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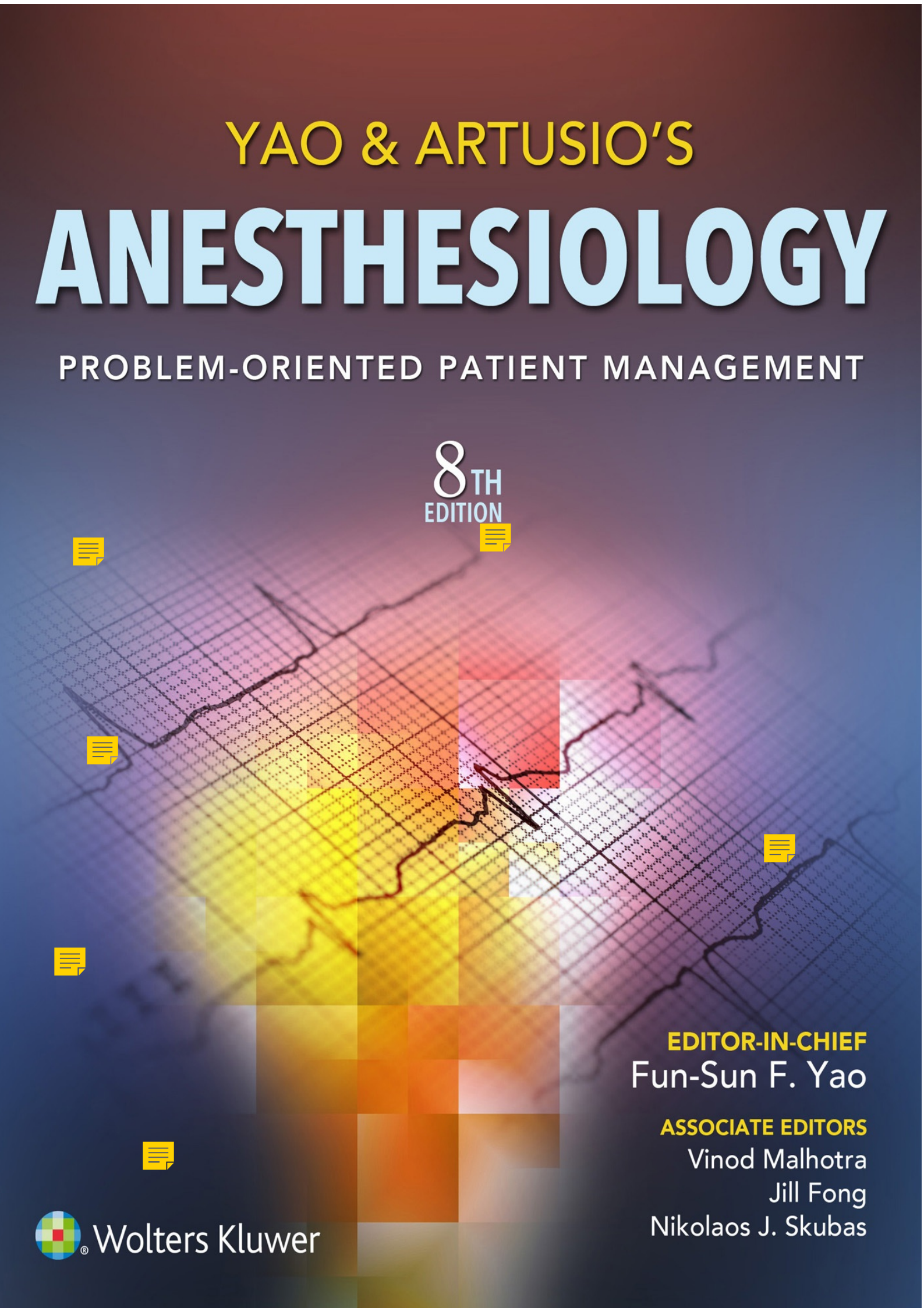
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YAO & ARTUSIO'S

ANESTHESIOLOGY

PROBLEM-ORIENTED PATIENT MANAGEMENT

8TH EDITION



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Dedication

*This book is dedicated to **Joseph F. Artusio Jr., MD** who has taught us not only to be good anesthesiologists but also to become better persons.*

Preface

Important advances in surgical procedures and in the clinical practice of anesthesiology have prompted the production of a new edition of this text. The book has been published in five languages: English, German, Japanese, Chinese, and Portuguese. The remarkable popularity of the first seven editions in the anesthesiology community both in the United States and abroad encouraged us to update and expand its subject matter. The eighth edition is written to further improve anesthesia management for sophisticated modern surgery.

As with our previous editions, *Yao & Artusio's Anesthesiology: Problem-Oriented Patient Management* was written to present a group of important clinical entities covering the most critical anesthetic problems. It is intended to provide logical and scientific fundamentals for individualized patient management.

In this eighth edition, *Yao & Artusio's Anesthesiology* is organized by organ systems into 12 sections consisting of 63 chapters. Each chapter begins with a brief case presentation, followed by essential problems of each disease covering four areas: (1) pathophysiology and differential diagnosis, (2) preoperative evaluation and preparation, (3) intraoperative management, and (4) postoperative anesthetic management. Using a question-and-answer format, the book is designed to stress anesthetic problems and to give the anesthesiologist the opportunity to organize his or her own ideas of patient care. A reasonable answer, with updated references, follows each question.

To maintain the fresh quality of the textbook, approximately one-quarter of the eighth edition consists of new chapters or contributions by new authors. The text originally reflected the clinical experience of the Department of Anesthesiology at Weill Cornell Medical College-The New York-Presbyterian Hospital. In this edition, experts from other prestigious institutions have contributed their invaluable opinions to make this book more universally acceptable and applicable. The material in the book is prepared for the education of the resident and the practicing anesthesiologist; it also serves as a review source for continuing education. The question-and-answer format, combined with current references, enhances its educational value.

We welcome comments, criticisms, and suggestions for future editions.

Acknowledgments

I wish to express my personal gratitude to the individual contributors. This book would not have been possible without their hard work and dedication. I am grateful to the associate editors: Jill Fong, MD, Vinod Malhotra, MD, and Nikolaos Skubas, MD, for their invaluable assistance. I would like to thank our editors at Lippincott Williams & Wilkins (Wolters Kluwer), Keith Donnellan, Nicole Dernoski, and Rodel Fariñas for their commitment to excellence. In addition, I am especially indebted to Hugh Hemmings, MD, for his advice and support. Above all, my deepest appreciation goes to my family, Tong-Yi, Ning-Yen, Jean-Kuan, and especially to my dear compassionate wife, Baw-Chyr Peggy Yao. Her understanding, patience, and encouragement made this book possible.

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Chapter 1
Asthma and Chronic Obstructive Pulmonary Disease

Fun-Sun F. Yao
Angela R. Selzer

A 55-year-old man with cholelithiasis is scheduled for laparoscopic cholecystectomy. He has a long history of asthma, has smoked two packs of cigarettes a day for the past 30 years, and reports dyspnea with moderate exertion (walking uphill). He sleeps on two pillows. There is no peripheral edema. Arterial blood gas (ABG) on room air shows the following: pH, 7.36; PCO_2, 60 mm Hg; PO_2, 70 mm Hg; CO_2 content, 36 mEq per L.

A. Medical Disease and Differential Diagnosis

1. What differential diagnosis is compatible with these symptoms?
2. What is the prevalence of asthma and chronic obstructive pulmonary disease (COPD)?
3. What is the etiology of asthma?
4. Discuss the pathogenesis of asthma. How is asthma distinguished from COPD?
5. What are the predisposing factors of bronchospasm?
6. What is the universal finding in ABGs during asthmatic attacks: hypoxemia or CO_2 retention?
7. Describe the abnormalities seen in spirometry, lung volumes, and lung capacities during an asthmatic attack.

B. Preoperative Evaluation and Preparation

1. How would you evaluate the patient preoperatively? What preoperative workup would you order?
2. How would you distinguish obstructive lung disease from restrictive lung disease by spirometry?
3. Define normal lung volumes and lung capacities. Give normal values for an average adult male.
4. What are flow-volume loops? Draw flow-volume loops for a healthy subject and patients with COPD, restrictive lung disease, fixed obstruction of the upper airway, variable extrathoracic obstruction, and variable intrathoracic obstruction.
5. Define closing volume (CV) and closing capacity (CC). What is the normal value of CV?
6. Why is the functional residual capacity (FRC) important in oxygenation?

7. How are FRC and CC affected by age and posture? How are they affected by anesthesia?
8. Give the equations for shunt (QS/QT) and dead space/tidal volume (VD/VT). What are their normal values?
9. Interpret the following ABG: pH, 7.36; PCO_2, 60 mm Hg; PO_2, 70 mm Hg; CO_2 content, 36 mEq per L.
10. What are the common physiologic causes of hypoxemia?
11. How would you prepare this asthmatic patient with COPD for surgery?
12. The patient comes to your perioperative clinic 2 weeks before surgery. He wants to know if his smoking puts him at increased risk during surgery. What do you tell him? Should he quit now?
13. You discover that the patient had a recent upper respiratory infection (URI), would you postpone surgery? For how long?
14. What medications would you expect the patient to have taken in the past or be taking at the present time?
15. Should the patient receive preoperative steroids? Why or why not?
16. What is the onset of action of intravenous steroid therapy in asthma?

C. Intraoperative Management

1. If the patient had a severe asthmatic attack in the operating room before the induction of anesthesia, would you

proceed with the anesthetic or postpone the surgery?

2. The patient did not have an asthmatic attack in the operating room and you proceed with induction. How would you induce anesthesia? Would you use a supraglottic airway instead of an endotracheal tube?
3. Would you use propofol for induction of anesthesia?
4. Would you use thiopental, methohexital, etomidate, or ketamine for induction?
5. Would you administer lidocaine for intubation?
6. If this is an emergency surgery and rapid sequence induction is indicated, how would you induce anesthesia in this patient?
7. Could a regional technique be used for this surgery? Discuss the advantages and disadvantages of neuraxial anesthesia in this patient for this surgery.
8. Would you choose an inhalational or an intravenous technique for maintenance of anesthesia?
9. What mechanisms produce bronchodilation from volatile anesthetics?
10. Which muscle relaxants would you use? Why?
11. How will you ventilate the patient? Will you use positive end-expiratory pressure (PEEP)? How can you detect the presence of auto-PEEP on your ventilator?
12. In the middle of surgery, peak inspiratory pressures suddenly increase. How do you manage this?
13. How would you give β_2-agonists? What is their mechanism of action on asthma?
14. If the patient does not respond to the aforementioned treatment and becomes cyanotic, what would you do?
15. What are the differential diagnoses of intraoperative bronchospasm?
16. The asthmatic attack was relieved with your treatment and the surgery was completed. Following emergence, the patient was found to be hypoventilating. What are the common causes of hypoventilation? What will be your approach to treat hypoventilation?
17. Would you consider a deep extubation in this patient?
18. If the patient cannot be extubated, what measures can you take to reduce the likelihood of bronchospasm with an endotracheal tube in place?

D. Postoperative Management

1. In patients with asthma, are there special considerations for the use of opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) for postoperative pain control?
2. Would you consider using a regional technique for analgesia?
3. The patient was breathing well and was extubated. Would you place this patient on supplemental oxygen in the recovery room? How much?

A. Medical Disease and Differential Diagnosis

A.1. What differential diagnosis is compatible with these symptoms?

The differential diagnoses of wheezing and dyspnea include bronchial asthma; COPD; acute left ventricular failure (cardiac asthma); upper airway obstruction by tumor or laryngeal edema; and endobronchial disease such as foreign body aspiration, neoplasms, bronchial stenosis, carcinoid tumors, recurrent pulmonary emboli, eosinophilic pneumonias, chemical pneumonias, and occasionally polyarteritis.

The triad of dyspnea, coughing, and wheezing, in addition to a history of periodic attacks, is quite characteristic of asthma. A personal or family history of allergic disease is valuable contributory evidence. The ability to trigger bronchospasm with histamine or methacholine administration is a hallmark characteristic of asthma. However, this airway hyperreactivity is typically present in patients with COPD as well. In patients such as this one, with a considerable smoking history, concomitant COPD and asthma is common, and airway obstruction with both reversible and irreversible components is frequently seen.

Severe COPD with systemic features is associated with a high perioperative mortality. The patient with advanced COPD has signs of wasting and nutritional deficiency. Signs of rightsided heart failure and cor pulmonale include jugular venous

distension, a split second heart sound, tricuspid or pulmonary insufficiency murmurs, hepatic enlargement, and peripheral edema.

Cardiac asthma, on the other hand, is a misnomer and refers to acute left ventricular failure. Although the primary lesion is cardiac, the disease manifests itself in the lungs. The symptoms and signs may mimic bronchial asthma, but the findings of moist basilar rales, gallop rhythms, blood-tinged sputum, peripheral edema, and a history of heart disease allow the appropriate diagnosis to be reached.

American Thoracic Society/European Respiratory Society Task Force. Standards for the diagnosis and management of patients with COPD. Published 2004. Updated September 8, 2005. http://www.thoracic.org/go/copd. Accessed November 11, 2014.

Longo DL, Fauci AS, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2084-2087, 2102-2116, 2151-2160.

A.2. What is the prevalence of asthma and chronic obstructive pulmonary disease (COPD)?

Asthma is one of the most common chronic diseases globally and currently affects approximately 300 million people. The prevalence of asthma has risen in affluent countries over the last 30 years but now appears to have stabilized. The prevalence of asthma in the United States is 8.7% of the adult population and 8.2% of children. It occurs at all ages, with a peak in children aged 5 to 9 years. In childhood, there is a 10:7 male/female preponderance, which is reversed in adulthood (6.5:10 male/female).

The greatest modifiable risk factor for asthma is smoking. Nonmodifiable risk factors include income (inversely proportional), ethnicity (Whites and Hispanics have a reduced risk, increased prevalence in African Americans), and environmental exposure.

Although deaths from asthma are rare, the annual rate of death from asthma is approximately 15-fold higher in adults older than 65 years than in children (37.2 vs. 2.6 per million).

The estimated worldwide prevalence of COPD is 210 million. In the United States, 14.1% of smokers carry a diagnosis of COPD, 7.1% of former smokers, and 2.9% of never smokers. The majority (71.2%) of COPD patients carry the diagnosis of at least one

comorbidity and have a significantly higher rate of hyperlipidemia, hypertension, coronary artery disease, diabetes, cancer, stroke, and chronic kidney disease than patients without COPD.

Asthma Facts: CDC's National Asthma Control Program Grantees. Published 2013. http://www.cdc.gov/asthma/reports_publications.htm. Accessed December 2, 2014.

Cunningham TJ, Ford ES, Rolle IV, et al. Associations of self-reported cigarette smoking with chronic obstructive pulmonary disease and co-morbid chronic conditions in the United States. *COPD*. 2015;12:276-286.

World Health Organization. *Global Surveillance, Prevention and Control of Chronic Respiratory Diseases: A Comprehensive Approach*. Geneva, Switzerland: World Health Organization; 2007.

A.3. What is the etiology of asthma?

Asthma is a heterogeneous disease with complex, multifactorial etiologies. The common denominator that underlies the asthmatic diathesis is a nonspecific hyperirritability of the tracheobronchial tree. Clinically, asthma is classified into two groups: allergic (extrinsic) and idiosyncratic (intrinsic). Allergic asthma is usually associated with a personal or family history of allergic diseases, positive skin reactions to extracts of airborne antigens, and increased levels of immunoglobulin E (IgE) in the serum. Immunologic mechanisms appear to be causally related to 25% to 35% of all cases and contributory in another 33%. Idiosyncratic asthma cannot be classified on the basis of immunologic mechanisms, and it is probably due to abnormality of the parasympathetic nervous system.

Bronchospasm is provoked when certain agents stimulate tracheobronchial receptors. Intraoperative bronchospasm is often cholinergically mediated. Afferent receptors in the bronchial mucosa can be an initiating event, although such an event is not always identifiable. Efferent parasympathetic fibers travel to bronchial smooth muscle where the stimulation of

the M3 cholinergic receptors on bronchial smooth muscle results in bronchoconstriction. After release of acetylcholine (Ach) at the M3 receptor, the Ach will stimulate the M2 muscarinic receptor, an inhibitory receptor that limits further release of Ach. Alterations of M2 receptor function may contribute to bronchospasm.

Fanta CH. Asthma. *N Engl J Med*. 2009;360:1002-1014.

Longo DL, Fauci AS, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2102-2116.

A.4. Discuss the pathogenesis of asthma. How is asthma distinguished from COPD?

Asthma is a chronic disease characterized by reversible expiratory airflow obstruction resulting from narrowing of the airways in response to various stimuli and a nonspecific hyperirritability of the tracheobronchial tree.

COPD is characterized by mucous hypersecretion, ciliary dysfunction, lung hyperinflation, and irreversible expiratory airflow obstruction.

The underlying mechanism of both conditions is thought to be chronic airway inflammation. Bronchial biopsies of asthmatics reveal infiltration by inflammatory cells and epithelial shedding from the mucosa.

With asthma, exposure to an initiating stimulus triggers inflammatory cells (mast cells, eosinophils, T lymphocytes, macrophages, basophils, neutrophils, and platelets) and structural cells (epithelial cells, fibroblasts, and airway smooth muscle cells) to release various mediators that lead to bronchospasm, vascular congestion, increased capillary permeability (edema of bronchial mucosa), and thick tenacious secretions (Fig. 1.1).

The net result is a reduction in airway diameter, an increase in airway resistance, decreased forced expiratory volumes and flow rates, hyperinflation of the lungs and thorax, increased work of breathing, alterations in respiratory tract muscle function, mismatched ventilation/perfusion, and altered blood gases.

In COPD, goblet cell hypertrophy, activated inflammatory cells (lymphocytes, neutrophils, and macrophages), and alteration in function of structural cells lead to increased mucus production, airway fibrosis, loss of alveolar attachments, and pulmonary vascular remodelling. The net result is hypersecretion of mucus, emphysema with peripheral airway collapse, impaired gas exchange, pulmonary hypertension, and right ventricular dysfunction.

The minority of COPD cases are a result of a genetic deficiency in antitrypsin levels, leading to an imbalance between antiproteinases and increased lung parenchymal destruction.

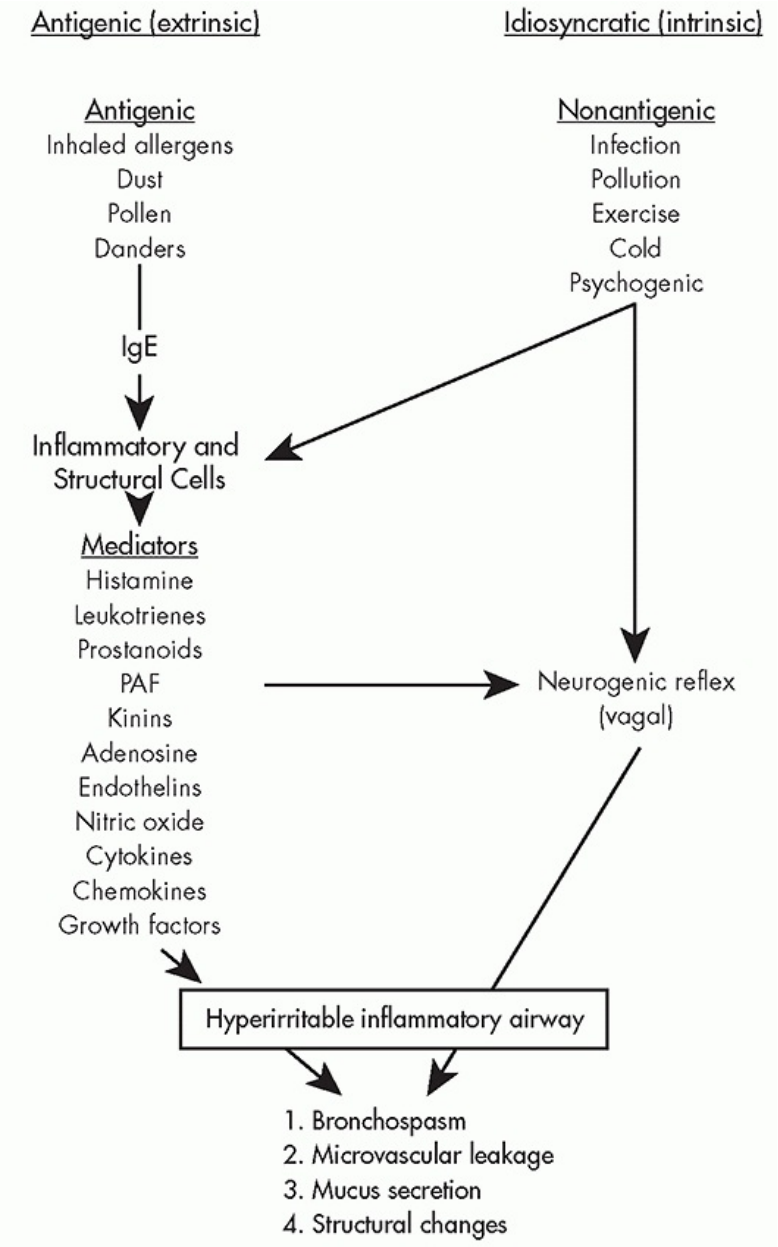


FIGURE 1.1 The pathogenesis of bronchial asthma. IgE, immunoglobulin E; PAF, platelet-activating factor.

American Thoracic Society/European Respiratory Society Task Force. Standards for the diagnosis and management of patients with COPD. Published 2004. Updated September 8, 2005. http://www.thoracic.org/go/copd. Accessed November 11, 2014.

Fanta CH. Asthma. *N Engl J Med*. 2009;360:1002-1014.

Longo DL, Fauci AS, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2102-2116, 2151-2160.

A.5. What are the predisposing factors of bronchospasm?

- *Allergens*. Inhaled allergens are common triggers of asthma. Airborne allergens are able to activate mast cells with bound IgE, immediately releasing bronchoconstrictor.
- *Infections*. Respiratory tract infections are among the most common stimuli that evoke acute asthmatic attacks.
- *Pharmacologic stimuli*. Drugs associated with bronchospasm include coloring agents such as tartrazine, β-adrenergic antagonists, acetylcholinesterase inhibitors, and sulfiting agents. Aspirin and other NSAIDs, such as indomethacin,

mefenamic acid, ibuprofen, fenoprofen, flufenamic acid, naproxen, and phenylbutazone, can worsen asthma

via inhibition of prostaglandin G/H synthetase 1 (cyclooxygenase type 1). All nonspecific β-blockers should be avoided in asthmatics because their use can lead to severe bronchospasm. The ultra-short-acting β-1 selective antagonists landiolol and esmolol can be safely used perioperatively in patients with airway hyperreactivity. Intraoperative bronchospasm is more likely to occur after administration of acetylcholinesterase inhibitors for neuromuscular blockade reversal. Adequate dosing of a concomitant anticholinergic is necessary to avoid this complication, and some advocate avoiding reversal altogether in an asthmatic patient with adequate return of neuromuscular function.

- *Environment and air pollution*. Some types of asthma, such as Tokyo-Yokohama or New Orleans asthma, tend to occur in individuals who live in heavy industrial or dense urban areas. Dry, cold air can also trigger bronchospasm in susceptible individuals.
- *Occupational factors*. Various compounds used in industry can cause asthma in susceptible individuals. Various names have been applied to this condition, such as meat wrapper's asthma, baker's asthma, and woodworker's asthma.
- *Exercise*. Asthma can be induced or made worse by physical exertion. The mechanism is linked to hyperventilation, which results in increased osmolality in airway lining fluid and triggers mast cell mediator release, resulting in bronchoconstriction.
- *Emotional stress.* Asthma can be induced by bronchoconstriction through the cholinergic reflex pathway.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2012:182-188.

Longo DL, Fauci AS, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2102-2116.

Yamakage M, Iwasaki S, Jeong SW, et al. Beta-1 selective adrenergic antagonist landiolol and esmolol can be safely used in patients with airway hyperreactivity. *Heart Lung*. 2009;38:48-55.

A.6. What is the universal finding in ABGs during asthmatic attacks: hypoxemia or CO_2 retention?

Hypoxemia is a universal finding during asthmatic attacks. Frank ventilatory failure with CO_2 retention is relatively uncommon because CO_2 has a diffusion capacity that is 20 times higher than that of oxygen. During acute asthmatic attacks, most patients try to overcome airway obstruction and hypoxia by hyperventilation. This results in hypocarbia and respiratory alkalosis. CO_2 retention is a late finding and indicates severe and prolonged airway obstruction, as in status asthmaticus.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2012:182-188.

Longo DL, Fauci AS, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2102-2116.

A.7. Describe the abnormalities seen in spirometry, lung volumes, and lung capacities during an asthmatic attack.

The forced vital capacity (FVC) is usually normal but may be decreased during a severe attack. The forced expiratory volume at 1 second (FEV_1) is sharply reduced, usually to less than 50% of the FVC, typically less than 40% of that predicted. The $FEF_{25\%-75\%}$ is sharply reduced as well. $FEF_{25\%-75\%}$ (also referred to as the maximum midexpiratory flow rate or MMEFR) is the forced expiratory flow rate during 25% and 75% of the vital capacity. Unlike the FEV_1, the $FEF_{25\%-75\%}$ is independent of patient effort. Other classic spirometry findings include a maximum breathing capacity (MBC) that is sharply reduced and a moderately decreased expiratory reserve volume (ERV). Conversely, the residual volume (RV) markedly increases, frequently approaching 400% of normal. This results in a net increase in *total lung*

capacity (TLC) and FRC, which frequently doubles.

Longo DL, Fauci AS, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2094-2116.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient preoperatively? What preoperative workup would you order?

A thorough history and examination provides crucial information to the anesthesiologist caring for a patient with COPD and asthma. A focused medical history should include physical status and exercise tolerance, recent or current presence of infectious symptoms, sputum quantity and quality, known triggers of attacks, most recent exacerbation, current medications and time of last use, last course of systemic steroids, recent medication changes, coexisting morbidities, oxygen dependence, presence of obstructive sleep apnea, smoking history, recent weight loss, previous surgery, and anesthesia.

A focused cardiopulmonary exam should occur. First, observe the patient's breathing and look for use of accessory muscles, pursed-lip exhalation, or cyanosis. Auscultation of the lungs can reveal wheezing, adventitious lung sounds, and hyperinflation. Auscultation of the heart may reveal a split second heart sound typical of cor pulmonale or the murmur of tricuspid or pulmonary regurgitation present in some patients with long-standing pulmonary hypertension. Additionally, jugular venous distension, peripheral edema, and hepatic enlargement may be present. Cachexia may also be seen.

Laboratory testing should include a complete blood count, serum electrolytes, electrocardiogram, urinalysis, and coagulation screening. Additionally, these patients should have a chest radiograph, a room air Spo2, and spirometry. Although not necessary in every patient, a computed tomography scan of the chest, detailed lung volume testing (including diffusion capacity of the lung for carbon monoxide [DLCO]), and a room air ABG would certainly be informative if available.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2012:182-195.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

Yamakage M, Iwasaki S, Namiki A. Guideline-oriented perioperative management of patients with bronchial asthma and chronic obstructive pulmonary disease. *J Anesth*. 2008;22:412-428.

B.2. How would you distinguish obstructive lung disease from restrictive lung disease by spirometry?

Table 1.1 summarizes the distinctions between the two types of lung diseases. In restrictive lung disease (e.g., pulmonary fibrosis and ankylosing spondylitis), the FVC is low because of limited expansion of the lungs or chest wall, although the FEV_1 is often not reduced proportionately, because airway resistance is normal. Therefore, the FEV_1/FVC percentage is normal or high.

In obstructive lung disease, the FEV_1/FVC is grossly reduced because the airway resistance is high. Normally, FEV_1 is more than 80% of FVC, and VC should be more than 80% of predicted value. The predicted values depend on body size, age, and sex. The FEV_1/FVC is less than 0.70 in COPD. The severity of COPD is determined by the FEV_1. Patients with an FEV_1

greater than 80% of predicted are considered to have mild COPD. Those with FEV_1 greater than 50% but less than 80% of predicted are classified as having moderate COPD. Severe cases of COPD have an FEV_1 that is less than 50% of predicted.

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TABLE 1.1 Differences between Obstructive and Restrictive Lung Diseases

	OBSTRUCTIVE	RESTRICTIVE
Vital capacity	N or ↓	↓
Total lung capacity	N or ↓	↓
Residual volume	↑	↓
FEV_1/FVC	↓	N or ↑
Maximum midexpiratory flow rate	↓	N
Maximum breathing capacity	↓	N

↓, decreased; ↑, increased; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; N, normal.

The TLC is increased in obstructive lung disease and decreased in restrictive lung disease. However, TLC cannot be obtained by routine screening spirometry.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:279-281.

Longo DL, Fauci AS, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2087-2094.

Rabe KF, Hurd S, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. GOLD executive summary. *Am J Respir Crit Care Med*. 2007;176:532-555.

B.3. Define normal lung volumes and lung capacities. Give normal values for an average adult male.

There are four basic “volumes” and four derived “capacities” that are combinations of these volumes (Fig. 1.2).

Tidal volume (VT) is the volume of air inhaled or exhaled during normal breathing. Normal VT is 500 mL or approximately 6 to 8 mL per kg.

Inspiratory reserve volume (IRV) is the maximum volume of gas that can be inhaled following a normal inspiration while at rest. Normal IRV is 2,000 to 3,000 mL.

Expiratory reserve volume (ERV) is the maximum volume of gas that can be exhaled after a normal expiration. Normal ERV is 1,000 mL.

Residual volume (RV) is the volume of gas remaining in the lungs after a forced exhalation. Normal RV is 1,500 mL.

Vital capacity (VC) is the maximum amount of gas that can be exhaled after a maximum inhalation. VC is the sum of VT, ERV, and IRV. Normal VC is approximately 60 to 70 mL per kg.

Inspiratory capacity (IC) is the maximum amount of gas that can be inhaled from the resting expiratory position after a normal exhalation. It is the sum of VT and IRV. Normal IC is 3,500 mL.

Functional residual capacity (FRC) is the remaining lung volume at the end of a normal quiet expiration. It is the sum of RV and ERV. Normal FRC is 2,500 mL or 30 to 40 mL per kg.

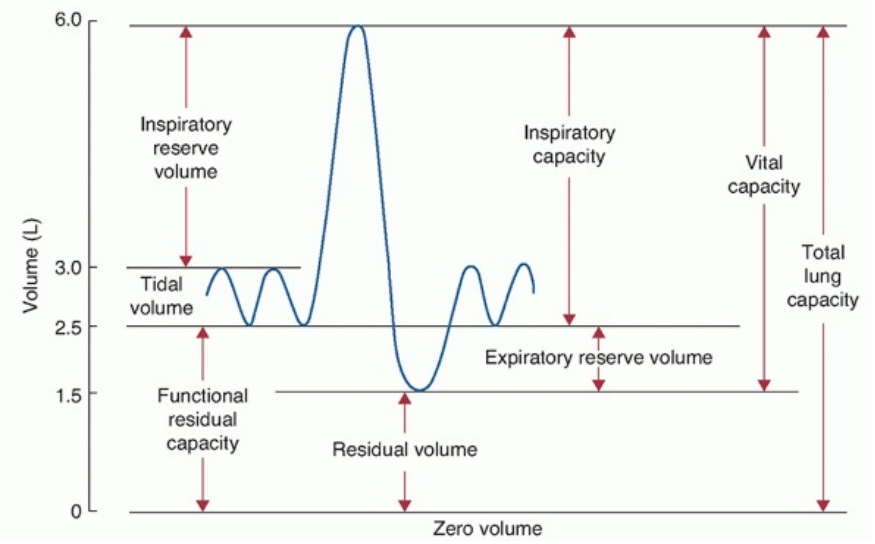


FIGURE 1.2 Lung volumes and lung capacities.

Total lung capacity (TLC) is the lung volume at the end of a maximum inspiration. It is the sum of VC and RV. Normal TLC is 5,000 to 6,000 mL for an adult man and 4,000 to 5,000 mL for an adult woman.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:279-281.

Longo DL, Fauci AS, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2087-2094.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Butterworth-Heinemann; 2010:33-35.

B.4. What are flow-volume loops? Draw flow-volume loops for a healthy subject and patients with COPD, restrictive lung disease, fixed obstruction of the upper airway, variable extrathoracic obstruction, and variable intrathoracic obstruction.

Flow-volume loops provide a graphic analysis of flow at various lung volumes. To perform the test, subjects are asked to inhale maximally (to TLC) and then exhale as forcefully and maximally as possible (to RV). This cycle is repeated. The flow (L/sec) is plotted on the y-axis and volume (L) on the x-axis (Fig. 1.3A). The test requires a compliant patient for accurate results—the majority of the test is effort dependent, including the entire inspiratory curve and both ends of the expiratory curve (near TLC and RV). The forced expiratory flow during 25% to 75% of VC ($FEF_{25\%-75\%}$), is reflective of the small to medium sized airways and is considered a relatively effort-independent value.

Normal flow-volume loop (Fig. 1.3A). Inspiratory limb of loop is symmetric and convex. Expiratory limb is linear. Airflow at the midpoint of inspiratory capacity and airflow at the midpoint of expiratory capacity are often measured and compared. Maximal inspiratory flow (MIF) at 50% FVC is greater than maximal expiratory flow (MEF) at 50% FVC because dynamic compression of the airways occurs during exhalation.

Obstructive disorder (e.g., emphysema, asthma) (Fig. 1.3B). Although all airflow is diminished, expiratory prolongation predominates, and MEF < MIF. Peak expiratory flow (PEF) is sometimes used to estimate degree of airway obstruction but depends on patient effort.

Restrictive disorder (e.g., interstitial lung disease, kyphoscoliosis) (Fig. 1.3C). The loop is narrowed because of diminished lung volumes. Airflow is greater than normal at comparable lung volumes because the increased elastic recoil of lungs holds the airways open.

Fixed obstruction of the upper airway (e.g., tracheal stenosis, goiter) (Fig. 1.3D). The top and bottom of the loops are flattened so that the configuration approaches that of a rectangle. Fixed obstruction limits flow equally during inspiration and expiration, and MEF = MIF.

Variable extrathoracic obstruction (e.g., unilateral vocal cord paralysis, vocal cord dysfunction) (Fig. 1.3E). When a single vocal cord is paralyzed, it moves passively with pressure gradients across the glottis. During forced inspiration, it is drawn inward, resulting in a plateau of decreased inspiratory flow. During forced expiration, it is passively blown aside, and expiratory flow is unimpaired. Therefore, MIF 50% FVC < MEF 50% FVC.

Variable intrathoracic obstruction (e.g., tracheomalacia) (Fig. 1.3F). During a forced inspiration, negative pleural pressure holds the floppy trachea open. With forced expiration, loss of structural support results in tracheal narrowing and a plateau of diminished flow. Airflow is maintained briefly before airway compression occurs.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:280.

Longo DL, Fauci AS, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2087-2094.

The Merck Manual: Professional Edition. http://www.merckmanuals.com/professional/pulmonary_disorders/tests_of_pulmonary_function_pft/airflow_lung_volumes_and_flow-volume_loop.html?qt=flow%20volume%20loops&alt=sh. Accessed November 11, 2014.)

B.5. Define closing volume (CV) and closing capacity (CC). What is the normal value of CV?

CC is the lung volume at which the small airways in the dependent parts of the lung begin to close. CC is the sum of CV and RV. CV is the volume above the RV at which small airways begin to close during expiration. It can be measured during the single-breath nitrogen test (Fig. 1.4) or with an inert tracer gas such as helium, xenon, or argon.

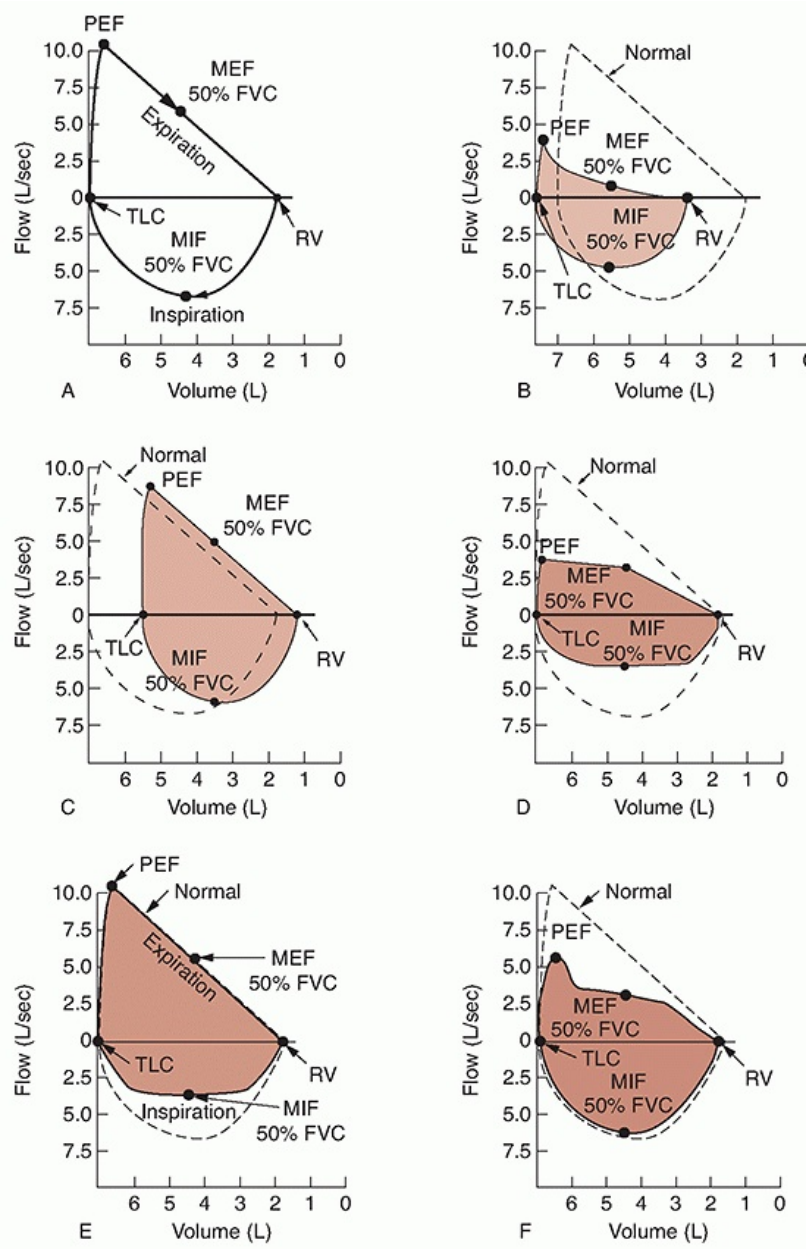


FIGURE 1.3 Flow-volume loops in a healthy person **(A)**, a patient with obstructive lung disease **(B)**, a patient with restrictive lung disease **(C)**, a patient with a fixed obstruction **(D)**, a patient with a variable extrathoracic obstruction **(E)**, and a patient with a variable intrathoracic obstruction **(F)**. FVC, forced vital capacity; MEF, maximal expiratory flow; MIF, maximal inspiratory flow; PEF, peak expiratory flow; RV, residual volume; TLC, total lung capacity. (From *The Merck Manual: Professional Edition*, with permission. http://www.merckmanuals.com/professional/pulmonary_disorders/tests_of_pulmonary_function_pft/airflow_lung_volumes_and_flow-volume_loop.html?qt=flow%20volume%20loops&alt=sh. Accessed November 11, 2014.)

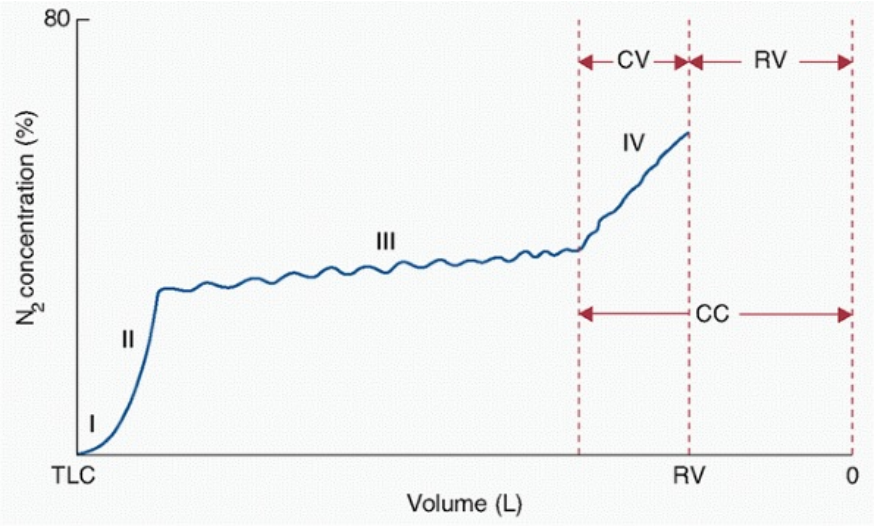


FIGURE 1.4 Closing volume measurement by single-breath nitrogen test. CC, closing capacity; CV, closing volume; RV, residual volume; TLC, total lung capacity.

In healthy young people, CV is approximately 10% of the VC, or 400 to 500 mL. CV and CC increase with age. CV is increased in patients with small airway disease and in chronic smokers.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Butterworth-Heinemann; 2010:36-38.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Churchill Livingstone; 2015:451-453.

B.6. Why is the functional residual capacity (FRC) important in oxygenation?

In a healthy young adult, FRC is above CC (FRC > CV + RV). Increases in CC and/or decreases in FRC can result in CC exceeding FRC and subsequent closure of the small airways during certain periods of normal tidal ventilation. Airway closure produces shunting, with perfusion of unventilated alveoli. Therefore, shunt (QS/QT) is increased and arterial oxygenation is decreased.

Perfusion to the lung occurs in both inspiratory and expiratory phases of respiration. The FRC, or lung volume remaining at end expiration, provides surface area for gas exchange during this phase of respiration. The greater the FRC, the more oxygenation occurs. Patients in the supine position, under general anesthesia, or with acute respiratory distress syndrome all have decreased FRC to varying degrees. PEEP increases FRC, improving oxygenation in the expiratory phase and reducing small airway collapse.

FRC can be measured by helium dilution, nitrogen washout, or body plethysmography.

Buist AS. The single-breath nitrogen test. *N Engl J Med*. 1975;293:438.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Butterworth-Heinemann; 2010:36-39.

B.7. How are FRC and CC affected by age and posture? How are they affected by anesthesia?

Posture has a dramatic effect on FRC. When a patient goes from upright to the supine position, FRC decreases approximately 30%. Body position does not affect CC.

Conversely, age has a greater effect on CC than on FRC. CC increases with age, whereas FRC does not change or increases only slightly. Therefore, CC will exceed FRC in healthy adults over the age of 44 years when in the supine position and in healthy adults over the age of 66 years in the upright position.

During anesthesia, FRC is reduced by approximately 20% with spontaneous breathing and by approximately 16% with artificial ventilation. This is due to changes in the chest

wall shape and diaphragm position. The change in FRC that can be ascribed to changes in diaphragm is on average less than 30 mL.

CC is reduced in parallel to FRC during anesthesia.

Gilmour I, Burnham M, Craig DB. Closing capacity measurements during general anesthesia. *Anesthesiology*. 1976;45:477.

Juno P, Marsh HM, Knopp TJ, et al. Closing capacity in awake and anesthetized-paralyzed man. *J Appl Physiol*. 1978;44:238.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Butterworth-Heinemann; 2010:36-39, 333-334.

Rehder K, Marsh HM, Rodarte JR, et al. Airway closure. *Anesthesiology*. 1977;47:40.

Wahba RWM. Perioperative functional residual capacity. *Can J Anaesth*. 1991;38:384-400.

B.8. Give the equations for shunt (QS/QT) and dead space/tidal volume (VD/VT). What are their normal values?

$$Q_S/Q_T = \frac{Cc'O_2 - CaO_2}{Cc'O_2 - C\bar{v}O_2} \qquad V_D/V_T = \frac{Paco_2 - P\bar{E}co_2}{Paco_2}$$

where $Cc'O_2$, CaO_2, and $C\bar{v}O_2$ are oxygen contents in pulmonary capillary, arterial, and mixed venous blood, respectively; QT is cardiac output; QS is shunt blood; and $PaCO_2$ and $P\bar{E}CO_2$ are partial pressures of CO_2 in arterial blood and the mixed expired gases, respectively.

Normal QS/QT is 4% to 5%, and VD/VT is approximately 0.3.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:276-278.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Butterworth-Heinemann; 2010:125-137.

B.9. Interpret the following ABG: pH, 7.36; PCO_2, 60 mm Hg; PO_2, 70 mm Hg; CO_2 content, 36 mEq per L.

The fraction of inspired oxygen (FIO_2) is essential to evaluate PaO_2. Assume the blood sample is obtained while the patient is breathing room air. The blood gases show mild hypoxemia and respiratory acidosis, compensated by metabolic alkalosis. The blood gases are compatible with COPD. PaO_2 levels in the patient with mild to moderate COPD are 60 to 80 mm Hg. A PaO_2 less than 60 mm Hg indicates severe COPD. In these patients, long-term oxygen therapy has been proven to provide a significant survival benefit.

COPD Working Group. Long-term oxygen therapy for patients with chronic obstructive pulmonary disease (COPD): an evidence based analysis. *Ont Health Technol Assess Ser*. 2012;12(7):1-64.

B.10. What are the common physiologic causes of hypoxemia?

From the shunt equation, arterial oxygen content is related to the change in pulmonary capillary oxygen content, venous oxygen content, and venous admixture. It is easier to classify hypoxemia into the following three categories.

Decreased pulmonary capillary oxygen tension

- Hypoventilation

- Low FIO_2
- Ventilation/perfusion mismatch from pulmonary parenchymal change
- Diffusion abnormality (rare)

Increased shunting

- Either intrapulmonary or cardiac

Reduced venous oxygen content

- Congestive heart failure—low cardiac output
- Increased metabolism—fever, hyperthyroidism, shivering
- Decreased arterial oxygen content—anemia

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Churchill Livingstone; 2015:466-469.

B.11. How would you prepare this asthmatic patient with COPD for surgery?

The preoperative preparation should include the following:

- Rule out or treatment of acute and chronic infection with appropriate antibiotics
- Relief of bronchial spasm with a bronchodilator
- Chest physiotherapy to improve sputum clearance and bronchial drainage
- Reversal of uncompensated or borderline cor pulmonale with diuretics, digitalis, improved oxygenation, and correction of acidemia by more efficient ventilation
- Correction of dehydration and electrolyte imbalance
- Familiarization with respiratory therapy equipment likely to be used in the postoperative period
- Cessation of smoking (see section B.12)
- Continuation of anti-inflammatory and bronchodilator therapy up to the time of surgery
- Initiation of steroid therapy with oral methylprednisolone 40 mg for 5 days before elective surgery for patients with newly diagnosed disease, poorly compliant patients, and patients with ongoing wheezing
- In select patients with COPD, 2 to 4 weeks of preoperative pulmonary rehabilitation has been shown to improve perioperative outcomes.

Edrich T, Sadovnikoff N. Anesthesia for patients with severe chronic obstructive pulmonary disease. *Curr Opin Anaesthesiol*. 2010;23:18-24.

Mujovic N, Mujovic N, Subotic D, et al. Preoperative pulmonary rehabilitation in patients with non-small cell cancer and chronic obstructive pulmonary disease. *Arch Med Sci*. 2014;10(1):68-75.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

B.12. The patient comes to your perioperative clinic 2 weeks before surgery. He wants to know if his smoking puts him at increased risk during surgery. What do you tell him? Should he quit now?

Smoking results in increased levels of carboxyhemoglobin, lower oxygen content, and decreased delivery of oxygen by hemoglobin to the tissues. These effects are dramatically improved with as little as 12 hours of smoking cessation.

Smoking also increases the risk of postoperative pulmonary complications (PPCs). These include respiratory failure, unplanned intensive care unit (ICU) admission, pneumonia, airway events during anesthesia, and increased need for

postoperative respiratory support. Smokers have an increased rate of wound-related complications and decreased bone healing after surgery. Although a cessation period of at least 8 weeks prior to surgery is optimal and results in improved mucociliary clearance, decreased sputum production, and a relative risk reduction in PPCs, it is highly recommended for patients to stop smoking at any time prior to surgery.

A persistent misconception in our specialty is that short-term smoking cessation (<4 weeks) is detrimental to the patient. Some have argued that a patient smoking 2 weeks before surgery should continue smoking to avoid *increased* risks associated with cessation. There is now a preponderance of evidence that debunks this myth. Short-term smoking cessation is *not* a risk factor for long-term perioperative complications. In contrast, the long-term detrimental effects of continued smoking are well known. Anesthesiologists should be aware that admission for surgery can be a powerful motivator for patients to quit smoking, providing a “teachable moment” for smoking cessation and frequently resulting in successful, long-term cessation. Therefore, this patient should be counseled to quit smoking as soon as possible.

Myers K, Hajek P, Hinds C, et al. Stopping smoking shortly before surgery and postoperative complications. *Arch Intern Med*. 2011;171(11):983-989.

Turan A, Mascha EJ, Roberman D, et al. Smoking and perioperative outcomes. *Anesthesiology*. 2011;114: 837-846.

Warner DO. Perioperative abstinence from smoking: physiologic and clinical consequences. *Anesthesiology*. 2006;104:356-367.

Yu S, Warner DO. Surgery as a teachable moment for smoking cessation. *Anesthesiology*. 2010;112:102-107.

B.13. You discover that the patient had a recent upper respiratory infection (URI), would you postpone surgery? For how long?

Respiratory tract infections are the most common stimuli that evoke acute exacerbations of asthma. Even healthy subjects have increased airway responsiveness to nonspecific stimuli transiently following a viral infection. It is unclear how long surgery should be delayed following a URI because airway hyperreactivity can last 2 to 8 weeks after the infection in both healthy subjects and patients with asthma. Cohen and Cameron reported that a child with a URI having endotracheal anesthesia has an 11-fold increased risk of respiratory complications. In addition, Tait and Knight found that laryngospasm and bronchospasm were significantly increased in healthy children 2 weeks after a URI. However, the data are controversial. A frequently cited retrospective study by Warner et al. found no increase in intraoperative bronchospasm in patients with asthma and a recent URI.

In this patient presenting for elective surgery with multiple risk factors for PPCs, postponing surgery at least 2 to 3 weeks after clinical recovery from the URI is reasonable.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:847.

Cohen MM, Cameron CB. Should you cancel the operation when a child has an upper respiratory infection? *Anesth Analg*. 1991;72:282-288.

Tait AR, Knight PR. Intraoperative respiratory complications in patients with upper respiratory tract infections. *Can J Anaesth*. 1987;34:300-303.

Warner DO, Warner MA, Barnes RD, et al. Perioperative respiratory complications in patients with asthma. *Anesthesiology*. 1996;85:460-467.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

B.14. What medications would you expect the patient to have taken in the

past or be taking at the present time?

The main drugs for asthma and COPD can be divided into rescue medications (bronchodilators) and controllers (for maintenance).

Patients with infrequent asthma symptoms are placed solely on a short-acting β_2-agonist (SABA). Alternatively, anticholinergic inhalers such as ipratropium may be given, although their slower onset of action makes them less preferred.

Patients with increased risk for exacerbations (including smokers) and/or those with frequent symptoms should be placed on controller therapy with a low-dose inhaled corticosteroid (ICS). In patients with severe symptoms, a long acting β_2-agonist or a high-dose ICS are added. Acute exacerbations are treated with a short course of oral corticosteroids.

Theophylline was a widely prescribed oral controller medication for asthma but has fallen out of favor secondary to its narrow therapeutic index, multiple drug interactions, and side effect profile. It may be prescribed in patients with COPD. Patients taking theophylline require routine level testing. They should continue theophylline in the perioperative period to avoid an asthma or COPD exacerbation secondary to withdrawal.

Other oral medications targeting the inflammatory component of asthma include the mast cell stabilizer cromolyn, the anti-IgE antibody omalizumab, and leukotriene receptor antagonists such as zafirlukast and montelukast. The phosphodiesterase-4 inhibitor roflumilast may be added to the treatment regimens of patients with severe COPD.

Longo DL, Fauci AS, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2102-2116, 2151-2160.

Global Initiative for Asthma. Global strategy for asthma management and prevention. Published 2014. http://www.ginasthma.org/. Accessed November 11, 2014.

Global Initiative for Asthma. Global strategy for the diagnosis, management, and prevention of COPD. Global initiative for chronic obstructive lung disease. Published 2014. http://www.goldcopd.org/. Accessed November 11, 2014.

B.15. Should the patient receive preoperative steroids? Why or why not?

All patients with known or suspected adrenal insufficiency should receive preoperative corticosteroid replacement therapy. This includes any patients treated with systemic steroids for more than 2 weeks within the previous 6 months. Under baseline conditions, the human adrenal

glands normally secrete approximately 30 mg of hydrocortisone (cortisol) per day. Under stress, up to 500 mg per day may be secreted. It is reasonable to replace 300 mg of hydrocortisone per day in the perioperative period. A 100-mg dose of hydrocortisone phosphate is given intravenously before induction and during surgery. Postoperatively, hydrocortisone phosphate 100 mg intravenously is given every 8 hours for 48 hours. The biologic half-life of hydrocortisone is 8 to 12 hours. If the patient received less than 2 weeks of systemic steroid therapy or more than 6 months previously *and* there are no signs of adrenal insufficiency, routine steroid preparation is not advised. However, intravenous steroid preparations should be available in the operating room in case intractable hypotension from adrenal insufficiency occurs during surgery.

The increasing understanding of the inflammatory component of reactive airway disease has led to greater appreciation of the importance of steroids in preventing and treating exacerbations. It has been recommended that systemic steroid preparation be used preoperatively in patients with moderate to severe asthma and a history of a need for systemic steroids in the past. In wheezing patients, oral methylprednisolone 40 mg daily for 5 days before surgery has been shown to decrease postintubation bronchospasm. The oft-cited concern that steroids increase the rate of wound complications is not well founded. A study of patients with asthma treated with steroids preoperatively found no increase in the incidence of wound infections or wound-healing problems.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:595.

Bishop MJ. Editorial views: preoperative corticosteroids for reactive airway. *Anesthesiology*. 2004;100: 1047-1048.

Silvanus M-T, Groeben H, Peters J. Corticosteroids and inhaled salbutamol in patients with reversible airway obstruction markedly decrease the incidence of bronchospasm after tracheal intubation. *Anesthesiology*.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

B.16. What is the onset of action of intravenous steroid therapy in asthma?

Although the bronchial effects of intravenous steroids are not immediate and are typically seen 4 to 6 hours after initial administration, their administration is nonetheless indicated with severe bronchospasm that has not resolved despite intense optimal bronchodilator therapy. A loading dose of hydrocortisone 4 mg per kg is given to achieve plasma cortisol levels above 100 μg per dL, followed by 3 mg per kg every 6 hours. Alternatively, methylprednisolone, 125 mg, may be given every 6 hours.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2012:188.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

C. Intraoperative Management

C.1. If the patient had a severe asthmatic attack in the operating room before the induction of anesthesia, would you proceed with the anesthetic or postpone the surgery?

First, medical treatment should be given to relieve the asthmatic attack. Elective surgery should be postponed, the patient reevaluated carefully, and his asthma better optimized. In the case of emergency surgery, such as acute appendicitis, the surgery can be performed after the asthmatic attack is successfully treated. Regional anesthesia, if feasible, should be considered. During surgery, the medical treatment should be continued.

C.2. The patient did not have an asthmatic attack in the operating room and you proceed with induction. How would you induce anesthesia? Would you use a supraglottic airway instead of an endotracheal tube?

The principles of anesthetic management for the asthmatic patient are threefold: to block airway reflexes before laryngoscopy and intubation, to relax airway smooth muscle, and to prevent release of biochemical mediators.

Before induction of general anesthesia, the patient should take two or three puffs of albuterol from a metered-dose inhaler (MDI). Propofol 2.5 mg per kg can be used for induction. Then, oxygen and a potent inhalation agent, such as sevoflurane, are administered by mask to achieve an adequate depth of anesthesia that suppresses hyperreactive airway reflexes sufficiently to permit tracheal intubation without triggering bronchospasm. The lesser pungency of sevoflurane (compared with desflurane and isoflurane) may decrease the likelihood of coughing, which can induce bronchospasm. Endotracheal intubation can be accomplished following injection of succinylcholine or other muscle relaxants. Prior to intubation, lidocaine may be administered (see section C.5).

Avoidance of intubation altogether is another approach. A supraglottic airway provides a unique opportunity for the clinician to control the airway without having to introduce a foreign body into the trachea. Kim and Bishop demonstrated a reversible increase in airway resistance in intubated patients under isoflurane anesthesia and showed that this increase was not present with supraglottic airway use. Therefore, it may be an ideal airway tool in the patient with asthma not at risk for reflux and aspiration.

Laparoscopic surgeries using a supraglottic airway have been reported by multiple centers for both gynecologic surgeries and cholecystectomies. Insufflation of the abdomen and manipulation of the bowel places these patients at increased aspiration risk. However, the use of a specialized supraglottic airway such as LMA-ProSeal can mitigate these effects by allowing for placement of an orogastric tube for drainage of the stomach and a larger cuff size that reduces both the risk for gastric inflation and aspiration of refluxed gastric contents.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams &

Kim ES, Bishop MJ. Endotracheal intubation, but not laryngeal mask airway insertion, produces reversible bronchoconstriction. *Anesthesiology*. 1999;90:391-394.

Maltby JR, Beriault MT, Watson NC, et al. The LMA ProSeal is an effective alternative to tracheal intubation in laparoscopic cholecystectomy. *Can J Anaesth*. 2002;49:857.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

C.3. Would you use propofol for induction of anesthesia?

Propofol may be the induction agent of choice for the hemodynamically stable patient with reactive airways. In comparison to induction with thiopental, thiamylal, or methohexital, 2.5 mg per kg propofol induction resulted in a significantly lower incidence of wheezing after tracheal intubation in asthmatic patients. The incidence of wheezing was 0%, 45%, and 26% in patients who received propofol, a thiobarbiturate, and oxybarbiturate, respectively. Another study in unselected patients found a significantly lower respiratory resistance after tracheal intubation following induction with propofol than with thiopental or etomidate. Nevertheless, propofol-induced bronchospasm has been reported in patients with allergic rhinitis and should be used with caution in patients with a high allergic component.

Eames WO, Rooke GA, Wu RS, et al. Comparison of the effects of etomidate, propofol, and thiopental on respiratory resistance following tracheal intubation. *Anesthesiology*. 1996;84:1307-1311.

Nishiyama T, Hanaoka K. Propofol-induced bronchoconstriction: two case reports. *Anesth Analg*. 2001;93:645-646.

C.4. Would you use thiopental, methohexital, etomidate, or ketamine for induction?

Thiopental and thiamylal are thiobarbiturates that have been demonstrated to release histamine. Methohexital and pentobarbital are oxybarbiturates that have not been shown to release histamine. This suggests that the sulfur atom is important in barbiturate-induced histamine release. Moreover, thiobarbiturates, but not oxybarbiturates, have been shown to lead to a thromboxane-mediated tracheal constriction in guinea pigs. For these reasons, methohexital may be preferred as the induction agent in patients with extreme sensitivity to histamine (asthmatics) or increased histamine releasability (atopics).

Because it provides only a light plane of anesthesia, airway instrumentation under thiopental anesthesia alone may trigger bronchospasm. However, it may be used cautiously in asthmatics provided that an adequate depth of anesthesia is achieved before airway stimulation.

Etomidate has not been shown to release histamine, does not depress myocardial function, and provides hemodynamic stability in critically ill patients. Both etomidate and thiopental afford no protection against wheezing after intubation and are therefore inferior to propofol in this regard.

Ketamine produces bronchodilation both through neural mechanisms and through release of catecholamines. In an actively wheezing patient, ketamine is the induction agent of choice, particularly with unstable hemodynamics.

Eames WO, Rooke GA, Wu RS, et al. Comparison of the effects of etomidate, propofol, and thiopental on respiratory resistance following tracheal intubation. *Anesthesiology*. 1996;84:1307-1311.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2012:187.

C.5. Would you administer lidocaine for intubation?

The administration of intravenous lidocaine 1 mg per kg 1 to 2 minutes prior to intubation to prevent reflex-induced bronchospasm is a long-standing practice that has recently been called into question. Paradoxical bronchospasm has

been demonstrated in patients with asthma. Therefore, intravenous lidocaine should be administered with caution in these patients.

Alternatively, topical endotracheal spray of lidocaine can be used. However, this practice can also *provoke* bronchoconstriction unless an adequate depth of anesthesia is achieved before administering it. In elderly patients with COPD, the addition of a lidocaine infusion (1 to 2 mg/kg/hr) to the anesthetic maintenance can augment an adequate plane of anesthesia for reduced airway hyperactivity without the detrimental effects on their cardiovascular systems.

Burches BR Jr, Warner DO. Bronchospasm after intravenous lidocaine. *Anesth Analg*. 2008;107:1260-1262.

Maslow AD, Regan MM, Israel E, et al. Inhaled albuterol, but not intravenous lidocaine, protects against intubation-induced bronchoconstriction in asthma. *Anesthesiology*. 2000;93:1198-1204.

McAlpine LG, Thomson NC. Lidocaine-induced bronchoconstriction in asthmatic patients: relation to histamine airway responsiveness and effect of preservative. *Chest*. 1989;96:1012-1015.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

C.6. If this is an emergency surgery and rapid sequence induction is indicated, how would you induce anesthesia in this patient?

Precautions to prevent both aspiration of gastric contents and bronchospasm must be considered simultaneously. The need to secure the airway rapidly and to ensure an adequate depth of anesthesia before intubation can be competing interests. Additionally, patients like this one frequently have cardiovascular comorbidities that must be considered.

Prior to induction, inhalation of β_2-agonists such as albuterol with an inhaler may be administered. The patient should then be adequately denitrogenated with 100% oxygen by mask.

Rapid sequence induction using adequate doses of propofol, methohexital, or ketamine should be administered. Ketamine (2 mg per kg) may be the induction agent of choice in patients without cardiac disease. In patients with ischemic heart disease, a moderate dose of fentanyl 5 μg per kg 2 to 3 minutes before the administration of propofol (1.5 mg per kg) or methohexital (1.5 mg per kg) to suppress airway reflexes and prevent tachycardia and hypertension caused by intubation.

Cisatracurium or vecuronium 1 mg should be given 3 minutes before administration of succinylcholine.

Martin DE, Rosenberg H, Aukburg SJ, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesth Analg*. 1982;61:680.

C.7. Could a regional technique be used for this surgery? Discuss the advantages and disadvantages of neuraxial anesthesia in this patient for this surgery.

For laparoscopic surgery, regional anesthesia can be used. Typically, this is performed with epidural anesthesia, which allows for repeated dosing to obtain an adequate level and

duration of anesthesia. Laparoscopic surgery requires a T4 to T5 dermatomal level. Even with adequate analgesia to this dermatome, patients will often complain of shoulder pain, which can be treated with intravenous narcotic administration. The advantages of regional anesthesia include the avoidance of instrumenting the airway, a decrease in the resultant risk of bronchospasm, and the ability to maintain the epidural postoperatively to reduce or even eliminate the need for postoperative narcotics.

However, the high level required for laparoscopic surgery has multiple effects on the respiratory system. First, patients with a high blockade lose sensory input from chest wall movement, and patients feel dyspneic, even in the presence of normal respiratory function. This feeling of dyspnea can be anxiety producing and in a patient with asthma can lead to bronchospasm.

More important, however, high levels of neuraxial anesthesia should be avoided in patients with severe respiratory disease who require accessory muscle contribution in order to maintain adequate ventilation. These patients will have reduced expiratory flow and minute ventilation under high neuraxial blockade and can become hypoxic and hypercarbic.

Newer surgical techniques, including the Natural Orifice Transluminal Endoscopic Surgery (NOTES), are being developed for minimally invasive cholecystectomy. These procedures may be done with a lower dermatomal level.

Vretzakis G, Bareka M, Aretha D, et al. Regional anesthesia for laparoscopic surgery: a narrative review. *J Anesth*. 2014;28:429-446.

C.8. Would you choose an inhalational or an intravenous technique for maintenance of anesthesia?

For maintenance of anesthesia, inhalation agents such as sevoflurane and isoflurane can be used. These agents are thought to be superior to desflurane because of its pungent odor that may cause airway irritation and trigger bronchospasm. At lower doses (<1.0 minimum alveolar concentration), the inhaled anesthetics inhibit chemically induced tracheal contractions in the order: *enflurane* ≥ *isoflurane* > *sevoflurane*. More recent clinical observations in humans indicate that sevoflurane at 1.1 minimum alveolar concentration may be the most effective agent, particularly in the presence of airway instrumentation. In addition, sevoflurane may have a more rapid onset of bronchodilation than isoflurane.

Desflurane has been shown to cause elevations in airway resistance and tissue mechanical parameters, with markedly enhanced airway narrowing in children with asthma or a recent URI. Therefore, desflurane should be avoided in children with susceptible airways.

Nitrous oxide can also be used, provided that the patient does not have pulmonary hypertension, a condition commonly present in patients with COPD.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:468-469.

Rock GA, Choi JH, Bishop MJ. The effect of isoflurane, halothane, sevoflurane and thiopental nitrous oxide on respiratory system resistance after tracheal intubation. *Anesthesiology*. 1997;86:1294-1299.

Von Ungern-Sternberg BS, Saudan S, Petak F, et al. Desflurane but not sevoflurane impairs airway and respiratory tissue mechanics in children with susceptible airways. *Anesthesiology*. 2008;108:216-224.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

C.9. What mechanisms produce bronchodilation from volatile anesthetics?

The volatile anesthetics relax airway smooth muscle primarily by directly depressing smooth muscle contractility. This action appears to result from direct effects on bronchial epithelium and airway smooth muscle cells and indirect inhibition of the reflex neural pathways. The mechanisms responsible for the direct relaxation effects involve decreases in intracellular calcium, an important regulator of smooth muscle reactivity. Several intracellular mediators responsible for mobilization of calcium ions are potential sites for the action of volatile anesthetics, but the predominant mechanism appears to be inhibition of cell membrane-associated voltage-dependent calcium channels, an action that decreases entry of calcium ions into the cytosol. Volatile anesthetic-induced increases in cyclic 3′,5′ adenosine monophosphate

(cAMP) cause decreases in free intracellular calcium by stimulating efflux of calcium and increasing uptake of calcium into the sarcoplasmic reticulum. This action contributes to airway smooth muscle relaxation. In addition, volatile anesthetics reduce calcium sensitivity as a result of inhibition of protein kinase C activity and inhibition of G protein function.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:468-469.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Churchill Livingstone; 2015:671-678.

C.10. Which muscle relaxants would you use? Why?

Muscle relaxants that cause histamine release should be avoided. Rocuronium, cisatracurium, and vecuronium are the preferred relaxants because the histamine release is insignificant. Additionally, their intermediate duration of action allows for early recovery without reversal with an anticholinesterase, which may precipitate bronchospasm. D-Tubocurarine can cause bronchospasm by histamine release. Metocurine and succinylcholine also cause histamine release but to a lesser extent. There is no evidence that succinylcholine is associated with increased airway resistance in patients with asthma. Atracurium, mivacurium, and doxacurium in high doses increase histamine release. Therefore, their use in asthmatics should be avoided.

Basta SJ. Modulation of histamine release by neuromuscular blocking drugs. *Curr Opin Anesth*. 1992;5:572.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Churchill Livingstone; 2015:978-980.

C.11. How will you ventilate the patient? Will you use positive end-expiratory pressure (PEEP)? How can you detect the presence of auto-PEEP on your ventilator?

There are competing interests involved in managing the ventilation of this patient with COPD undergoing laparoscopic surgery. Peak inspiratory pressures (PIPs) should be kept at a minimum, end-expiratory time needs to be adequate to overcome air trapping, and hypercarbia from insufflation with CO_2 must be compensated for.

A pressure control ventilation mode would be preferable to volume control because it results in lower PIPs at similar tidal volumes. However, the laparoscopic technique leads to increasing airway resistance and increasing PIPs, so the tidal volumes must be watched closely because they will decrease with insufflation of the abdomen and PIP set on the ventilator will need to be increased as the case proceeds.

High PIP should be avoided, especially in patients with emphysema and blebs, because a pneumothorax can result from barotrauma. PIP should never be greater than 50 cm H_2O, and plateau pressures should be kept below 30 cm H_2O to minimize barotrauma.

The inspiratory-to-expiratory time ratio (I:E ratio) can be increased in order to reduce PIP. However, in this patient, the I:E ratio will likely need to be *reduced* in order to allow for complete expiration in the setting of expiratory obstruction and avoid air trapping. Allowing for an adequate expiratory time is a key component in the ventilatory management of patients with obstructive pulmonary disease.

Adequate minute ventilation will need to be maintained and should be increased as the case proceeds and insufflated CO_2 is absorbed into the bloodstream and exhaled through the alveoli. Minute ventilation may need to increase as much as 60% in order to maintain normocarbia. Absorbed CO_2 can result in hypercapnia that lingers well into the postoperative period.

Achieving adequate minute ventilation with sufficient expiratory time and reasonable PIP can be a difficult task. In patients with severe pulmonary disease, it may be impossible. In this scenario, alternatives to traditional laparoscopy should be discussed with the surgeon. Gasless laparoscopic techniques that do not require insufflation of the abdomen are preferable, when feasible. These techniques utilize abdominal wall lifting to avoid necessitating a pneumoperitoneum.

The application of PEEP during positive pressure ventilation is a controversial issue. This type of PEEP is also referred to as extrinsic PEEP and must be differentiated from intrinsic or auto-PEEP. Intrinsic PEEP occurs in patients with COPD or asthma because outflow

obstruction leads to air trapping. In ventilators equipped with an expiratory hold control, intrinsic PEEP can be measured during positive pressure ventilation. PEEP applied by the ventilator should be subtracted from the airway pressure measured during the expiratory hold time in order to obtain intrinsic PEEP. When extrinsic PEEP is lower than intrinsic PEEP, it can improve ventilation, especially in the spontaneously ventilating patient. Extrinsic PEEP reduces the amount of negative pressure required to generate a breath and therefore reduces the work of breathing.

However, extrinsic PEEP that exceeds intrinsic PEEP can worsen air trapping and hyperinflation. Excessive PEEP also results in decreased venous return, decreased left ventricular compliance, and increased pulmonary capillary resistance. All of these changes lead to hypotension.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:282.

Reddy RM, Guntupalli KK. Review of ventilatory techniques to optimize mechanical ventilation in acute exacerbation of chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2007;2(4):442-452.

Slinger P. Don't make things worse with your ventilator settings: how you manage the lungs during the perioperative period affects postoperative outcomes. In *IARS 2013 ReviewCourse Lectures*. San Francisco, CA: International Anesthesia Research Society; 2013:38-46.

C.12. In the middle of surgery, peak inspiratory pressures suddenly increase. How do you manage this?

The most common cause of bronchospasm during surgery is inadequate depth of anesthesia. The patient with asthma has an extremely sensitive tracheobronchial tree. When the level of anesthesia is too light, the patient may develop bucking, straining, or coughing as a result of the foreign body (endotracheal tube) in the trachea and then bronchospasm. Therefore, during surgery, the initial treatment of bronchospasm is not to administer β-agonist but rather to increase FIO_2 and deepen anesthesia.

First, increase the FIO_2. Then, bag ventilate in order to manually assess pulmonary compliance and auscultate the lungs to assess for wheezing. Bilaterally diminished breath sounds are present during severe bronchospasm, or a mechanical obstruction of the tube. Unilaterally decreased breath sounds may indicate a main-stemmed endotracheal tube or, rarely, a pneumothorax. Once bronchospasm is confirmed, prior to deepening anesthesia, take a blood pressure. If normal or high, deepen anesthesia by increasing the concentration of inhalation agents, such as sevoflurane or isoflurane, which are direct bronchodilators, or administer an incremental dose of propofol. This has the advantage of deepening anesthesia without relying on alveolar ventilation (which is decreased during bronchospasm) for administration. Likewise, in a patient with a low to normal blood pressure, an incremental dose of ketamine both deepens anesthesia and bronchodilates. The patient should be continuously ventilated with a volume-cycled ventilator.

Second, relieve mechanical stimulation. Pass a catheter through the endotracheal tube to suction secretions and determine whether there is an obstruction, kinking of the tube, or overinflation of the endotracheal tube cuff. The cuff of the endotracheal tube can be deflated, the tube moved back 1 to 2 cm, and the cuff reinflated. Occasionally, the endotracheal tube slips down and stimulates the carina of the trachea, causing severe bronchospasm during light anesthesia. Surgical stimulation, such as traction on the mesentery, intestine, or stomach, should be stopped temporarily because it stimulates a vagal reflex and can cause bronchospasm.

Third, start medical intervention if the previously mentioned treatment does not break the bronchospasm or anesthesia cannot be deepened secondary to hypotension. The cornerstone of the treatment of intraoperative bronchospasm is inhalation of β_2-agonists such as albuterol, which induce further bronchodilation even in the presence of adequate inhalational anesthesia. Because of rain-out in the endotracheal tube, a large dose (8 to 10 puffs) should be given to achieve adequate therapeutic levels. If bronchospasm continues despite optimal bronchodilation therapy, high-dose intravenous corticosteroids are indicated (see sections B.15 and B.16). Epinephrine 5 to 10 μg can be given intravenously, but caution should be taken as it can exacerbate tachycardia and tachyarrhythmias.

Alternatively, a continuous infusion of epinephrine 0.5 to 2 μg per minute in adults can provide maintenance bronchodilation with fewer adverse effects.

A patient with severe, refractory bronchospasm may require ventilation with a ventilator equipped to generate very high inspiratory pressures. An ICU ventilator can generate inspiratory pressures as high as 120 cm H_2O. Most anesthesia machines cannot deliver adequate alveolar ventilation because the circuit has too much compressible volume (tubing compliance) and the ventilator does not have sufficient driving power. The major disadvantage of an ICU ventilator is its inability to use inhalational anesthetics. Some newer anesthesia machines incorporate an ICU-type ventilator with vaporizers and oxygen mixers. They may be ideal for this situation.

Heliox is an oxygen/helium mixture that, secondary to its lower density to air, can permit higher flow rates at lower pressures, theoretically improving delivery of oxygen during bronchospasm. However, due to its expense and controversy of use in asthma, it is not routinely used.

Finally, although not available at all centers, venovenous extracorporeal membrane oxygenation (VV-ECMO) may be established in order to adequately oxygenate the blood when all other measures have failed. ECMO is expensive, requires specially trained personnel, and is an invasive treatment modality associated with a number of potential complications. However, it is a potentially lifesaving measure that should be considered in select cases of severe, refractory hypoxemia secondary to respiratory disease.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2012:188.

Liu LL, Aldrich JM, Shimabukuro DW, et al. Rescue therapies for acute hypoxemic respiratory failure. *Anesth Analg*. 2010;111:693-702.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

C.13. How would you give β_2-agonists? What is their mechanism of action on asthma?

Historically, it was fashionable to treat episodes of severe asthma with intravenous sympathomimetics such as isoproterenol. This approach no longer appears justifiable. Isoproterenol infusions can induce ventricular arrhythmias during halothane anesthesia and is clearly associated with myocardial damage. Even the intravenous administration of β_2-selective agents such as terbutaline and albuterol offers no advantage over the inhaled route.

β_2-Agonists such as albuterol, levalbuterol, and terbutaline may be administered through MDI adapters or small-volume jet nebulizers to the anesthetic circuit. Because MDI adapters are not very efficient in the intubated patient, 8 to 10 puffs are needed to break acute bronchospasms.

Adrenergic stimulants produce bronchodilation through action on β-adrenergic receptors. β-Agonists increase intracellular cAMP by activating adenyl cyclase, which produces cAMP from adenosine triphosphate. Increased cAMP promotes bronchial relaxation and inhibits the release of mediators from mast cells (Fig. 1.5).

Fanta CH. Asthma. *N Engl J Med*. 2009;360:1002-1014.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2012:185-188.

Longo DL, Fauci AS, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2102-2116.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

C.14. If the patient does not respond to the aforementioned treatment and becomes cyanotic, what would you do?

The ABG values should be determined immediately. In a severe, prolonged asthmatic attack, there will be combined respiratory and metabolic acidosis resulting from CO_2 retention and lactic acidosis from tissue hypoxia. Hypercarbia, hypoxemia, and acidemia promote arrhythmias and impair the response to bronchodilator therapy. $NaHCO_3$ should be given to correct the acidosis because β-agonists are not effective in severe acidosis. At the same time,

bronchodilator therapy should be continued or increased. Further treatment options are outlined in section C.12. Consultation with senior staff or a physician in pulmonary medicine may be necessary.

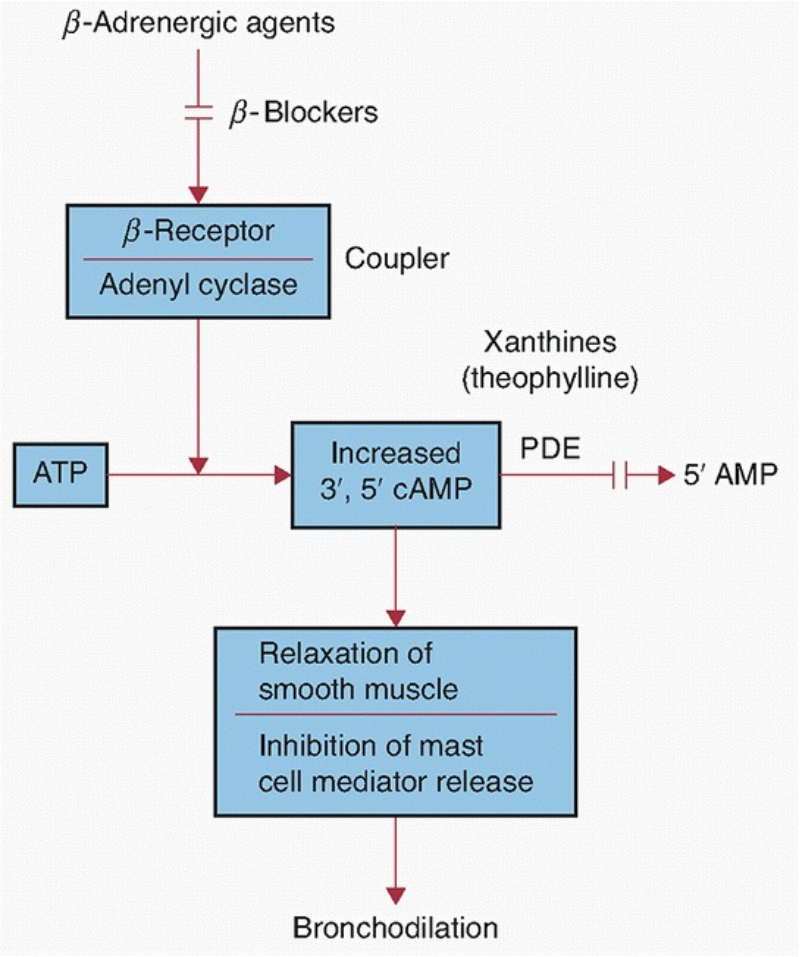


FIGURE 1.5 Cyclic adenosine monophosphate (cAMP) pathways involved in bronchodilator action. 3′,5′, cAMP, cyclic 3′,5′ adenosine monophosphate; AMP, adenosine monophosphate; ATP, adenosine triphosphate; PDE, phosphodiesterase. (From Hirshman C. Airway reactivity in humans: anesthetic implications. *Anesthesiology*. 1983; 58:170, with permission.)

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

C.15. What are the differential diagnoses of intraoperative bronchospasm?

The causes of wheezing and increased airway pressure include the following:

- Mechanical obstruction of endotracheal tube
  - Kinking
  - Solidified secretions or blood
  - Overinflation of tracheal tube cuff
- Inadequate depth of anesthesia
- Pulmonary edema
- Tension pneumothorax (especially consider in a patient with emphysema and blebs)
- Aspiration pneumonitis
- Pulmonary embolism
- Endobronchial intubation
- Persistent coughing and straining

- Asthmatic attack

If the bronchospasm occurs with or without evidence of a rash or angioedema, an allergic reaction should be considered. Common causes of intraoperative allergies include latex, neuromuscular blocking drugs (NMBDs), and antibiotics. In the setting of hypotension and/or

bradycardia, anaphylaxis is high on the differential. Administration of likely inciting agents should cease; epinephrine 5 to 10 μg, diphenhydramine, and steroids should be given. An infusion of epinephrine may be necessary. A tryptase level should be sent to confirm the diagnosis, and the patient should be notified in writing of the potential reaction so that follow-up allergy testing can be obtained.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2012:188.

C.16. The asthmatic attack was relieved with your treatment and the surgery was completed. Following emergence, the patient was found to be hypoventilating. What are the common causes of hypoventilation? What will be your approach to treat hypoventilation?

The following are common causes of apnea or hypoventilation at the end of surgery:

- Respiratory center depression by inhalational anesthetics, opioids, or mechanical hyperventilation (low $PaCO_2$)
- Peripheral blockade by muscle relaxants
- Hypothermia

In a patient with severe asthma, avoiding the use of an anticholinesterase, such as neostigmine, to reverse a nondepolarizing relaxant may be beneficial because neostigmine may trigger bronchospasm by cholinergic and prosecretory effects. However, any patient without sustained tetany of train-of-four, stimulation should be reversed.

If reversal is required, larger than customary doses of glycopyrrolate or atropine should be administered to minimize the possibility of bronchospasm. Although atropine or glycopyrrolate given simultaneously with neostigmine may prevent bronchospasm, the duration of action of neostigmine can outlast that of a vagolytic agent, especially in the presence of renal insufficiency, and lead to delayed bronchospasm. Intraoperatively, it is advisable to use inhalation agents to potentiate relaxants and to use smaller amounts of intermediate-acting relaxants for surgery.

If the patient does not appear to have any of the aforementioned causes of hypoventilation but is still inadequately ventilating, extubation should be delayed.

Hazizai A, Hatija A. Bronchospasm caused by neostigmine. *Eur J Anaesthesiol*. 2006;23:85-86.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Churchill Livingstone; 2015:2930-2931.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

C.17. Would you consider a deep extubation in this patient?

To avoid bronchospasm triggered by coughing and bucking caused by laryngeal and pharyngeal reflexes during emergence and extubation, patients may be extubated at surgical (deep) levels of anesthesia. However, the risks of aspiration, airway obstruction, and hypoventilation should be weighed against the benefits. With a history of severe COPD, chronic hypoxemia, and CO_2 retention, the patient was not a good candidate for extubation while deeply anesthetized. A systematic approach for emergence and extubation is illustrated in Figure 1.6. However, the guidelines do not include all possible patient-surgical-anesthetic conditions. Certainly, the practitioner's clinical judgment is of utmost importance regarding the decision to extubate.

Lien CA, Koff H, Malhotra V, et al. Emergence and extubation: a systemic approach. *Anesth Analg*. 1997;85:1177.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

C.18. If the patient cannot be extubated, what measures can you take to reduce the likelihood of bronchospasm with an endotracheal tube in place?

Loading doses of lidocaine, followed by continuous infusion, as described in section C.5, may be administered intravenously to prevent bronchoconstriction induced by stimulation of the

endotracheal tube. β_2-Agonists such as albuterol may be administered through MDI adapter to prevent bronchospasm. Alternatively, a supraglottic airway may be used to replace the endotracheal tube for control of ventilation and to avoid tracheal stimulation.

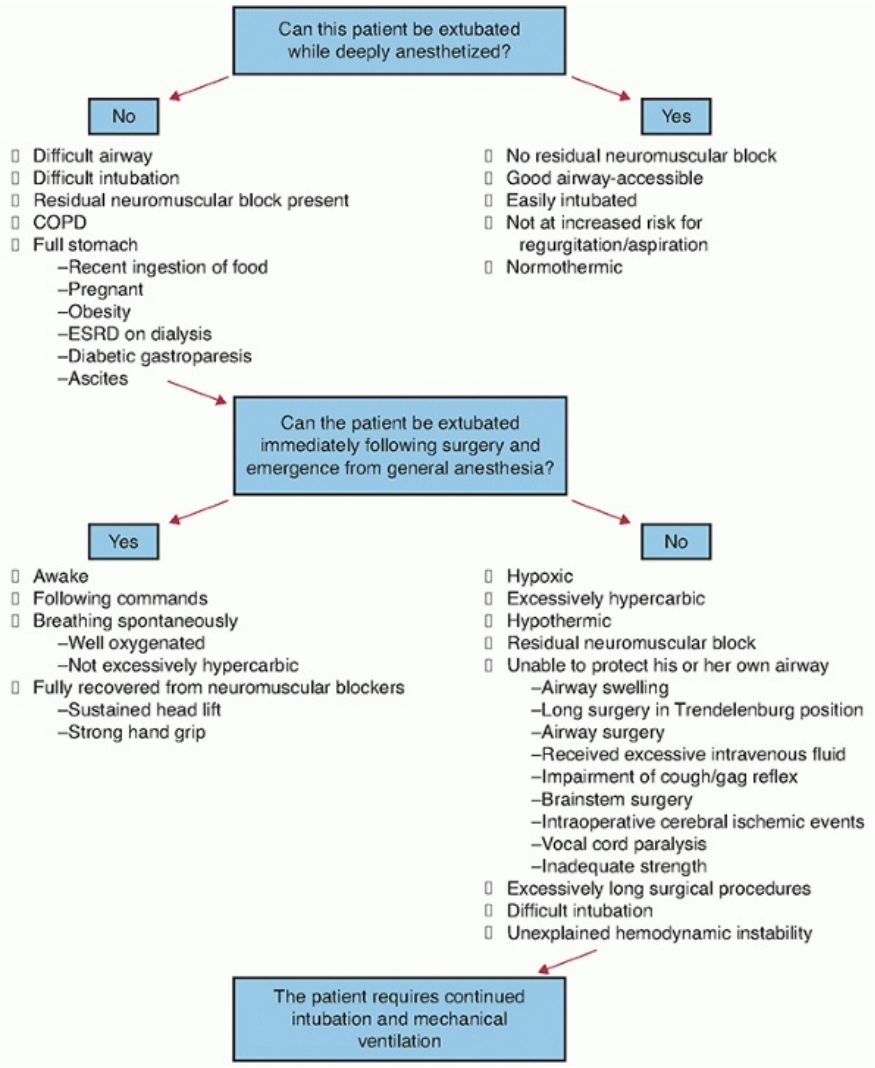


FIGURE 1.6 A systematic approach to emergence and extubation. COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Churchill Livingstone; 2012:182-188.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57-i65.

D. Postoperative Management

D.1. In patients with asthma, are there special considerations for the use of opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) for postoperative pain control?

Opioids should be used very carefully because prolonged respiratory depression may further compromise the airway. Morphine is avoided because of possible histamine release

and increased central vagal tone, which may cause bronchospasm. Meperidine may be a better choice for postoperative analgesia because of its spasmolytic action. Narcotics should be titrated carefully to control pain and not depress respiration. Poor pain control may compromise respiration because of splinting of the thoracic cage and decreased ability to cough.

An estimated 4% to 11% of asthmatics have a sensitivity toward NSAIDs, known as aspirin-sensitive respiratory disease (ASRD). NSAIDs block the cyclooxygenase-mediated conversion of arachidonic acid to prostaglandins, thereby shunting arachidonic acid toward the formation of bronchoconstricting leukotrienes. Patients with ASRD are more likely to have an irreversible component to their obstructive airway disease, more likely to have frequent exacerbations, and more likely to have had a history of severe attacks and oral steroid use. Persistent rhinorrhea, nasal polyps, and nasal congestion are common symptoms. Most patients with ASRD are unaware of the diagnosis. If a focused preoperative history reveals any of the aforementioned symptoms, NSAIDs should be avoided.

Farooque SP, Lee TH. Aspirin-sensitive respiratory disease. *Annu Rev Physiol*. 2009;71:465-487.

Longo DL, Fauci AS, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2102-2116.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Churchill Livingstone; 2015:877-879.

D.2. Would you consider using a regional technique for analgesia?

Were this surgery to be accomplished laparoscopically, a regional technique for analgesia is typically not necessary. However, in a patient with severe respiratory disease, the complete avoidance of systemic narcotics may be desired in order to reduce the risk of PPCs. In this case, epidural analgesia is preferred. The epidural may be placed before surgery and may be used as an adjunct or alternative to general anesthesia (see section C.7). The complete analgesia that can be obtained with epidural anesthesia allows for patients to avoid “splinting” secondary to abdominal pain and improves postoperative respiratory recovery.

Contraindications to epidural anesthesia include patient refusal and anticoagulation. In patients unable to receive neuraxial anesthesia, an alternative is the transversus abdominis plane (TAP) block. A study of 43 patients undergoing laparoscopic cholecystectomy showed decreased postoperative opiate use and mean discharge time from postanesthesia care unit (PACU) in patients receiving a TAP block as compared to those with conventional port site infiltration. A TAP block consists of two to four injections of local anesthetic (typically bupivacaine, ropivacaine, or liposomal bupivacaine) providing 12 to 36 hours of pain relief. Unlike an epidural, once the block is performed and following a period of adequate postblock monitoring, no special equipment is necessary and patients can be discharged home. However, a TAP block only covers surgical incision pain and does not affect internal surgical pain. Therefore, a multimodal pain regimen will still be required.

Tolchard S, Davies R, Martindale S. Efficacy of the subcostal transversus abdominis plane block in laparoscopic cholecystectomy: comparison with conventional port-site infiltration. *J Anaesthesiol Clin Pharmacol*. 2012;28(3):339-343.

Vretzakis G, Bareka M, Aretha D, et al. Regional anesthesia for laparoscopic surgery: a narrative review. *J Anesth*. 2014;28:429-446.

D.3. The patient was breathing well and was extubated. Would you place this patient on supplemental oxygen in the recovery room? How much?

Patients with COPD who receive supplemental oxygen tend to breathe with lower tidal volumes. Additionally, oxygen therapy may abolish hypoxic pulmonary vasoconstriction in poorly ventilated areas, increasing blood flow to these areas and proportionally decreasing blood flow to other lung regions with normal or high ventilation:perfusion ratios. Both of the

mechanisms lead to increased dead space ventilation, causing an increase in $PaCO_2$.

The belief that supplemental oxygen in patients with COPD leads to hypercarbia through the abolition of hypoxic respiratory drive is not evidence based. Adequate oxygen concentration must be used in the presence of hypoxemia. Of current available evidence, it is recommended to administer supplemental oxygen in order to maintain a PaO_2 greater than

65 mm Hg. Lower PaO_2 values are associated with increased pulmonary artery pressures and lead to right ventricular strain and dysfunction.

COPD is not a contraindication for continuous positive airway pressure (CPAP), and patients who are felt to benefit from noninvasive positive pressure ventilation (NIPPV) postoperatively should be provided with that treatment. CPAP is especially important in patients with COPD because the application of CPAP counterbalances the intrinsic PEEP present in these patients. When necessary, hypoventilation can be assisted or controlled by artificial ventilation.

Gomersall CD, Joynt GM, Freebairn RC, et al. Oxygen therapy for hypercapnic patients with chronic obstructive pulmonary disease and acute respiratory failure: a randomized controlled pilot study. *Crit Care Med*. 2002;30:113-116.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia, PA: Butterworth-Heinemann; 2005;191:381.

Slinger P. Don't make things worse with your ventilator settings: how you manage the lungs during the perioperative period affects postoperative outcomes. *IARS 2013 ReviewCourse Lectures*. San Francisco, CA: International Anesthesia Research Society; 2013:38-46.

Chapter 2
Bronchoscopy, Mediastinoscopy, and Thoracoscopy

Alessia Pedoto
Paul M. Heerdt
Fun-Sun F. Yao

A 60-year-old man has suffered from cough, intermittent hemoptysis, and weight loss for 2 months. He has smoked one pack of cigarettes per day for 40 years. A chest radiograph 1 month ago revealed a right middle lobe infiltrate that was treated with antibiotics without clinical improvement. Subsequent evaluation revealed a carcinoma. He is now scheduled for fiberoptic bronchoscopy, mediastinoscopy, and possible video-assisted thoracoscopic (VATS) lobectomy.

A. Medical Disease and Differential Diagnosis

1. How is the diagnosis of lung carcinoma made? What is your prediction for the most likely type of malignancy?
2. What are the less common manifestations of bronchogenic carcinoma?
3. The patient has a long history of cigarette smoking. What is the significance of this finding?

B. Preoperative Evaluation and Preparation

1. How would you evaluate the patient prior to surgery?
2. What are the pulmonary function guidelines that indicate an increased risk for morbidity and mortality?

C. Intraoperative Management

1. How would you premedicate, monitor, and anesthetize this patient?
2. How many types of bronchoscopes are available and what are the intraoperative considerations of each one?
3. What are the indications for cervical mediastinoscopy? Are there potential complications?
4. The decision was made to proceed with a thoracoscopic right middle lobectomy. How would this alter your management?
5. What are the indications for single-lung ventilation and how is it accomplished?
6. What are the contraindications to the use of double-lumen endotracheal tubes (DLTs)?
7. Would you use a right- or left-sided DLT?
8. How do you know that the tube is in the correct position?
9. How many types of bronchial blockers are available? What are the advantages and disadvantages of bronchial blockers?
10. How will systemic oxygenation be monitored during single-lung ventilation? What is the mechanism of pulse oximetry?
11. The patient was placed in the lateral decubitus position. Describe the effects of lateral positioning on pulmonary blood flow and respiration.
12. What is hypoxic pulmonary vasoconstriction (HPV)?

13. What are the effects of anesthetic agents on HPV and their clinical implications?
14. Discuss pulmonary blood flow distribution, shunt flow, and PaO_2 ($FIO_2 = 1.0$) during single-lung ventilation in the lateral position.
15. How could you improve oxygenation during single-lung ventilation?

16. A right middle lobectomy was performed. Would you extubate the trachea at the end of the procedure?

D. Postoperative Management

1. What are the immediate life-threatening complications that follow lobectomy or pneumonectomy?
2. Why is it important to control postoperative pain? How would you achieve this?

A. Medical Disease and Differential Diagnosis

A.1. How is the diagnosis of lung carcinoma made? What is your prediction for the most likely type of malignancy?

The initial presenting symptoms in patients with lung cancer are constitutional and nonspecific, mainly related to metastatic disease. Nonproductive cough, dyspnea, hemoptysis, and chest pain, along with an unresolved lung infiltrate on chest radiography, should suggest carcinoma. In the attempt to make early diagnosis, the American Cancer Society has issued preliminary guidelines for screening high-risk patients using low-dose computed tomography imaging. Recommended candidates include “apparently healthy” subjects aged between 55 and 74 years with a smoking history of at least 30 packs per year, who are current smokers or quit within the past 15 years. The main limitation of this test is the 23.3% incidence of false-positive results, which may lead to further testing including surgical biopsy. Biomarkers from large airway epithelial cells or buccal mucosal biopsies are being investigated and may represent early diagnostic options in the future. At the present time, the initial diagnostic and staging procedures are done in the operating room under general anesthesia. This includes flexible bronchoscopy with airway washings and brush biopsy, possibly followed by ultrasound-guided transbronchial biopsy (endobronchhial ultrasound [EBUS]) of the mediastinal lymph nodes. Additional areas for biopsy include palpable lymph nodes in the neck or axilla, needle aspiration biopsy, mediastinoscopy, and possibly exploratory thoracoscopy or thoracotomy. An extensive evaluation must be performed to exclude metastases which would contraindicate major surgery.

Cancers of the lung account for 16% of all malignancies and nearly 27% of cancer-related deaths worldwide. Bronchogenic carcinomas represent the vast majority of lung cancers in patients requiring surgical resection and can be classified into four major types: small cell, large cell, squamous cell, and adenocarcinoma. For surgical purposes, lung tumors are classified as non-small cell or small cell. The former are amenable to surgical resection, while the latter tend to be nonresectable and are treated medically.

The TNM classification is used in the staging of bronchogenic carcinomas and helps to predict the response to therapy. *T* designates tumor site, size, and local extent; *N*, the presence and location of regional lymph node involvement; and *M*, the presence of distal metastases beyond the ipsilateral hemithorax. In general, small cell carcinomas that spread beyond possible resection by the time of presentation are primarily managed with chemotherapy, with or without radiation, and lead to a 5-year survival of approximately 20%. In contrast, non-small cell cancers found to be localized at the time of presentation should be considered for primary resection. The 5-year survival can be as high as 85% for small tumors without regional lymph node involvement or metastases (stage I). Approximately 45% of patients present with circumscribed extrapulmonary disease or lymphatic spread to the ipsilateral mediastinal or subcarinal lymph nodes (stage IIIa). Their 5-year postresection survival is less than 20%.

Kasper DL, Fauci AS, Hauser S, et al, eds. *Harrison's Principles of Internal Medicine*. 19th ed. New York: McGraw-Hill; 2015:506-522.

Kathuria H, Gesthalter Y, Spira A, et al. Updates and controversies in the rapidly evolving field of lung cancer screening, early detection, and chemoprevention. *Cancers (Basel)*. 2014;6:1157-1179.

Spiro SG, Gould MK, Colice GL. Initial evaluation of patients with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest*. 2007;132:149S-160S.

Wender R, Fontham ET, Barrera E Jr, et al. American Cancer Society lung cancer screening guidelines. *CA Cancer J Clin*. 2013;63:107-117.

A.2. What are the less common manifestations of bronchogenic carcinoma?

Other manifestations of lung tumors are primarily related to mass effects or altered metabolism. In addition to bronchial obstruction and possible postobstructive pneumonia, mass effects include invasion into the chest wall and pleura, compression of great vessels (e.g., superior vena cava syndrome) and heart, tracheobronchial displacement, paresis of the recurrent laryngeal or phrenic nerves and of the sympathetic chain. Pancoast syndrome can present with pain and upper extremity weakness secondary to invasion of the brachial plexus as well as the first and second thoracic and eighth cervical nerve roots. Recognized metabolic manifestations of small cell lung tumors include symptoms that resemble those of Cushing syndrome (from ectopic adrenocorticotropic hormone production), carcinoid syndrome, hypercalcemia and hypophosphatemia (resulting from ectopic parathyroid hormone or parathyroid hormone-related peptides), hypokalemia (caused by ectopic adrenocorticotropic hormone secretion), and hyponatremia (from inappropriate secretion of antidiuretic hormone and possibly atrial natriuretic factor). Neurologic paraneoplastic syndromes include Lambert-Eaton myasthenic syndrome, peripheral neuritis involving both motor and sensory components, cerebellar degeneration, retinopathy, limbic encephalopathy, and autonomic neuropathy. An autoimmune process has been suggested for these findings, and it seems to be more common in patients with limited disease.

Extrathoracic spread of the tumor can affect the bones, liver, adrenal glands, intra-abdominal and subcutaneous lymph nodes, brain, and spinal cord, contributing to the nonspecific presentation of the cancer.

Kasper DL, Fauci AS, Hauser S, et al, eds. *Harrison's Principles of Internal Medicine*. 19th ed. New York: McGraw-Hill; 2015:506-522.

Spiro SG, Gould MK, Colice GL. Initial evaluation of patients with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest*. 2007;132:149S-160S.

A.3. The patient has a long history of cigarette smoking. What is the significance of this finding?

Cigarette smoking still remains the leading cause of lung cancer in the United States. Tobacco exposure leads to chronic obstructive pulmonary disease (COPD), which includes chronic bronchitis and emphysema, and is strongly associated with an increased incidence of stroke, myocardial infarction, and cancer (lung, oral cavity, larynx, and esophagus). Pulmonary hypertension from chronic hypoxemia and subsequent cor pulmonale may also occur.

Eight percent to 17% of patients with lung cancer who are scheduled for surgical resection are still smoking at the time of surgery. Current tobacco use increases the risk of postoperative respiratory failure, pneumonia, aspiration, air leak, atelectasis, as well as 1-year mortality. Preoperative smoking cessation is strongly recommended, but it is unclear how long is needed to see a significant reduction in postthoracotomy complications. Carboxyhemoglobin concentrations decline substantially within 12 hours of smoking cessation. In patients undergoing thoracic surgery, the benefits of smoking cessation must be balanced with the risk of local tumor growth and metastatic spread, which may preclude resectability. Four weeks has been suggested as an acceptable time by several studies in this population. A combined approach including counseling and polypharmacology has been shown to increase the success rate and decrease relapses after hospital discharge.

Carson KV, Usmani ZA, Robertson TA, et al. Smoking cessation interventions for lung cancer patients. *Lung Cancer Manage*. 2013;2:61-74.

DeHoyos A, DeCamp M. Preoperative smoking cessation for lung resection patients. In: Ferguson MK, ed. *Difficult Decision in Thoracic Surgery: An Evidence-Based Approach*. 3rd ed. London: Springer-Verlag; 2014:85-98.

Kathuria H, Gesthalter Y, Spira A, et al. Updates and controversies in the rapidly evolving field of lung cancer screening, early detection, and chemoprevention. *Cancers (Basel)*. 2014;6:1157-1179.

Mason DP, Subramanian S, Nowicki ER, et al. Impact of smoking cessation before resection of lung cancer: a

Society of Thoracic Surgeons General Thoracic Surgery Database study. *Ann Thorac Surg*. 2009;88:362-370.

Pedoto A, Heerdt PM. Postoperative care after pulmonary resection: postanesthesia care versus intensive care unit. *Curr Opin Anaesthesiol*. 2009;22:50-55.

Wong J, Lam DP, Abrishami A, et al. Short term preoperative smoking cessation and postoperative complications: a systematic review and meta-analysis. *Can J Anaesth*. 2012;59:268-279.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient prior to surgery?

Preoperative evaluation should investigate cardiac risks in case of perioperative cardiac disease, lung function, gas exchange capacity, and cardiopulmonary reserve. The main goal is to identify in advance those at risk for major postoperative complications and optimize their functional status. The first step should include a complete history, physical examination, and laboratory tests (e.g., complete blood count, basic metabolic profile, coagulation study, electrocardiogram, chest radiography, and computed tomographic imaging). A positive smoking history, especially if current, cough, sputum production, orthopnea, and dyspnea should be further investigated. An abnormal exercise tolerance, such as the inability to climb at least three flights of stairs or walk for 6 minutes, may indicate a patient with compromised cardiorespiratory function and unable to tolerate the stress of anesthesia and surgery. A brief review of symptoms, physical limitations, interval changes, and airway anatomy is usually performed before entering the operating room.

In addition to routine preoperative testing, patients scheduled for lung resection usually undergo pulmonary function testing to help define the relative risks of the planned resection. Respiratory function can be assessed by:

- **Respiratory mechanics:** evaluated via forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), and the ratio between residual volume and total lung capacity (RV/TLC). Flow-volume loops may be helpful to document the location of the obstruction (small vs. large airway) and its severity. Post bronchodilator FEV_1 and FEV_1/FVC paired with clinical symptoms are used to determine the severity of COPD.
- **Cardiopulmonary reserve:** evaluated with maximal oxygen uptake (VO_2 max), stair climbing, 6-minute walk, and shuttle walk. VO_2 max is the gold standard for aerobic capacity and cardiorespiratory fitness. Patients with VO_2 max value less than 10 mL/kg/min are at increased risk for postoperative morbidity and mortality.
- **Lung parenchymal function:** Diffusing lung capacity for carbon monoxide (DLCO), partial pressure of oxygen in the arterial blood (PaO_2), and partial pressure of arterial carbon dioxide ($PaCO_2$). Predicted postoperative DLCO and FEV_1 less than 40% to 44% are significant independent predictors for increased postoperative morbidity and mortality.

Brunelli A, Kim AW, Berger KI, et al. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013;143(suppl 5):e166S-e190S.

Licker M, Triponez F, Diaper J, et al. Preoperative evaluation of lung cancer patients. *Curr Anesthesiol Rep*. 2014;4:124-134.

Ravenel JG, ed. *Lung Cancer Imaging*. New York: Springer Science; 2013:69-78.

B.2. What are the pulmonary function guidelines that indicate an increased risk for morbidity and mortality?

The reported mortality from lung resection is between 2% and 4%, mainly as a result of pneumonia, respiratory failure, bronchopleural fistula, empyema, and pulmonary embolism. Respiratory insufficiency occurs in approximately 5% of patients following lung resection

and is associated with a 50% mortality rate. Advanced age and the increased incidence of concomitant nonpulmonary disease seem to contribute to this outcome. An increased risk of postoperative complications can be predicted by the following:

TABLE 2.1 Minimal Pulmonary Function Test Criteria for Various-Sized Pulmonary Resections

TEST	UNIT	NORMAL	PNEUMONECTOMY	LOBECTOMY	BIOPSY OR SEGMENTAL
MBC	L/min	>100	>50	>40	>25
MBC	Percentage predicted	100%	>50%	>40%	>25%
FEV_1	Liters	>4	>2.1-1.7	>1.2-1.0	>0.6-0.9
FEV_1	Percentage	>80% FVC	>50% FVC	>40% FVC	>40% FVC
$FEV_{25\%-75\%}$	Liters	>2	>1.6	>0.6-1.6	>0.6

FEV_1, forced expiratory volume in first second; $FEV_{25\%-75\%}$, forced expiratory volume from 25% to 75% of forced vital capacity; FVC, forced vital capacity; MBC, maximum breathing capacity.

- **Spirometry:** Spirometric parameters, such as FEV_1/FVC ratio and FEV_1 (reflective of the degree of airway obstruction), as well as static volumes (such as inspiratory and TLC), are used to define the severity of COPD. Several studies have indicated a strong correlation between predicted postoperative FEV_1 and DLCO and a respective increase in morbidity and mortality, especially for open procedures and extensive dissection. Concerning values are summarized in Table 2.1.
- **Arterial blood gases:** Historically, hypercapnia ($PaCO_2$ greater than 45 mm Hg) was considered an exclusion criterion for lung resection. However, no independent correlation has been found with an increased mortality. Patients who are hypercapnic often have a low predicted postoperative FEV_1 and an abnormal exercise capacity, which preclude surgery. Preoperative hypoxemia (PaO_2 less than 50 mm Hg, and percentage of available hemoglobin saturated with oxygen [SaO_2] less than 90%) has been associated with an increased risk of postoperative complications. However, baseline hypoxemia can be the result of ventilatory mismatch caused by obstructive tumors that once resected may theoretically improve gas exchange.

Other factors influencing outcome include patient comorbidities and functional status, the extent and location of the proposed surgical resection, and whether the patient has undergone preoperative induction chemotherapy. An improvement in both surgical and anesthetic techniques has broadened the criteria for surgical respectability. As evident from lung volume reduction studies, patients with severely impaired pulmonary function (e.g., FEV_1 less than 1 L) can still undergo surgical resection under general anesthesia without prohibitive risk for postoperative complications. Moreover, the development of minimally invasive surgical techniques has raised the question of whether standard selection criteria should always be adopted.

Emphasis has been directed toward integrating multiple aspects of the preoperative evaluation (e.g., respirometry, ventilation-perfusion scanning, extent of planned resection, patient functional status) into the estimate of postoperative function. Better postoperative analgesia techniques, early ambulation, and thromboprophylaxis have all contributed to

improve outcomes after major lung resection in patients at high risk.

Boffa DJ, Allen MS, Grab JD, et al. Data from The Society of Thoracic Surgeons General Thoracic Surgery database: the surgical management of primary lung tumors. *J Thorac Cardiovasc Surg*. 2008;135:247-254.

Matsubara Y, Takeda S, Mashimo T. Risk stratification for lung cancer surgery: impact of induction therapy and extended resection. *Chest*. 2005;128:3519-3525.

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Pedoto A, Heerdt PM. Postoperative care after pulmonary resection: postanesthesia care versus intensive care unit. *Curr Opin Anaesthesiol*. 2009;22:50-55.

C. Intraoperative Management

C.1. How would you premedicate, monitor, and anesthetize this patient?

Current practice in most institutions dictates that patients arrive at the hospital the day of surgery; thus, traditional oral or parenteral premedication before transport to the operating room is largely obsolete. Bronchoscopy and mediastinoscopy are generally ambulatory procedures, necessitating a relatively rapid hospital discharge. Because lung resection in this patient is only a possibility, intravenous midazolam immediately on entry into the operating room would seem appropriate for anxiolysis and subsequent amnesia. If not contraindicated, a small intravenous dose (0.2 mg) of glycopyrrolate can be considered as an antisialagogue, particularly in patients who smoke.

EBUS-guided lymph node biopsy has become more popular in the past decade, as a minimally invasive highly accurate alternative to cervical mediastinoscopy for staging of lung cancer. It can be performed either via the esophagus or the trachea under sedation or general anesthesia. The former is indicated for a limited number of biopsies, whereas the latter works better in case of complete staging of the mediastinum. On-site cytologic exam is usually performed during the procedure. Mediastinal, hilar, lobar, and interlobar lymph nodes are accessible with this technique with a complication rate of 1.4%. Coughing (if the airway is not adequately topicalized) and bronchospasm are potential intraoperative complications. The incidence of pneumothorax is rare and depends on the location of the lymph node to biopsy rather than the type of anesthesia and the ventilation modality. Bleeding is also a rare instance, therefore not requiring aggressive reversal of anticoagulation as for mediastinoscopy.

Cervical mediastinoscopy is now reserved for small lymph nodes not readily accessible via EBUS. During mediastinoscopy, intermittent compression or occlusion of the innominate artery can occur. Therefore, the blood pressure cuff should be placed on the left arm and the pulse oximeter on the right hand. In the case of innominate artery compression, a damping of the pulse oximetry trace will be evident while blood pressure measurements will remain accurate. Although rare, injury to vascular structures (such as the azygos veins and innominate artery) can occur, potentially necessitating sternotomy. Patient positioning and placement of electrocardiography leads should be considered accordingly. Arterial access is not routinely used for this procedure unless the patient has clinical indications for continuous hemodynamic monitoring. In this case, the catheter should be placed in the left radial artery as well to avoid falsely low readings related to innominate artery compression. Body temperature should be monitored, and a warming blanket applied. Despite the potential of being a short procedure, hypothermia can occur, especially in the elderly patients. Induction, maintenance of anesthesia, and muscle relaxation can be achieved with relatively short-acting agents. Propofol is usually used for induction of general anesthesia followed by rocuronium, vecuronium, or cisatracurium to facilitate tracheal intubation via a singlelumen endotracheal tube (ETT). Anesthesia can be maintained with a potent inhalational agent in oxygen or air, if oxygen saturation tolerates it. Two to 3 μg per kg of fentanyl often provides sufficient analgesia for the procedure. Local anesthetic can be infiltrated in the wound by the surgeon at the beginning or at the end of the procedure. Nonsteroidal antiinflammatory drugs (NSAIDs) are used by some providers as adjuvant agents; nevertheless, the potential for bleeding in a closed space in ambulatory patients should be considered. Finally, many clinicians choose to avoid the use of nitrous oxide because of the potential for the mediastinoscope to enter the pleural space and create a pneumothorax.

Eapen GA, Shah AM, Lei X, et al. Complications, consequences, and practice patterns of endobronchial ultrasound-

guided transbronchial needle aspiration: results of the AQuIRE registry. *Chest*. 2013;143:1044-1053.

Harris CL, Toloza EM, Klapman JB, et al. Minimally invasive mediastinal staging of non-small-cell lung cancer: emphasis on ultrasonography-guided fine-needle aspiration. *Cancer Control*. 2014;21:15-20.

Molins L, Fibla JJ, Pérez J, et al. Outpatient thoracic surgical programme in 300 patients: clinical results and economic impact. *Eur J Cardiothorac Surg*. 2006;29:271-275.

Rami-Porta R, Call S. Invasive staging of mediastinal lymph nodes: mediastinoscopy and remediastinoscopy. *Thorac Surg Clin*. 2012;22:177-189.

Slinger P, ed. Perioperative lung injury. In: Slinger P, ed. *Principle and Practice of Anesthesia for Thoracic Surgery* . New York: Springer; 2011:201.

C.2. How many types of bronchoscopes are available and what are the intraoperative considerations of each one?

Four types of bronchoscopes are currently in use: flexible fiberoptic, bronchoscopy (EBUS), rigid ventilating, and rigid Venturi.

The *flexible fiberoptic bronchoscope* can be used either in sedated patients under local anesthesia (allowing examination of vocal cords movements) or under general anesthesia with a supraglottic airway or an ETT. For the awake or sedated examination, viscous lidocaine can be gargled to anesthetize the upper airway, and a 2% or 4% lidocaine solution inhaled via nebulizer mask to reach the lower airway. Bilateral superior laryngeal nerve blocks or transtracheal block can be added, however, not as popular as in the past due to the potential complications. Intravenous sedation can be achieved with 0.5-mg increments of midazolam, 10 μg of remifentanil boluses or a propofol infusion. Alternatively, dexmedetomidine (as a bolus of 0.5 to 1 μg per kg over 10 minutes followed by a continuous infusion of 0.2 to 1.5 μg/kg/hr) can also be used; its main advantage consisting of amnesia and vagolysis without impaired ventilation. When compared to propofol, the main disadvantage seems to be the prolonged recovery time, limiting its use in the ambulatory setting. If the oropharynx is adequately anesthetized, a supraglottic airway can be inserted without discomfort in sedated patients and used to assist ventilation at higher FIO_2 concentrations.

EBUS can be done with either sedation or general anesthesia, depending on the number and locations of the lymph nodes to biopsy. Good topical anesthesia is paramount to prevent coughing and bronchospasm, independently of the technique used. The EBUS bronchoscope is a 6.9-mm outer diameter flexible bronchoscope with a latex balloon tip, coupled with a 7.5-MHz convex ultrasound probe. When the balloon is inflated with normal saline, it allows a tight adhesion to the airway wall facilitating ultrasound identification of the lymph nodes. A 21-gauge needle is used through a dedicated channel of the bronchoscope for real time biopsy. Color Doppler is available to differentiate the lymph nodes from vascular structures. In the sedated patient, or if a supraglottic airway device is used, particular attention should be used to avoid vocal cord trauma due to the positioning of the optical view at a 30-degree angle. Intravenous steroids may be used to prevent inflammation and edema. In nonintubated patients, local anesthetic toxicity may result from larger doses used to tolerate the longer procedure and abolish the cough reflex. If ETT is used, an 8.5 mm internal diameter (ID) ETT is recommended to accommodate the bronchoscope and ventilate. In the presence of precarinal lymphadenopathy, the ETT may need to be placed high in the trachea, leaving the balloon between vocal cords. Trauma may occur in case of prolonged procedures and in the absence of paralysis. Other complications include pneumo- and hemomediastinum, pneumothorax, mediastinitis, and bacteremia.

Rigid bronchoscopy usually necessitates general anesthesia. Although spontaneous ventilation has been used, the risk of tracheal trauma is high with coughing. If not contraindicated, muscle relaxation is usually used. The rigid ventilating bronchoscope has a side-port adapter that can be attached to either the anesthesia machine or the jet ventilator, allowing the delivery of a high flow rate. A variable air leak usually exists around the bronchoscope, so high flow rates of inspired gases or packing of the oropharynx are needed. Significant loss of volatile anesthetic into the operating room environment needs to be considered; thus, the use of total intravenous technique is a good alternative.

The *rigid Venturi-effect bronchoscope* relies on an intermittent high-flow (20 to 60 L per minute), high-pressure (50 psi) oxygen jet to entrain air and insufflate the lungs. The jet is delivered through a reducing valve (25 psi) into a 16- or 18-

gauge needle inside and roughly parallel to the lumen of the bronchoscope. Major disadvantages of this bronchoscope are the lack of control of the inspired oxygen concentration and the inability to administer inhaled anesthetics. Accordingly, anesthesia should be maintained by intravenous techniques. Inadequate ventilation can result in hypercapnia.

Rigid bronchoscopic procedures can be relatively short; therefore, continuous succinylcholine infusion still remains an option for these procedures. If not contraindicated, small doses of nondepolarizing muscle relaxants can also be used. When followed

by another procedure, an intermediate-duration nondepolarizing muscle relaxant is often desirable.

José RJ, Shaefi S, Navani N. Anesthesia for bronchoscopy. *Curr Opin Anesthesiol*. 2014;27:453-457.

Metha AC, Jain P, eds. *Interventional Bronchoscopy: A Clinical Guide*. New York: Springer Science; 2013:85-106.

C.3. What are the indications for cervical mediastinoscopy? Are there potential complications?

Cervical mediastinoscopy was the gold standard to evaluate disease in the mediastinum and staging of lung cancer. However, with the introduction of the EBUS, cervical mediastinoscopy has become less popular. Independently of the technique used, if lymph nodes are positive for malignancy by frozen section, the patient is probably not a surgical candidate and the planned lung resection aborted.

Conventional cervical mediastinoscopy involves a small incision at the sternal notch for the insertion of the mediastinoscope and sampling of the lymph nodes. The pleural space is generally not entered intentionally, and, therefore, a chest tube is not indicated. Occult pneumothorax can occur as a complication, so a chest radiograph is usually obtained before discharge. Complications during mediastinoscopy are relatively rare (1% to 2%) and generally result from trauma to adjacent structures (pleura, trachea, esophagus, superior vena cava, azygos vein, innominate artery, pulmonary artery, and aorta) or nerve injury (recurrent laryngeal or phrenic nerve). Should a major vascular structure be perforated, blood loss can be rapid and profound, necessitating emergent sternotomy. Because packing or vascular clamps may be applied to the superior vena cava, clinicians should always have a plan for establishing venous access in the lower extremity.

Ehrenwerth J, Brull SJ. Anesthesia for thoracic diagnostic procedures. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. 3rd ed. Philadelphia, PA: Churchill Livingstone; 2003:174-195.

Wilson RS. Anesthesia for bronchoscopy and mediastinoscopy. In: Youngberg JA, Lake CL, Wilson RS, eds. *Cardiac, Vascular, and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:660-669.

C.4. The decision was made to proceed with a thoracoscopic right middle lobectomy. How would this alter your management?

Minimally invasive procedures include either a video-assisted thoracoscopic (VATS) or a robotic assisted (RATS) approach. Robotic thoracic procedures present some unique challenges when compared to VATS.

In both cases, patients are **positioned** in the lateral decubitus and the bed maximally flexed. For robotic cases, the bed may be rotated 90 to 180 degrees from the original position and hence far away from the anesthesiologist. This is to allow the robot to be docked. Extensions for the intravenous tubing and the breathing circuit may be necessary. For the same purpose, the upper arm is suspended and sometimes abducted away from the chest cavity. Unnatural positioning with stretching of the brachial plexus can lead to potentially permanent damage. This can occur if the robotic arms are resting on the patient's arm or head.

Optimal **lung isolation** and **collapse** are needed to enhance lung visualization during the case and allow full motion of the instruments. Because the chest cavity remains partially closed, lung collapse is slower than for the open approach. Carbon dioxide (CO_2) insufflation may be used to expedite the process at the price of a tension pneumothorax physiology.

Leftsided DLTs are commonly used due to their higher margin of safety and the ability to quickly collapse the lung. Once the patient is positioned and the robot docked, it is quite difficult to gain access to the airway. Bronchial blockers may be an alternative, but they may require repositioning during the case. Because of the variable takeoff the right upper lobe, right-sided DLT are not the preferred choice.

Intravenous access should be placed before final positioning and draping because patient access will be limited. An **arterial line** (in the dependent radial artery) may be beneficial in patients undergoing robotic procedures for hemodynamic monitoring, although not uniformly regarded as necessary for lung resection via thoracotomy, and highly institution-dependent. In order to optimize lung collapse, and facilitate the instruments motion, the chest is sometimes

insufflated with carbon monoxide (CO). This “iatrogenic tension pneumothorax” may be associated a transient increase in peak airway pressures and a decrease in venous return with significant hypotension and decreased lung compliance. In the majority of cases, it is transient and responds to pressors or temporary decrease of the insufflation pressures. Suggested values should be less than 10 to 15 mm Hg, whereas peak inspiratory pressures should be less than 30 cm H_2O. Minute ventilation should be adjusted to maintain normocapnia.

Hemodynamic collapse can also be caused by unexpected bleeding, *arrhythmias* or, in rare cases, contralateral *pneumothorax* (more common during robotic esophagectomy). Bleeding can be more difficult to control in robotic cases than VATS because the robotic arms limit the access to the chest, causing delays in making an incision or performing cardiopulmonary resuscitation (CPR). Maneuvers that help to decrease bleeding involve increasing the insufflation pressure for the CO_2 (potentially worsening systemic hypotension) and having temporary apnea to prevent mediastinal swings and facilitate compression/clipping of the source of bleeding.

The duration of surgery depends on the expertise of the surgeon and the operating room staff. VATS and robotic cases are usually longer than open procedures, especially during the learning phase, exposing patients to prolonged anesthesia and lung collapse. Intraoperative costs are increased when the robot is compared to the VATS approach.

Campos JA. Update on lung separation techniques. *Revista Mexicana de Anestesiologia*. 2011;34:S270-S277.

Campos J, Ueda K. Update on anesthetic complications of robotic thoracic surgery. *Minerva Anestesiol*. 2014;80(1):83-88.

Kroth M, Chalikonda S, eds. *Essentials of Robotic Surgery*. New York: Springer International Publishing; 2015:165-177.

Walsh AM, Losher J. Arterial oxygenation and management of hypoxemia during VATS. *Curr Opin Resp*. 2014;4:170-176.

C.5. What are the indications for single-lung ventilation and how is it accomplished?

Absolute and relative indications for lung separation are listed in Table 2.2. Several techniques can be used to provide single-lung ventilation, including DLTs, bronchial blocking catheters passed outside or inside the ETT, ETTs with incorporated bronchial blocking catheters (Univent® ETT, Teleflex, Triangle Park, NC), or conventional ETTs placed endobronchially. Newer DLTs include the VivaSight® (ETView Medical Ltd, Misgav, Israel) (a left-sided DLT with a high-resolution built-in video camera at the tip of the tracheal lumen which allows a continuous view of the airway when connected to a monitor), the Silbroncho® (Teleflex, Triangle Park, NC) left-sided DLT (a silicone-made DLT with a wire-reinforced tip), and the Cliny® (Create Medic Co, Ltd, Yokohama, Japan) right-sided DLT (a device with an oblong cuff and two ventilation slots for the upper lobe). Currently, DLTs remain the most common method for achieving lung isolation. Although DLTs of variable design and material have been used in the past (e.g., Robertshaw, Carlens, and White), the models most commonly used today are disposable and made of polyvinylchloride. Such a tube was the chosen for this procedure. DLTs are available in five sizes: 28, 35, 37, 39, and 41 French (size in French = 3.14 × external diameter in millimeters or 4 × the internal diameter + 2) and two sides (right and left). Although the general rule is that average-sized Caucasian men usually accommodate a 39-French and average-sized women a 37-French, there is no clear correlation between age, height, weight, and DLT size. In the Asian population, this correlation becomes even less reliable, warranting a review of the chest imaging. Accordingly, some clinicians advocate the use of small DLTs in all patients. Radiographic or computed tomographic imaging have been used to measure the airway size, but they have been questioned across gender and ethnicity. A properly sized DLT should pass atraumatically through the glottis, advance easily into the trachea and bronchus, and exhibit an air leak when the bronchial cuff is deflated.

Several types of bronchial blockers are available (see section C.9), presenting a good option for lung isolation in patients who have difficult airways, when postoperative mechanical ventilation is needed, in case of a fresh tracheostomy or in the pediatric population. Lobar blockade can also be accomplished by blockers, especially after pneumonectomy, or in case one-lung ventilation (OLV) is not tolerated. Disadvantages of blockers include slow lung collapse, especially in patients with severe COPD, dislodgment of the catheter tip during surgical manipulation of the hilum, or being stapled in the bronchial stump.

TABLE 2.2 Indications for Single-Lung Ventilation

ABSOLUTE	
1. To isolate from spillage or contamination	• Infection: Bronchiectasis and lung abscess • Massive hemorrhage
2. To control the distribution of ventilation	• Bronchopleural fistula • Bronchopleural cutaneous fistula • Giant unilateral lung cyst or bulla • Tracheobronchial tree disruption or trauma • Surgical procedures on major conducting airway (i.e., pneumonectomy or sleeve resection) • Life-threatening hypoxemia resulting from unilateral lung disease • Unilateral bronchopulmonary lavage (pulmonary alveolar proteinosis)
3. To facilitate surgical exposure	• Video- and robotic-assisted thoracoscopic surgery
RELATIVE	
1. Facilitation of surgical exposure—high priority	• Thoracic aortic aneurysm • Pneumonectomy • Upper lobectomy • Mediastinal exposure • Pulmonary resection via median sternotomy
2. Facilitation of surgical exposure—low priority	• Esophageal resection • Middle and lower lobectomies and segmental resection • Procedures on the thoracic spine
3. Severe hypoxemia resulting from unilateral lung disease	

Independently of the technique chosen, single-lung ventilation is associated with certain disadvantages and complications. The most notable is the large and variable alveolar-to-arterial oxygen tension difference ($PAO_2 - PaO_2$) that occurs as a result of continued perfusion to the nondependent nonventilated lung. The incidence of severe hypoxemia and hypercarbia is relatively small and often the result of DLT malposition resulting from overinflation of the endobronchial cuff, surgical manipulation of the bronchus, or head extension or flexion during positioning. Other complications include traumatic laryngitis and tracheobronchial rupture resulting from bronchial cuff overinflation, forceful placement, or airway pathology.

Heir SJ, Purugganan R, Jackson TA, et al. A retrospective evaluation of the use of video-capable double-lumen endotracheal tubes in thoracic surgery. *J Cardiovasc Thorac Anesth*. 2014;28:882-884.

Licker M, Le Guen M, Diaper J, et al. Isolation of the lung: double lumen tubes and endobronchial blockers. *Trends Anaesth Crit Care*. 2014;4:47-54.

Miller RD, ed. *Miller's Anesthesia*. 10th ed. New York: Churchill Livingstone; 2015:1942-2006.

Pedoto A. How to choose the double-lumen tube size and side: the eternal debate. *Anesthesiol Clin*. 2012;30(4):671-681.

C.6. What are the contraindications to the use of double-lumen endotracheal tubes (DLTs)?

Placement of a DLT should be carefully considered in the following situations:

- Patients whose upper airway anatomy may preclude safe insertion of the tube (recessed jaw, prominent teeth, bull neck, anterior larynx, mandibular surgery, and neck radiation)
- Patients with lesions present somewhere along the pathway of the tube that could be traumatized, such as airway stricture or endoluminal tumors

- Small patients for whom a no. 35 French tube is too large to fit comfortably through the larynx, and a no. 28 French tube is considered too small
- Critically ill patients who have a single-lumen tube already in place and who cannot tolerate cessation of mechanical ventilation and positive end-expiratory pressure (PEEP) for a short period of time

Under these circumstances, single-lung ventilation can be achieved via an endobronchial blocker. Endobronchial placement of a single-lumen tube for lung isolation is an alternative but suboptimal option. The tip of the ETT can cause direct distal airway trauma, whereas significant airway compression with potential mucosal ischemia may occur if the cuff bulges at carina. When placed on the right side, the right upper lobe can also be occluded by the cuff of the tube, preventing the ability to ventilate.

Campos JA. Update on lung separation techniques. *Revista Mexicana de Anestesiologia*. 2011;34:S270-S277.

Licker M, Le Guen M, Diaper J, et al. Isolation of the lung: double lumen tubes and endobronchial blockers. *Trends Anaesth Crit Care*. 2014;4:47-54.

Miller RD, ed. *Miller's Anesthesia*. 10th ed. New York: Churchill Livingstone; 2015:1942-2006.

C.7. Would you use a right- or left-sided DLT?

A left-sided DLT is generally preferable for most procedures due to its margin of safety. The left mainstem bronchus is much longer than the right (approximately 5.0 to 5.5 cm vs. 1.5 to 2.0 cm), allowing small movements of the tube without obstructing a bronchial division. The variable origin of the right upper lobe (1.5 to 2.0 cm below carina) may complicate maintaining a good placement of a right-sided tube. Nevertheless, in an institution in which the use of right-sided DLT is routine, no difference was found in the incidence of hypoxemia, hypercarbia, or high airway pressures when compared to left-sided DLTs. A right-sided DLT is indicated in the case of pathology of the left mainstem bronchus, such as large exophytic lesions, significant bronchial stenosis, tracheobronchial disruption, endobronchial stent, and distortion by an adjacent tumor or a thoracoabdominal aneurysm. Other indications include left pneumonectomy, sleeve resection, or lung transplantation to avoid the presence of a “foreign body” in the surgical field that could be included in the staple line or prevent suturing of the donor lung. At the end of a pneumonectomy, the stump can be protected from positive pressure ventilation by leaving the tracheal side clamped until the patient returns to spontaneous ventilation; for a left lung transplant or a sleeve resection, the right lung continues being ventilated during the reconstruction phase. The only absolute

contraindication for right-sided DLTs use is the presence of an anomalous takeoff of the right upper bronchus above the tracheal carina, commonly referred to as a “pig bronchus.”

Campos JA. Update on lung separation techniques. *Revista Mexicana de Anestesiologia*. 2011;34:S270-S277.

Ehrenfeld JM, Walsh JL, Sandberg WS. Right- and left-sided Mallinckrodt double-lumen tubes have identical clinical performance. *Anesth Analg*. 2008;106:1847-1852.

Licker M, Le Guen M, Diaper J, et al. Isolation of the lung: double-lumen tubes and endobronchial blockers. *Trends Anaesth Crit Care*. 2014;4:47-54.

Miller RD, ed. *Miller's Anesthesia*. 10th ed. New York: Churchill Livingstone; 2015:1942-2006.

Pedoto A. How to choose the double-lumen tube size and side: the eternal debate. *Anesthesiol Clin*. 2012;4:671-681.

C.8. How do you know that the tube is in the correct position?

Recommended insertion techniques for a DLT include direct laryngoscopy followed by fiberoptic guidance in the appropriate mainstem. Blind insertion is not recommended due to the potential of airway injury. Auscultation alone is unreliable to confirm the position of a double-sided lumen due to a possible decrease in breath sounds, especially in patients with COPD. The position of the device should be reconfirmed once the patient is in the lateral decubitus prior to lung collapse.

During bronchoscopy, the tracheal cartilaginous rings are anterior and the tracheal membrane is posterior. Therefore, right versus left can be discerned by the relationship of the mainstem bronchi to the anterior cartilaginous rings and the posterior membrane (Fig. 2.1A). In addition, the right upper lobe takeoff (which usually arises from the lateral aspect of the

right mainstem bronchus, just below the tracheal carina) is a useful landmark when the airway anatomy has been obscured by bleeding, edema, or radiation-induced changes or has been distorted by extrinsic compression. Left-sided DLT position and depth are confirmed by inserting the fiberoptic bronchoscope in the tracheal lumen. The entire right mainstem bronchus should be visible, and the tracheal lumen orifice of the DLT should be 1 to 2 cm above the tracheal carina. When properly positioned, the upper part of the blue endobronchial cuff is visualized just below the tracheal carina in the left mainstem bronchus (Fig. 2.1B). If a right-sided DLT is used, correct positioning is confirmed by visualization of the bronchial cuff in the right mainstem bronchus (Fig. 2.1C) and visualization of the right upper lobe orifice through a slot on the lateral surface of the DLT (Fig. 2.1D). For both left-sided and right-sided tubes, the bronchoscope should also be inserted in the bronchial lumen to evaluate the distance between the tip of the tube and the distal bifurcation of the bronchus. DLT position should be reconfirmed after the patient is positioned laterally, before inflating the blue cuff and isolating the lung.

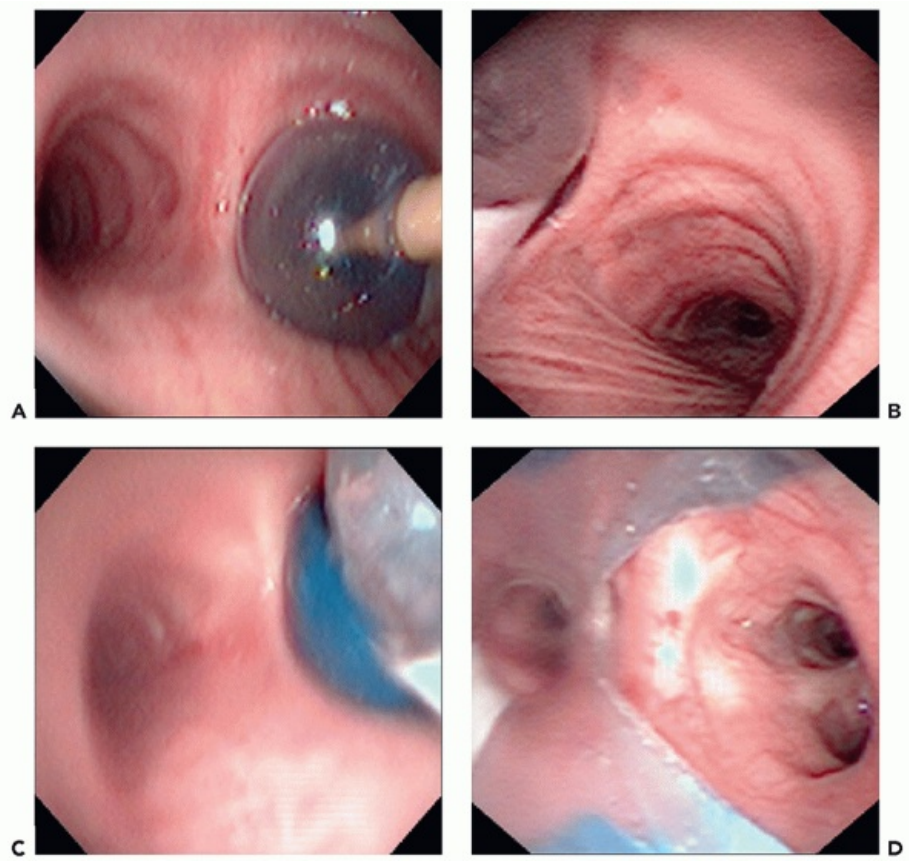


FIGURE 2.1 Representative bronchoscopic images of a bronchial blocker and DLT placement. **A.** Normal tracheal anatomy with cartilaginous rings anteriorly and membranous trachea posteriorly; this helps define left versus right. A bronchial blocking catheter is seen in the right mainstem bronchus. **B.** Placement of a left-sided DLT; the upper portion of the endobronchial cuff is evident as well as the orifice of the right upper lobe just below tracheal carina. **C.** Placement of a right-sided DLT; the upper portion of the endobronchial cuff is evident in the right mainstem bronchus. **D.** The orifice of the right upper lobe visualized through the slot on the lateral aspect of the bronchial side of a right-sided DLT.

When the *VivaSight*® tube is used, placement and repositioning can be facilitated by the high-resolution built-in camera. The main advantage for its use is during robotic cases

because of the patient being far away from the anesthesiologist and the robotic arms very close to the patient head, making adjustments to the DLT difficult. The ability to ventilate is not affected by the presence of the camera. The main disadvantage is the fogging of the camera by secretions, especially during right-sided procedures and the bigger outer diameter, which may cause airway injury during the placement. The lack of a camera on the bronchial side still requires the use of a fiberoptic bronchoscope to assess secondary carina.

Campos JA. Update on lung separation techniques. *Revista Mexicana de Anestesiologia*. 2011;34:S270-S277.

Campos J, Ueda K. Update on anesthetic complications of robotic thoracic surgery. *Minerva Anestesiol*. 2014;80(1):83-88.

Lee GK. Airway apparatus for thoracic surgery. *Anaesth Intensive Care Med*. 2014;15:499-504.

Licker M, Le Guen M, Diaper J, et al. Isolation of the lung: double lumen tubes and endobronchial blockers. *Trends Anaesth Crit Care*. 2014;4:47-54.

C.9. How many types of bronchial blockers are available? What are the

advantages and disadvantages of bronchial blockers?

Several blockers are available, leaving ample preference of choice to the operator and the institution. Advantages and disadvantages of blockers are listed in Table 2.3.

- **Fogarty embolectomy catheters** (Edwards Lifesciences, Irvine, CA) can be used to isolate the lung, although not specifically made for this purpose. No. 7 French Fogarty catheters come with either a 12- or 20-mL high-pressure, low-volume balloon in both latex and nonlatex models. They have a metallic stylet that can be bent to facilitate endobronchial placement. In the case of dislodgment, the stylet can be reinserted and the blocker repositioned. Fogarty catheters have no communicating central channel; therefore, continuous positive airway pressure (CPAP) or suction cannot be applied intraoperatively. Lung collapse occurs by absorption of oxygen. Therefore, prior to inflating the balloon, it is recommended that ventilation be discontinued and the circuit of the ventilator depressurized as long as the patient tolerates it. The catheters are usually placed outside a single-lumen ETT and positioned via fiberoptic bronchoscopy (Fig. 2.1A). If placed inside the ETT, a connector such as a two-swivel adaptor is needed to facilitate insertion of both the catheter and a bronchoscope.
- **Arndt blockers** (Cook Medical Inc, Bloomington, IN) (wire-guided endobronchial blocker) are available in no. 5, 7, and 9 French catheter with elliptical or spherical cuffs (low pressure, high volume), the latter particularly advantageous to isolate the right lung. They are usually inserted through the ETT via a three-way connector (catheter, bronchoscope, ventilation circuit). Their positioning is facilitated via Seldinger technique by an inner wire with a loop at the distal tip, where the flexible bronchoscope is placed. The wire is then removed once the blocker is in position, leaving an inner lumen that allows suctioning or CPAP. Once the wire loop has been removed, it can be reinserted, allowing repositioning of the blocker in case of dislodgment.

TABLE 2.3 Advantages and Disadvantages of Bronchial Blockers

ADVANTAGES	DISADVANTAGES
◦ Able to use in adults and children too small to fit a double-lumen tube ◦ Difficult airway ◦ If double-lumen tube contraindicated ◦ Placed inside the ETT ◦ No need to change ETT in the case of postoperative mechanical ventilation	◦ Unable to suction efficiently ◦ Need to be positioned via fiberoptic bronchoscopy ◦ Difficult for right mainstem position and RUL isolation, when the takeoff is too close to the carina ◦ Tracheal occlusion if proximal dislodgment ◦ Cross ventilation if the cuff is not completely inflated ◦ Possible stapling in the stump if not retracted at the appropriate time

ETT, endotracheal tube; RUL, right upper lobe.

- **Cohen blockers** (Cook Medical Inc, Bloomington, IN) are similar in shape to the Arndt blockers, but they use a positioning “wheel” to facilitate placement. By turning the wheel in a clockwise fashion, the distal portion of the blocker deflects to the left. The main advantage of this blocker is its placement in the left mainstem because of its steep angle. Disadvantages include cost and the fact that the wheel is very delicate. They also come in only one size (no. 9 French).
- **EZ blockers** (Teleflex, Triangle Park, NC) are blockers with a Y-shaped bifurcation at the end fitted with two inflatable cuffs and a hollow channel in the center. The cuffs are highpressure, low-volume, and color-coded. The blocker is placed inside the ETT, with the end on a horizontal plane to facilitate the placement of the Y across carina. Final position needs to be confirmed via fiberoptic because sometimes the two cuffs tend to go in the right mainstem. The main advantage of this blocker is its stability, making it useful when patient access is limited. The presence of the two cuffs makes sequential lung isolation feasible with a blocker in place.
- **Univent® tubes** (Teleflex, Triangle Park, NC) consist of an ETT with a built-in silicon bronchial blocking catheter. The main advantage is the ability of leaving the device in place in case of postoperative mechanical ventilation. However, this device is not commonly used in the United States because of its bulkiness. The outer diameter ranges from 9.7 to

13.7 mm (for a 6.0 to 8.0 mm inner diameter tube), with the potential to cause subglottic edema and stenosis in case of long-term use. The inner diameter is quite narrow, making suctioning or fiberoptic bronchoscopy difficult. The silicon blocker in the Univent® is available as an isolated item (**Fuji blocker**). It is a high-volume low-pressure system with a preformed “hockey stick” bend at the tip and a double stylet. It has a spherical cuff (ideally more suited to isolate the right mainstem bronchus) and two different sizes (no. 4.5 French and 9 French). The **Coopdech** blocker (Daiken Medical Co, Tokyo, Japan) is similar in shape to the Fuji blocker but offers the extra option of an auto-inflate balloon with an auto-inflate button, allowing the use of one hand while maneuvering the fiberoptic bronchoscope.

Blockers can be used to rescue nonworking DLT by placing the device inside the lumen of the nondependent lung. This may be needed if the bronchial cuff ruptures in a patient already positioned, or for lobar collapse in case of DLT dislodgment and inability to appropriately reposition it in the mainstem bronchus. The DLT may be left in the original place or withdrawn and used as a single-lumen tube.

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C.10. How will systemic oxygenation be monitored during single-lung ventilation? What is the mechanism of pulse oximetry?

Pulse oximetry is still the hallmark for monitoring arterial oxygenation during lung resection, decreasing the need for repeated measurements of arterial blood gases. This technique uses spectrophotoelectric oximetric principles to determine oxygen saturation. Pulse oximeters are multiple-wavelength plethysmographs. The amplitude of the pulse is a function of arterial distention, hemoglobin oxygen saturation of the arterial blood inflow, and light wavelength. Hemoglobin saturation in the arterial blood is the result of the ratio between the pulse amplitude of red (660 nm = deoxyhemoglobin) and infrared (940 nm = oxyhemoglobin) light. Pulsatile waveform is a characteristic of arterial blood flow, so there is no interference from surrounding venous blood, skin, connective tissue, or bone. Arterial pulsations cause changes in light absorption, which are used to calculate oxygen saturation. Adequate finger pulsation generally is lost with hypothermia of a few degrees, hypotension (mean blood pressure less than 50 mm Hg), and infusion of vasoconstrictive drugs. Accuracy of the measurement is also lost for values below 70% and can be affected by dyshemoglobinemias (such as carboxyhemoglobin, methemoglobin, and sulfhemoglobin) as well as intravenous

dye injection. The use of arterial oxygen saturation to monitor organ perfusion has been recently questioned by data of cerebral desaturation in the absence of arterial desaturation.

Cerebral oximetry has recently become a popular monitor of brain perfusion during thoracic and cardiac anesthesia. The technique uses near-infrared spectroscopy (NIRS) to integrate venous and arterial hemoglobin oxygen saturation signals in a ratio of 3:1. The presence of autoregulatory mechanisms guarantees that the brain is perfused and oxygenated at the expenses of other organs. Therefore, when significant cerebral desaturation occurs (<65%), it is likely that other organs have already been exposed to the same insult and are at higher risk for damage. Cerebral oximetry can be used to monitor distant organ perfusion. Specifically, brain hypoperfusion seems to correlate with renal ischemia and subsequent acute renal failure (ARF). The magnitude and the duration of mean arterial pressure values below autoregulation limits appear to correlate with the incidence of postoperative ARF after cardiac surgery. ARF is a known complication after anatomic lung resection. At the present time, there are no studies correlating its incidence with cerebral desaturation. Postoperative changes in mental status have been reported for prolonged periods of cerebral desaturation after thoracic procedures. Proposed physiologic mechanism include hypoxemia during OLV, mediastinal shift with reduced cardiac output related to the lateral decubitus and increased shunting, and central venous pressure (CVP) secondary to hypoxic vasoconstriction.

Plethysmography has been used as a noninvasive method to guide fluid replacement in anesthetized patients undergoing major surgery, including cardiac cases. Available devices collect data via continuous analysis of the plethysmographic waveform during the respiratory cycle. Their reliability during OLV and in the lateral decubitus still

remains to be investigated and is lost with small tidal volumes, open chest and sustained arrhythmias, drug-induced vasoconstriction, hypothermia, and low cardiac output.

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C.11. The patient was placed in the lateral decubitus position. Describe the effects of lateral positioning on pulmonary blood flow and respiration.

In both upright and supine positions, the right lung receives approximately 55% of the total blood flow, whereas the left lung receives the remaining 45%. In the lateral decubitus position, gravity causes a vertical gradient in blood flow distribution. Therefore, perfusion of the dependent lung is significantly greater than the nondependent counterpart. When the right lung is nondependent, it receives 45% of the total blood flow while 55% perfuses the dependent left lung. When the left lung is nondependent, it receives 35% of the total blood flow, while right lung receives 65%. Therefore, the average blood flow of the nondependent lung is approximately 40% of the total blood flow with the dependent lung being perfused with the remaining 60% (Fig. 2.2).

Respiratory Effects

The lateral decubitus position causes mechanical interference with chest wall movements, and a decrease in lung expansion. Specifically, the dependent chest wall is constricted by the operating room table, the lateral movements are limited by the bolsters or the “beanbag” used to hold the patient in position, whereas the upper expansion is reduced by the weight of the mediastinum. The flexion at the hips causes a theoretical improvement of the diaphragmatic motion, especially in morbidly obese patients. However, the caudad displacement of the abdominal organs is counteracted by the negative effects of general anesthesia and

muscle relaxation. The end result is a gravity-induced mismatch of ventilation and perfusion while in the lateral position, with redistribution of blood flow toward the dependent lung. Compression by the mediastinal contents results in an increase in atelectasis and hypoventilation. In the awake, spontaneously breathing subject, the lower (dependent) diaphragm is still able to contract more efficiently, maintaining ventilation in the dependent lung and matching the increased perfusion. In contrast, when the patient is anesthetized, with or without paralysis, most of the ventilation is preferentially switched to the more compliant upper lung, while perfusion increases in the lower lung. The end result is an increased degree of ventilation/perfusion mismatch.

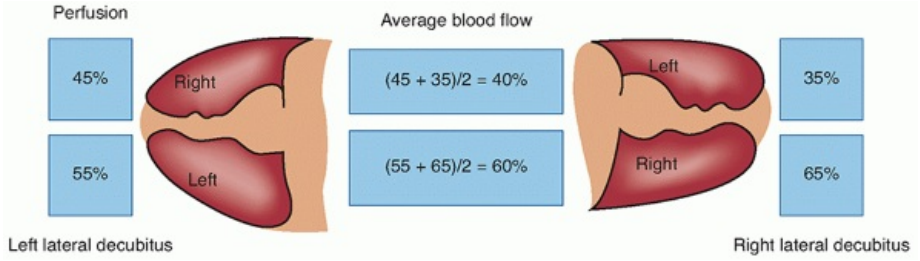


FIGURE 2.2 Changes in blood perfusion with the lateral decubitus position.

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C.12. What is hypoxic pulmonary vasoconstriction (HPV)?

HPV is an autoregulatory mechanism to prevent ventilation/perfusion mismatch and improve arterial oxygenation. Proposed mechanisms include an increase in reactive oxygen species in the pulmonary arterial smooth muscle, activation of redox-based oxygen sensors, and an increase in intracellular calcium. HPV is triggered by a decrease in PaO_2 within the lung from low FIO_2, hypoventilation, or atelectasis. The selective increase of vascular resistance in the hypoxic parenchyma diverts blood away to the better ventilated normoxic lung, decreasing the amount of shunt flow. This is a biphasic response that starts within 15 to 30 minutes from lung collapse, culminates at 120 minutes, and takes hours to reverse after normoxia is restored.

Increasing evidence indicates that significant systemic oxidative stress can be elicited by hyperoxic reperfusion of a lung in which HPV has been sustained for an extended period of time. Although the exact ramifications of this insult remain to be clarified, clinical data suggest an association between the magnitude of the oxidative stress and postoperative cardiopulmonary complications. Recommendations to decrease reexpansion injury include reinflating the collapsed lung with less than 100% FIO_2 as well as using protective lung strategies. The lowest FIO_2 possible is also recommended.

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C.13. What are the effects of anesthetic agents on HPV and their clinical implications?

Any drug that causes vasodilatation may inhibit hypoxic vasoconstriction. Several clinical studies have failed to demonstrate a decrease in HPV during single-lung ventilation and total

intravenous anesthesia. Intravenous anesthetics, such as thiopental, ketamine, morphine, and fentanyl have no direct effect

on HPV. In contrast, inhalational anesthetics have been shown to inhibit HPV in a dose-related fashion but usually at concentrations much higher than used clinically. Other nonanesthetic drugs such as β-agonists and antagonists, calcium channel blockers, nitrovasodilators, and theophylline may influence the effects of inhalation anesthetics on shunting and arterial oxygenation during single-lung ventilation. There is no good evidence that neuroaxial blockade affects HPV, unless causing a decrease in cardiac output or systemic vasodilatation.

- The end result of an increased shunt on PaO_2 depends on the absolute level of the initial shunt and the inspired oxygen concentration used. Even when shunt is increased, PaO_2 usually remains well above 100 mm Hg, with minimal changes in oxygen saturation and content.
- Inhalational agents inhibit HPV, but they also decrease cardiac output and oxygen consumption and may cause a decrease in mixed venous oxygen tension. If cardiac output decreases more than oxygen consumption, there will be a decrease in PvO_2, which is a potent stimulus for HPV. A low cardiac output will result in a decreased perfusion of the collapsed lung (where there is an increase in pulmonary vascular resistance as a result of HPV). Nevertheless, the presence of chronic and irreversible vascular disease in the nondependent lung may impair HPV response.
- The presence of disease in the dependent lung will decrease the ability of accepting blood flow redistribution, thereby decreasing the local HPV effect.
- Direct surgical manipulation may cause the release of vasoactive substances, such as thromboxane and prostacyclins, promoting local vasodilatation and blunting HPV, with a subsequent increase in shunt.
- Metabolic or respiratory acidosis and hypothermia are also associated with an impairment in HPV.

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C.14. Discuss pulmonary blood flow distribution, shunt flow, and PaO_2 (FIO_2 = 1.0) during single-lung ventilation in the lateral position.

When the nondependent lung is collapsed, HPV will increase pulmonary vascular resistance and decrease lung blood flow in this area. If no complicating factors exist, HPV should decrease blood flow to that lung by approximately 50%, causing a total reduction from 40% to 20% of the total. The resulting nondependent/dependent lung blood flow ratio during OLV should be 20%:80%.

Once atelectatic, all the blood flowing into the nonventilated lung is shunt flow. Therefore, OLV creates an obligatory right-to-left transpulmonary shunt that was not present during double-lung ventilation. During single-lung ventilation, an ideal total shunt flow of 20% would be expected, if no shunt existed during double-lung ventilation (ignoring the normal 1% to 3% physiologic amount from the bronchial, pleural, and thebesian circulation). PaO_2 with a fractional inspired O_2 concentration (FIO_2) equal to 1 should be approximately 280 mm Hg if hemodynamic and metabolic states are normal. Clinically, PaO_2 (FIO_2 = 1) ranges from 150 to 250 mm Hg.

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C.15. How could you improve oxygenation during single-lung ventilation?

When hypoxia occurs during single-lung ventilation, the goal is to optimize the match between ventilation and perfusion on the dependent lung or increase the amount of oxygen in the shunted blood of the collapsed lung.

Ventilated lung

a. Optimize ventilation

- Use 100% oxygen.
- Check the position of the DLT with a fiberoptic bronchoscope.
- Ventilate manually to determine whether higher or lower tidal volumes or inspiratory pressures are beneficial.
- Set minute ventilation to maintain $PaCO_2$ at 40 mm Hg (hypocapnia may inhibit HPV in the nondependent lung, whereas hyperventilation may increase airway pressure and promote blood flow to the nonventilated lung).
- Apply 5 cm H_2O of PEEP. It may be beneficial if larger tidal volumes delivered manually improved arterial saturation (i.e., recruitable alveoli). Alternatively, if tidal volumes are too large, adding PEEP may overdistend alveoli that are already open and compress blood vessels, diverting blood to the nonventilated lung and worsening the shunt.
- Use two-lung ventilation intermittently.

b. Increase perfusion

- Selective vasodilators (inhaled nitric oxide, inhaled prostacyclin PGI_2)

Collapsed lung

a. Oxygenate shunt blood: A variety of approaches have been described but must be carefully considered for minimally invasive procedures because most involve some degree of lung reexpansion and therefore may affect surgical visualization.

- Insufflate oxygen continuously: A flow of about 3 L per minute allowed to freely circulate will often increase arterial oxygen saturation 3% to 4%.
- Intermittent single breath with oxygen
- Partially reexpand the nonventilated lung then keep the lumen side closed.
- Apply continuous CPAP.
- Differential CPAP to the collapsed lung and PEEP to the ventilated lung has been described but is rarely necessary and generally impractical for VATS procedures.
- High-frequency ventilation to the nonventilated lung

b. Decrease the shunt

- Use drugs to augment HPV (phenylephrine, norepinephrine, almitrine).
- Clamp lobar vessels or the pulmonary artery of the nonventilated lung temporarily (rarely necessary).

Miller RD, ed. *Miller's Anesthesia*. 10th ed. New York: Churchill Livingstone; 2015:1942-2006.

C.16. A right middle lobectomy was performed. Would you extubate the trachea at the end of the procedure?

After routine lung resection, the trachea can be extubated as long as the patient meets all criteria and has adequate analgesia. If the patient cannot maintain adequate oxygenation and ventilation, postoperative mechanical support is indicated. Under most circumstances, the DLT should be changed to a single-lumen ETT. DLTs have a large outer diameter, which can cause airway edema and trauma if left in place for prolonged time; they are likely to move with patient

movement, and it is difficult to suction through them. Spontaneous ventilation avoids the potential hazards of positive pressure on the suture lines of the new bronchial stump or parenchymal air leaks. The combination of modest CPAP and pressure support ventilation is usually preferable to controlled intermittent mandatory ventilation for postoperative mechanical ventilation.

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D. Postoperative Management

D.1. What are the immediate life-threatening complications that follow lobectomy or pneumonectomy?

Serious complications after lobectomy include lobar collapse, massive hemorrhage caused by loosening of pulmonary vessels ligatures, bronchopleural fistula from disruption of a bronchial stump, and pulmonary torsion and infarction resulting from increased mobility of a lobe. Mediastinal shift, pleural effusion, hemothorax, chylothorax, empyema, and pulmonary edema can also occur. Deep venous thrombosis can lead to pulmonary embolus.

Pneumonectomy can be complicated by supraventricular arrhythmias, acute respiratory insufficiency, nerve injuries (phrenic, vagus, or recurrent laryngeal) during radical hilar dissection or excision of mediastinal tumors, cardiac herniation (in the case of intrapericardial approach), acute right heart failure, and right-to-left shunting across a patent foramen ovale as a result of increased pulmonary vascular resistance and increased right ventricular pressure. Postpneumonectomy syndrome is a rare complication characterized by mediastinal shift ipsilateral to the side of surgery with herniation of the hyperinflated lung in the same direction.

Slinger PD, ed. *Principle and Practice of Anesthesia for Thoracic Surgery* . 2011:601-607.

D.2. Why is it important to control postoperative pain? How would you achieve this?

Adequate postoperative analgesia is important not only for patient comfort but also to minimize pulmonary complications, allowing the patient to breathe deeply, cough effectively, and ambulate. Several options are available, depending on the institution and surgical preferences.

Enhanced recovery pathways have been developed to decrease postoperative complications and expedite discharge recommending a multimodal analgesic approach.

Epidural and Intrathecal Analgesia

A trend has been shown toward a decrease in morbidity and mortality after open lung resection since the introduction of regional analgesia. Thoracic (or lumbar) epidural analgesia is commonly achieved with a continuous infusion of a local anesthetic alone or in combination with an opiate. In order to reduce the volume required to produce an effect and lessen the chance of hypotension and motor weakness, the catheter is usually placed as close as possible to the dermatomes to be covered. A low concentration of local anesthetic such as bupivacaine 0.1% or 0.05% combined with an opiate (e.g., fentanyl 5 to 10 μg per mL, hydromorphone 8 μg per mL, or sufentanil 0.1 μg per mL) produces synergistic effects with a reduction of the sympathetic blockade associated with the use of a more concentrated local anesthetic alone. In addition, the presence of local anesthetics seems to increase the affinity of the narcotic for the opioid receptors. Potential complications of thoracic epidural technique can be related to the placement (inadvertent dural puncture, trauma to the spinal cord, hematoma) or drug administration (intravascular injection of local anesthetics with resultant cardiovascular and central nervous system toxicity). In addition, clinicians should carefully consider the patient's use of long-acting antiplatelet medications.

Intrathecal injection of opiates can be used pre- or intraoperatively for 18 to 24 hours postoperative pain relief. However, when compared to epidural injection, intrathecal opiates (in particular morphine) are associated with an increased incidence of late respiratory depression (4% to 7% compared to less than 1% for epidural administration).

The advantages of neuraxial techniques compared to systemic opiates include selective blockade of spinal pain receptors with minimal sympathetic blockade, no loss of motor function, and greater predictability of pain relief. Epidural opiates in combination with local anesthetics block the presynaptic and postsynaptic neuron cells of the substantia gelatinosa of the

spinal cord by passive diffusion across the dura into the cerebrospinal fluid. The lipophilic narcotics, such as fentanyl 0.1 mg, methadone 5 mg, and meperidine 30 to 100 mg, have a relatively short onset of action (less than 12 minutes). They provide significant pain relief in 20 to 30 minutes, which can last for 6 to 7 hours. In contrast, a hydrophilic opiate such as morphine (5-mg dose) has a relatively slow onset of action (15 to 30 minutes),

provides maximal pain relief in 40 to 60 minutes, and has duration of action of more than 12 hours. Urinary retention, pruritus, nausea, and vomiting are additional side effects. The narcotic antagonist naloxone can reverse them all, including the analgesia, so it must be used cautiously. Overall, unlike epidural local anesthetic, epidural opioids have not been shown to decrease the incidence of postoperative respiratory complications. Epidural analgesia is used less often for minimally invasive procedure, favoring a combination of other techniques.

Systemic Opioids and Adjuvants

Systemic administration of opiates is often used alone or in combination with other modalities to control postoperative pain, especially for minimally invasive procedures. Patientcontrolled analgesia, often in combination with NSAIDs, can be used in the postoperative period. When used as a single modality, systemic opioids require plasma concentrations that are usually associated with sedation, potential respiratory depression, hypoventilation, inhibition of cough, and reduced sighing. Even when used as patient-controlled analgesia, pain control is often suboptimal because of fluctuations in the drug plasma concentration. NSAIDs such as ketorolac, diclofenac, ketoprofen, and indomethacin can be used as adjuvants to parenteral opiates, particularly for the treatment of shoulder pain associated with chest tube placement. Potential side effects for NSAIDs include gastric bleeding, platelet dysfunction, and renal insufficiency in patients who are severely fluid restricted, especially the elderly. Intravenous acetaminophen can be added to potentiate analgesia if not contraindicated.

Low-dose intravenous ketamine infusion (0.2 μg/kg/hr) has been used as an adjuvant in the perioperative period, especially in patients with chronic pain. Psychomimetic side effects are a possibility but rare at this dosage. Intravenous dexmedetomidine can also be used as an adjuvant as a continuous infusion of 0.2 to 0.4 μg/kg/hr without a bolus. Its central α_2-agonism potentiates analgesia, allowing a decrease in intravenous narcotics and in MAC of inhaled agents. Hypotension, bradycardia, and sedation are potential side effects.

Intercostal and Paravertebral Nerve Block

Intercostal and paravertebral nerve blocks with long-acting local anesthetics can be used to control pain after thoracoscopy or thoracotomy. Single injections have a short duration (6 to 8 hours when bupivacaine is used); therefore, catheters are recommended. Intercostal blocks can be done under direct vision by the surgeon before closing the chest cavity or percutaneously before awakening the patient. The intercostal nerves to be blocked are at the level of the incision and two or three interspaces above and below. Of the three main sensory divisions of the intercostal nerve (posterior, lateral, and anterior cutaneous nerve), the posterior branch cannot be blocked with this approach, limiting its usefulness in the case of a posterolateral incision. There is controversy on the quality of analgesia with this technique alone when compared with the epidural route. Intercostal catheters are indicated as part of a multimodality treatment when neuroaxial blocks are contraindicated (e.g., patients on anticoagulation or tumor involvement of the epidural space) or for minimally invasive procedures. The use of extended release formulation of bupivacaine (Exparel®, Pacira Pharmaceuticals, Inc, Parsippany, NJ) may increase the duration of the block to 72 hours, improving the quality of analgesia, especially when paired with other adjuvants. The risk of systemic toxicity is increase due to the high rate of systemic absorption of the local anesthetic from the intercostal space. At the present time, Exparel® use for intercostal blockade is being trialed in humans. The few reported cases where the drug was used did not show permanent nerve damage or toxicity, although the degree of analgesia was reported comparable to thoracic epidural use.

Paravertebral blocks and catheters can be used preoperatively or postoperatively, in combination with parenteral opiates and NSAIDs, or as an alternative to thoracic epidural analgesia. In order to be effective, multiple levels need to be blocked. The failure rate for this technique is relatively high (6% to 10%) and can be decreased by locating the space via ultrasound guidance or under direct vision by the surgeon before closing the chest. Pneumothorax (especially if bilateral blocks are attempted), hypotension, local anesthetic toxicity because of the high vascularity of the area, and inadvertent total spinal are all potential risks. Advantages compared with epidural analgesia include less hypotension, less nausea or vomiting, and the ability to block just the surgical side.

Intrapleural Regional Analgesia

Intrapleural analgesia utilizes the percutaneous introduction of a catheter between the parietal and visceral pleura for the injection of local anesthetic. Analgesia is thought to occur as a result of (1) diffusion of local anesthetic through the parietal pleura and the innermost intercostal muscle to the intercostal nerves (where the block occurs), (2) block of the intrathoracic sympathetic chain, and (3) direct action of local anesthetic on nerve endings within the pleura. Nevertheless, the quality of analgesia is extremely variable and unfavorable compared to other modalities. The local anesthetic can be lost through the thoracotomy drainage, it can be diluted by extravasated blood and tissue fluid in the pleural space, or it can be sequestered and channeled because of the decreased movements of the operated lung. Moreover, in the sitting position, the local anesthetic pools in the costophrenic angle, limiting the quality of analgesia. The use of multiple or fenestrated catheters may achieve a more even distribution over the pleura and improve the quality of analgesia. However, this technique is rarely used today.

Cryoanalgesia

Long-lasting (3 to 4 weeks up to 6 months) intercostal nerve block can be obtained by cryoablation. Two 30- to 60-second freeze cycles (−60°C), separated by a 5-second thaw period, are applied to each of the nerves selected. Although cryoanalgesia was initially shown to effectively relieve pain and improve postoperative pulmonary function, more detailed studies have revealed a significant incidence of paresthesia and postthoracotomy pain syndrome.

Transcutaneous Electrical Nerve Stimulation

Transcutaneous electrical nerve stimulation (TENS) relies on the application of brief pulses of current via electrodes to the affected area. The advantages of TENS include low cost, ease of application, and lack of undesirable side effects. Nevertheless, TENS has a weak analgesic effect. It is generally reserved for adjunctive use with narcotics to relieve mild to moderate postthoracotomy pain. It is ineffective if the pain is severe and is contraindicated in patients with pacemakers, defibrillators, and infusion pumps because the current could produce interference.

Shoulder Pain after Lung Resection

Independently from the analgesia technique used and the surgical approach, approximately 80% of patients who have undergone lung resection complain of ipsilateral shoulder pain that is unresponsive to epidural block or systemic opioid. Possible causes for shoulder pain include referred pain from diaphragmatic irritation, chest tube placement (too far at the apex of the hemithorax), the posterior end of a large posterolateral incision, or surgical positioning in patients with arthritis. Shoulder pain usually responds to anti-inflammatory agents and often resolves on the second postoperative day. Phrenic nerve infiltration and brachial plexus block have been used but have the potential of causing diaphragmatic dysfunction.

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Chapter 3
Aspiration and Postoperative Respiratory Failure

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A 62-year-old woman presents to the emergency department with a small bowel obstruction. She is vomiting and hypotensive and appears to aspirate. She is emergently intubated, fluid resuscitated, and brought to the operating room for emergency laparotomy.

A. Aspiration

1. What are the risk factors for perioperative aspiration?
2. How does large volume aspiration affect the respiratory system?
3. How should you manage the patient after an aspiration event?
4. How would you prevent aspiration during emergency surgery?

B. Postoperative Respiratory Failure

After successful lysis of abdominal adhesions, the patient recovers well and is extubated at the completion of surgery. Subsequently, she develops progressive hypoxemic respiratory failure while in the postanesthesia care unit.

1. How can you predict which patients will develop postoperative respiratory failure?
2. How can intraoperative anesthesia management prevent respiratory failure?
3. What is the pathogenesis of postoperative respiratory failure?
4. What is the diagnostic approach to postoperative respiratory failure?

C. Indications for Ventilator Support

The patient has worsening hypoxemia and tachypnea despite treatment with high-flow supplemental oxygen.

1. What are the indications for noninvasive positive pressure ventilation (NIPPV)?
2. What are the indications for emergency endotracheal intubation?

D. The Acute Respiratory Distress Syndrome

The patient is intubated for respiratory failure. She has bilateral pulmonary infiltrates on chest x-ray and is severely hypoxemic.

1. What is the definition and etiology of the acute respiratory distress syndrome (ARDS)?
2. Explain the pathophysiology of ARDS.
3. What role does ventilator-induced lung injury (VILI) play in ARDS?

E. Management of Mechanical Ventilation

- Which mode of mechanical ventilation will you choose? Describe the features of that mode.
- How should you set the fraction of inspired oxygen (FIO_2)?
- How should you set the positive end-expiratory pressure (PEEP)?
- What tidal volume and inspiratory pressure target should you set?

F. Management of Refractory Respiratory Failure

The patient remains hypoxemic on FIO_2 of 0.8.

1. What else can you promote additional lung recruitment?
2. What rescue strategies can you use for refractory ARDS?

G. Adjunctive Management of Respiratory Failure

Since intubation, the patient has become hypotensive.

1. What is the cause and treatment of the hemodynamic instability associated with mechanical ventilation?
2. What is the adjunctive medical therapy for ARDS?

H. Liberation of the Patient from Mechanical Ventilation

The patient slowly recovers over the next 3 days.

1. Explain the importance of the decision to extubate the patient or continue mechanical ventilation.
2. How will you prepare the patient for liberation from the ventilator?
3. How will you recognize when the patient is ready for extubation?

A. Aspiration

A.1. What are the risk factors for perioperative aspiration?

Clinically significant aspiration is a relatively rare complication of anesthesia. The reported incidence is 1 to 5 per 10,000 patients, although it is more common in certain situations, such as traumatic brain injury. About half of the cases of perioperative aspiration occur during induction of anesthesia. Although an emergency indication for surgery is a major risk factor for aspiration, the majority of cases occur during elective procedures. Increased gastric pressure, decreased lower esophageal sphincter tone, and blunted protective airway reflexes promote aspiration. Therefore, risk factors for aspiration include full stomach, pregnancy, bowel obstruction, gastroesophageal reflux, obesity, gastrointestinal motility disorders, and neurologic conditions. Airway manipulation in an unfasted patient or an inadequate depth of anesthesia may increase the risk of aspiration. Many anesthetics reduce lower and upper esophageal sphincter tone and diminish protective airway reflexes. The appropriate use of laryngeal mask airways does not increase the risk of aspiration, although it may induce gastroesophageal reflux. Certain surgical procedures such as laparoscopic insufflation of the abdomen and bowel manipulation are associated with increased rates of aspiration.

Kluger MT, Short TG. Aspiration during anaesthesia: a review of 133 cases from the Australian Anaesthetic Incident Monitoring Study (AIMS). *Anaesthesia*. 1999;54(1):19-26.

Lockey DJ, Coats T, Parr MJ. Aspiration in severe trauma: a prospective study. *Anaesthesia*. 1999;54(11): 1097-1098.

Marik PE. Aspiration pneumonitis and aspiration pneumonia. *N Engl J Med*. 2001;344(9):665-671.

Ng A, Smith G. Gastroesophageal reflux and aspiration of gastric contents in anesthetic practice. *Anesth Analg*. 2001;93(2):494-513.

Smith G, Ng A. Gastric reflux and pulmonary aspiration in anaesthesia. *Minerva Anestesiol*. 2003;69(5):402-406.

A.2. How does large volume aspiration affect the respiratory system?

Aspiration of gastric and oropharyngeal contents causes three overlapping syndromes. First, aspiration of large particulate matter may obstruct the airways and lead to atelectasis. Acute aspiration pneumonitis is more common and is

a result of chemical burning of the tracheobronchial tree and pulmonary parenchyma by gastric and oral fluids. Finally, aspiration of bacteria from the oropharynx or a superinfection of the chemical pneumonitis may result in aspiration pneumonia.

Mendelson originally described aspiration pneumonitis in 66 obstetrical patients who aspirated gastric contents during anesthesia. Respiratory distress and cyanosis developed

within 2 hours after aspiration event. All patients (except two who had airway obstruction from solid food particles) recovered within 24 to 36 hours without antibiotics and had radiographic resolution. Signs and symptoms of aspiration pneumonitis include cough, wheeze, dyspnea, hypoxia, fever, tachypnea, and crackles on lung auscultation. Radiography usually demonstrates diffuse bilateral infiltrates.

Aspiration pneumonitis may be mild and elude clinical detection. Rarely, aspiration is fulminant and rapidly fatal. Most patients rapidly improve after aspiration and have clearing of radiographic lung infiltrates. Occasionally, patients initially improve but then develop progressive lung infiltrates on chest radiograph. These infiltrates probably represent secondary bacterial infection or ARDS. The volume and pH of the aspirated fluid are important factors affecting the degree of lung injury. In adults, approximately 25 mL of gastric acid with pH <2.5 is considered a clinically relevant threat. Smaller volumes may produce a milder syndrome. Bile may elicit a potent inflammatory response and has been identified in patients' endotracheal tubes. Atelectasis, peribronchial hemorrhage, pulmonary edema, and degeneration of bronchial epithelial cells all develop within minutes of aspiration. By 4 hours, the alveoli fill with polymorphonuclear leukocytes and fibrin and hyaline membranes form. Hyaline membranes form within 4 hours. The lung becomes grossly edematous and hemorrhagic with alveolar consolidation.

Aspiration pneumonia may result from a superimposed infection of the chemical injury or inhalation of microorganisms from the oropharynx. Poor dentition is a risk factor for aspiration pneumonia. Common bacteria include *Haemophilus influenzae*, Streptococci, and other anaerobes. The oral flora changes in chronically ill patients and those in health care settings for greater than 48 to 72 hours. In these patients, gramnegative bacteria and resistant *Staphylococcus* may colonize the oropharynx and cause pneumonia.

James CF, Modell JH, Gibbs CP, et al. Pulmonary aspiration—effects of volume and pH in the rat. *Anesth Analg*. 1984;63(7):665-668.

Marik PE. Aspiration pneumonitis and aspiration pneumonia. *N Engl J Med*. 2001;344(9):665-671.

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Mylotte JM, Goodnough S, Gould M. Pneumonia versus aspiration pneumonitis in nursing home residents: prospective application of a clinical algorithm. *J Am Geriatr Soc*. 2005;53(5):755-761.

Teabeaut JR II. Aspiration of gastric contents; an experimental study. *Am J Pathol*. 1952;28(1):51-67.

Wu YC, Hsu PK, Su KC, et al. Bile acid aspiration in suspected ventilator-associated pneumonia. *Chest*. 2009;136(1):118-124.

A.3. How should you manage the patient after an aspiration event?

Awake patients capable of airway protection should be placed in the upright or recovery position and encouraged to cough. However, clinicians may need to suction or rescue the airway if the patient has impaired protective airway reflexes. Supplemental oxygen should be administered for hypoxemia. Clinicians should avoid noninvasive ventilation because of the risk of gastric insufflation unless there is no further risk of additional vomiting. There is no evidence supporting lavage with saline or sodium bicarbonate. Gastric acid is rapidly neutralized by the physiologic response. When possible, the stomach should be emptied with a nasogastric tube. A chest radiograph should be ordered. In select circumstances, a bronchoscopy may be necessary for airway clearance and evaluation especially if airway obstruction is suspected. Bronchoscopy can provide quantitative lower respiratory tract cultures from bronchoalveolar lavage or protected brushings. These techniques can distinguish aspiration pneumonitis from pneumonia.

Although some animal studies support the use of corticosteroids in aspiration pneumonitis, there is no evidence of benefit in human studies. Moreover, the literature does not support the routine use of antibiotics immediately after aspiration. However, patients should be followed closely to identify the development of a secondary infection. If the clinicians diagnose aspiration pneumonia, they should choose antibiotics that provide coverage against oral flora including gram-negative coverage for patients with nosocomial

colonization. This may include extended spectrum beta lactamases inhibitors such as piperacillin-tazobactam.

Allewelt M, Schüler P, Bölcskei PL, et al. Ampicillin + sulbactam vs clindamycin +/− cephalosporin for the treatment of aspiration pneumonia and primary lung abscess. *Clin Microbiol Infect*. 2004;10(2):163-170.

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Downs JB, Chapman RL Jr, Modell JH, et al. An evaluation of steroid therapy in aspiration pneumonitis. *Anesthesiology*. 1974;40(2):129-135.

Dudley WR, Marshall BE. Steroid treatment for acid-aspiration pneumonitis. *Anesthesiology*. 1974;40(2): 136-141.

Marik PE. Aspiration pneumonitis and aspiration pneumonia. *N Engl J Med*. 2001;344(9):665-671.

Matthay MA, Rosen GD. Acid aspiration induced lung injury. New insights and therapeutic options. *Am J Respir Crit Care Med*. 1996;154(2 pt 1):277-278.

Ott SR, Allewelt M, Lorenz J, et al. Moxifloxacin vs ampicillin/sulbactam in aspiration pneumonia and primary lung abscess. *Infection*. 2008;36(1):23-30.

van Westerloo DJ, Knapp S, van't Veer C, et al. Aspiration pneumonitis primes the host for an exaggerated inflammatory response during pneumonia. *Crit Care Med*. 2005;33(8):1770-1778.

A.4. How would you prevent aspiration during emergency surgery?

Certain measures may help reduce the risk of perioperative aspiration. These include adequate fasting, prophylactic antiemetics, rapid sequence intubation (RSI), limited tidal volumes if bag ventilation used, and extubation when patient has return of laryngeal reflexes. Anti-acid medications can increase gastric pH; however, their use is only supported by expert opinion.

RSI involves preoxygenation followed by intubation using an induction agent and neuromuscular blockade without face-mask ventilation. There are no prospective randomized controlled trials that show whether RSI reduces the incidence of aspiration. However, RSI has been shown to decrease the time to achieve successful intubation, which may be beneficial when the risk of aspiration is high. The value of cricoid pressure during intubation remains controversial.

d'Escrivan T, Guery B. Prevention and treatment of aspiration pneumonia in intensive care units. *Treat Respir Med*. 2005;4(5):317-324.

de Souza DG, Doar LH, Mehta SH, et al. Aspiration prophylaxis and rapid sequence induction for elective cesarean delivery: time to reassess old dogma? *Anesth Analg*. 2010;110(5):1503-1505.

Neilipovitz DT, Crosby ET. No evidence for decreased incidence of aspiration after rapid sequence induction. *Can J Anaesth*. 2007;54(9):748-764.

Ng A, Smith G. Gastroesophageal reflux and aspiration of gastric contents in anesthetic practice. *Anesth Analg*. 2001;93(2):494-513.

Wallace C, McGuire B. Rapid sequence induction: its place in modern anaesthesia. *Contin Educ Anaesth Crit Care Pain*. 2014;14(3):130-135.

B. Postoperative Respiratory Failure

After successful lysis of abdominal adhesions, the patient recovers well and is extubated at the completion of surgery. Subsequently, she develops progressive hypoxemic respiratory failure while in the postanesthesia care unit.

B.1. How can you predict which patients will develop postoperative respiratory failure?

Respiratory failure commonly complicates the postoperative period and is strongly associated with an increased mortality. A number of clinical prediction rules exist to predict the risk of postoperative pulmonary complications. Predisposing factors include a high American Society of Anesthesiologists (ASA) Physical Status Classification, poor functional status, and hypoalbuminemia. Lung diseases such as obstructive airways dysfunction and extrapulmonary diseases such as liver cirrhosis, congestive heart failure, and renal failure also predispose patients to respiratory failure. Additional risk factors include emergency indications for surgery, prolonged procedural time, and the requirement for large volume fluid and blood product resuscitation. Because of their effects on respiratory mechanics,

thoracoabdominal surgeries, especially aortic aneurysm repair, are particularly high-risk procedures.

Canet J, Gallart L, Gomar C, et al. Prediction of postoperative pulmonary complications in a population-based surgical cohort. *Anesthesiology*. 2010;113(6):1338-1350.

Johnson RG, Arozullah AM, Neumayer L, et al. Multivariable predictors of postoperative respiratory failure after general and vascular surgery: results from the patient safety in surgery study. *J Am Coll Surg*. 2007;204(6):1188-1198.

Neto AS, Hemmes SN, Barbas CS, et al. Incidence of mortality and morbidity related to postoperative lung injury in patients who have undergone abdominal or thoracic surgery: a systematic review and meta-analysis. *Lancet Respir Med*. 2014;2(12):1007-1015.

B.2. How can intraoperative anesthesia management prevent respiratory failure?

An extensive literature has evaluated the role of limiting tidal volumes to prevent VILI. Ventilation with tidal volumes greater than 8 mL per kg ideal body weight (IBW) is a risk factor for postoperative pulmonary complications in thoracic and abdominal surgery. Moreover, a randomized controlled trial in major abdominal surgery demonstrated that restricting tidal volumes from 6 to 8 mL per kg IBW decreased the incidence of postoperative respiratory failure. This intervention was part of a lung-protective strategy, which combined restricted tidal volumes with PEEP as compared to large tidal volumes without PEEP. Because the intervention also included PEEP, we cannot ascribe the full benefit to tidal volume restriction. In sum, the current data support targeting tidal volumes to less than 8 mL per kg IBW. The optimum dose of intraoperative PEEP is less clear. A meta-analysis revealed that a no PEEP approach was a risk factor of postoperative pulmonary complications in thoracic and abdominal surgery. However, a randomized trial during high-risk abdominal surgery did not demonstrate a benefit from high PEEP and recruitment maneuvers. As a whole, the current evidence supports the use of moderate PEEP (approximately 5 cm H_2O) during surgery and using higher PEEP and recruitment maneuvers when the patient's physiology suggests derecruitment.

Cypel M, Fan E. Lung injury after abdominal and thoracic surgery. *Lancet Respir Med*. 2014;2(12):949-950.

Futier E, Constantin JM, Paugam-Burtz C, et al. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. *N Engl J Med*. 2013;369(5):428-437.

Hemmes SN, Gama de Abreu M, Pelosi P, et al. High versus low positive end-expiratory pressure during general

anaesthesia for open abdominal surgery (PROVHILO trial): a multicentre randomised controlled trial. *Lancet*. 2014;384(9942):495-503.

Neto AS, Hemmes SN, Barbas CS, et al. Incidence of mortality and morbidity related to postoperative lung injury in patients who have undergone abdominal or thoracic surgery: a systematic review and meta-analysis. *Lancet Respir Med*. 2014;2(12):1007-1015.

B.3. What is the pathogenesis of postoperative respiratory failure?

Numerous mechanisms contribute to the pathogenesis of postoperative respiratory failure (Fig. 3.1). A combination of postoperative pain, recumbent position, anesthetics, and impaired secretion clearance leads to collapse of dependent lung regions. Atelectasis increases shunt fraction, diminishes respiratory system compliance, and commonly contributes to postoperative respiratory failure.

Treating postoperative patients with high concentrations of inspired oxygen can lead to absorption atelectasis. Normally, the consumption of oxygen by peripheral tissues creates a small gradient between the gas tensions in the alveoli and pulmonary capillary blood. The gradient is normally small compared to the total gas tensions because nitrogen is the most abundant gas in both compartments. Nitrogen acts as a pneumatic splint in the lung by limiting the magnitude of the gas tension gradient between the alveoli and pulmonary capillary. Breathing high FIO_2 denitrogenates the body and increases the partial pressure of oxygen in alveolar gas much more than in mixed venous blood. Without nitrogen, venous blood becomes very hypobaric relative to alveolar gas. Therefore, high FIO_2 increases the gas tension gradient, which drives gas from the alveoli to the pulmonary capillary blood. This promotes the collapse of poorly ventilated alveoli (Fig. 3.2).

In the postoperative period, bronchospasm and impaired mucociliary clearance can decrease the rate of expiratory airflow and increase the work of breathing. Residual sedation and neuromuscular blockade may weaken respiratory muscles and diminish protective

muscle tone in the upper airway. Shock causes acidosis and hypoperfusion of respiratory muscles leading to respiratory failure. In particular, clinicians should consider the diagnosis of occult hemorrhage in any postoperative patient who develops respiratory failure. However, the clinician must also consider the opposite problem of fluid overload. Fluid accumulation in the lungs, chest wall, pleura, and peritoneum is a common problem and may decrease respiratory compliance and worsen gas exchange.

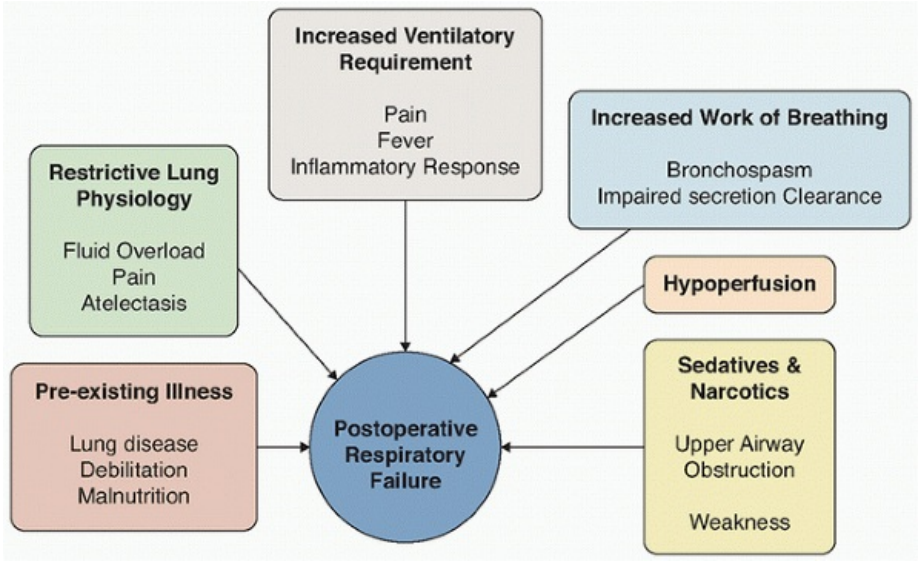


FIGURE 3.1 Pathogenesis of postoperative respiratory failure.

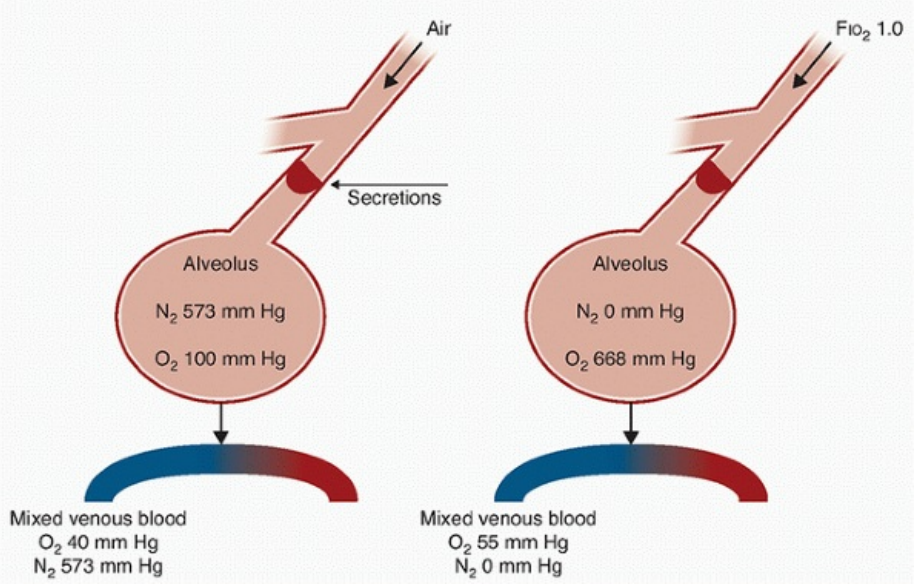


FIGURE 3.2 Nitrogen content of inspired air prevents alveolar collapse. On the left, secretions obstruct the airway while the patient was breathing room air. There is a small oxygen gradient between the alveolus and mixed venous blood. On the right, secretions obstruct the airway after denitrogenation. As a result, the mixed venous blood is very hypobaric compared with the alveolus. The alveolus will tend to collapse as O_2 rapidly flows down its pressure gradient. CO_2 and H_2O have been omitted for simplicity. (Adapted from West JB. *Respiratory Physiology*. 4th ed. Baltimore: Williams & Wilkins; 1990.)

TABLE 3.1 Differential Diagnosis of Postoperative Respiratory Failure

Aspiration Pneumonitis Exacerbation of obstructive sleep apnea	Atelectasis Wound infections Abdominal compartment syndrome	Pneumonia Upper airway obstruction Diaphragmatic palsy from scalene nerve block	Bleeding and shock Neuromuscular weakness	Pleural Effusions Exacerbation of underlying lung disorder Acute respiratory distress syndrome	Pulmonary embolism Pulmonary edema

The systemic inflammatory response to major surgery or an acute illness will increase rates of tissue oxygen consumption and carbon dioxide (CO_2) production. The increased ventilatory requirement may impose an unsustainable burden on a respiratory system impaired by the aforementioned factors. This is especially true in the setting of debility, malnutrition, and chronic lung disease.

Aubier M, Trippenbach T, Roussos C. Respiratory muscle fatigue during cardiogenic shock. *J Appl Physiol Respir Environ Exerc Physiol*. 1981;51(2):499-508.

West JB. *Respiratory Physiology—The Essentials*. 9th ed. Baltimore: Lippincott Williams & Wilkins; 2012.

B.4. What is the diagnostic approach to postoperative respiratory failure?

The history of the patient's illness provides key evidence for determining the cause of respiratory failure. The clinician

should review the past medical history, anesthesia record, operative reports, and perform a careful physical examination. The integration of these data should generate a short list of diagnostic possibilities (Table 3.1). Laboratory testing can help exclude or confirm diagnoses.

Arterial blood gas analysis can help triage disease severity and identify alveolar hypoventilation, increased alveolar-arterial oxygen gradient, and acid-base status. Additional labs including complete blood count, metabolic profile, and coagulation parameters are important part of the early evaluation. Chest x-rays are an essential part of the diagnostic approach to respiratory failure. However, their interobserver variability is high and their diagnostic accuracy is limited in acute respiratory failure.

Point-of-care diagnostic ultrasound can aid the diagnosis of acute respiratory failure (Table 3.2). In critically ill patients, pulmonary ultrasound is superior to chest x-ray in identifying pneumothorax, consolidation, pleural effusion, and lung edema. The use of basic echocardiography to identify right or left heart dysfunction can improve diagnostic accuracy. This approach can help distinguish cardiogenic from noncardiogenic causes of pulmonary edema and raise the suspicion for pulmonary embolism. Ultrasonography, like all clinical skills, requires expert training.

Pulmonary emboli (PE) are common in the postoperative period. PE cause tachycardia, tachypnea, and mildly reduce SpO_2. Large PE may cause shock. An abrupt increase in arterial to end-tidal PCO_2 gradient can be a sign of increased alveolar dead space from PE. If a clinician suspects PE, a computed tomography (CT) angiography is the best test. Ventilation-perfusion scintigraphy is an alternative if CT angiography cannot be performed. Given the

high-case fatality rate of untreated PE, therapeutic anticoagulation is indicated when PE is strongly suspected or confirmed. Clinicians must carefully consider the risk of bleeding from surgery sites or neuraxial anesthesia.

TABLE 3.2 Pulmonary Ultrasound Findings

Sliding lung (rules out pneumothorax)	Consolidation	A lines (normal finding)
Lung point (rules in pneumothorax)	B lines (interstitial edema)	Pleural effusion
Diaphragm movement (rules out diaphragmatic palsy)		

Pneumonia is the most important postoperative infection. Surgery, hospitalization, and illness alter the host's bacterial flora and lead to pneumonia with antibiotic-resistant organisms. A chest x-ray, arterial blood gas, and blood cultures should be obtained in all patients suspected of having health care-associated pneumonia. In the case of ventilatorassociated pneumonia, clinical diagnosis may be inaccurate. Quantitative cultures of the lower respiratory tract obtained from bronchoalveolar lavage or protected brushings can assist the diagnosis.

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Bataille B, Riu B, Ferre F, et al. Integrated use of bedside lung ultrasound and echocardiography in acute respiratory failure: a prospective observational study in ICU. *Chest*. 2014;146(6):1586-1593.

Hemnes AR, Newman AL, Rosenbaum B, et al. Bedside end-tidal CO_2 tension as a screening tool to exclude pulmonary embolism. *Eur Respir J*. 2010;35(4):735-741.

Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice

Guidelines. *Chest*. 2012;141(2 suppl):e419S-e494S.

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van Belle A, Büller HR, Huisman MV, et al. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. *JAMA*. 2006;295(2):172-179.

Xirouchaki N, Magkanas E, Vaporidi K, et al. Lung ultrasound in critically ill patients: comparison with bedside chest radiography. *Intensive Care Med*. 2011;37(9):1488-1493.

C. Indications for Ventilator Support

The patient has worsening hypoxemia and tachypnea despite treatment with high-flow supplemental oxygen.

C.1. What are the indications for noninvasive positive pressure ventilation (NIPPV)?

NIPPV may be an alternative to endotracheal intubation in some situations. NIPPV can deliver high flow rates of oxygen, maintain PEEP, stent open the upper airway, and unload the work of breathing. Careful patient selection and recognition of contraindications to its use are essential. In this patient, the vomiting due to bowel obstruction is likely a contraindication to a trial of noninvasive ventilation (Table 3.3). Generally, the etiology of the respiratory failure and the type of mask interface are more important determinants of treatment success than the mode of NIPPV. The clinical indications with the best supporting evidence for NIPPV are acute cardiogenic pulmonary edema, obstructive sleep apnea, and exacerbations of chronic obstructive pulmonary disease. In cardiogenic pulmonary edema, the application of positive pressure can markedly reduce left ventricular preload and afterload. Bilevel and continuous positive airway pressure (CPAP) modes are both effective in cardiogenic pulmonary edema. Although there is little data from randomized controlled trials, there is a compelling physiologic rationale for the use of noninvasive ventilation for respiratory failure due to neuromuscular weakness and obesity-hypoventilation syndrome.

The clinical trial data for NIPPV in other causes of postoperative respiratory failure are mixed. Clinicians must exercise caution when using NIPPV for acute hypoxemic respiratory failure. Although it can help avoid intubation in some situations, about half of the patients treated with NIPPV for ARDS or pneumonia ultimately require intubation. Patients with multiorgan dysfunction are more likely to require intubation. Unfortunately, the largest randomized trial of NIPPV for acute hypoxemic respiratory found no benefit. This trial used CPAP mode, which improved gas exchange. However, there was a markedly increased mortality rate among patients who failed NIPPV. There was also an alarmingly high rate of cardiac arrest during rescue intubation in this setting. This risk is likely due to the sudden derecruitment and loss ventilation during the intubation process.

TABLE 3.3 Use of Noninvasive Positive Pressure Ventilation in Acute Respiratory Failure

POSSIBLE INDICATIONS	CONTRAINDICATIONS
Increased dyspnea	Respiratory arrest
Tachypnea	Unable to fit/wear mask
Excessive work of breathing	Progressive shock
Hypoventilation	Multiorgan dysfunction

Obstructive sleep apnea	Poor airway protection
Hypercapnia	Recent upper-airway or gastrointestinal surgery
Hypoxia	No patient cooperation
	Progressive and severe clinical instability
	Vomiting/hematemesis

Adapted from Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet*. 2009;374:250-259.

Antonelli M, Conti G, Moro ML, et al. Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study. *Intensive Care Med*. 2001;27(11):1718-1728.

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Delclaux C, L'Her E, Alberti C, et al. Treatment of acute hypoxemic nonhypercapnic respiratory insufficiency with continuous positive airway pressure delivered by a face mask: a randomized controlled trial. *JAMA*. 2000;284(18):2352-2360.

Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet*. 2009;374(9685):250-259.

C.2. What are the indications for emergency endotracheal intubation?

Endotracheal intubation is performed for impending or actual respiratory failure. The possible indications for emergency endotracheal intubation are shown in Figure 3.3. Often, a combination of problems drives the decision to intubate. In borderline situations, a need to transport the patient or a worsening trajectory of acute illness may tip the balance in favor of intubation.

Laghi F, Tobin MJ. Indications for mechanical ventilation. In: Tobin MJ, ed. *Principles and Practice of Mechanical Ventilation*. 2nd ed. New York: McGraw-Hill; 2006:129-162.

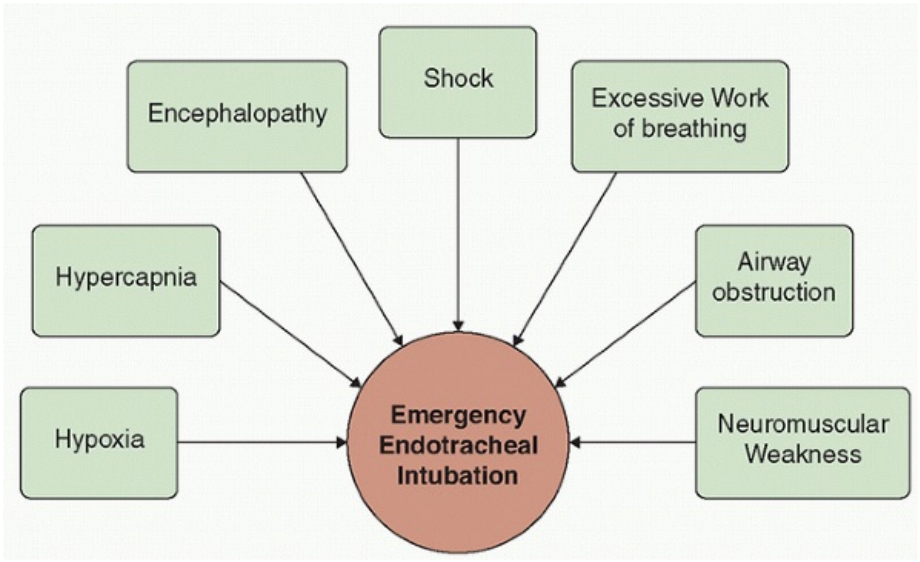


FIGURE 3.3 Possible indications for emergency endotracheal intubation.

D. The Acute Respiratory Distress Syndrome

The patient is intubated for respiratory failure. She has bilateral pulmonary infiltrates on chest x-ray and is severely hypoxemic.

D.1. What is the definition and etiology of the acute respiratory distress syndrome (ARDS)?

ARDS is a clinical syndrome of rapidly progressive respiratory failure characterized by severe hypoxemia and bilateral pulmonary infiltrates. ARDS occurs after or during an insult to the lungs or other organs and is not due to hydrostatic (cardiogenic) edema. The characteristic pathologic finding is diffuse alveolar damage (DAD).

The research definition of ARDS has evolved over time. A previous classification distinguished ARDS from acute lung injury (ALI) based on the severity of hypoxemia. The current consensus is called the Berlin (Germany) definition of ARDS (Fig. 3.4). This definition removed the distinction of ALI. This case definition encompasses a number of distinct disease processes. A significant proportion of patients meeting the diagnostic criteria for ARDS do not have DAD on biopsy or autopsy.

There are approximately 175,000 cases of ARDS each year in the United States although the incidence has been decreasing. Worse outcomes are associated with severe hypoxemia, increased dead space, and the presence of concomitant organ failure. The case fatality rate of ARDS has decreased from ˜40% in the late 1990s to ˜25% in the mid-2000s. The most common etiologies of ARDS include pulmonary and nonpulmonary infections, large volume aspiration of gastric contents, trauma, acute pancreatitis, drug reactions, and transfusions of blood products.

Ferguson ND, Fan E, Camporota L, et al. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. *Intensive Care Med*. 2012;38(10):1573-1582.

Malhotra A. Low-tidal-volume ventilation in the acute respiratory distress syndrome. *N Engl J Med*. 2007;357(11):1113-1120.

Matthay MA, Ware LB, Zimmerman GA. The acute respiratory distress syndrome. *J Clin Invest*. 2012;122(8):2731-2740.

Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307(23):2526-2533.

Rubenfeld GD, Caldwell E, Peabody E, et al. Incidence and outcomes of acute lung injury. *N Engl J Med*. 2005;353(16):1685-1693.

Thille AW, Esteban A, Fernández-Segoviano P, et al. Comparison of the Berlin definition for acute respiratory distress syndrome with autopsy. *Am J Respir Crit Care Med*. 2013;187(7):761-767.

Ware LB, Matthay MA. The acute respiratory distress syndrome. *N Engl J Med*. 2000;342(18):1334-1349.

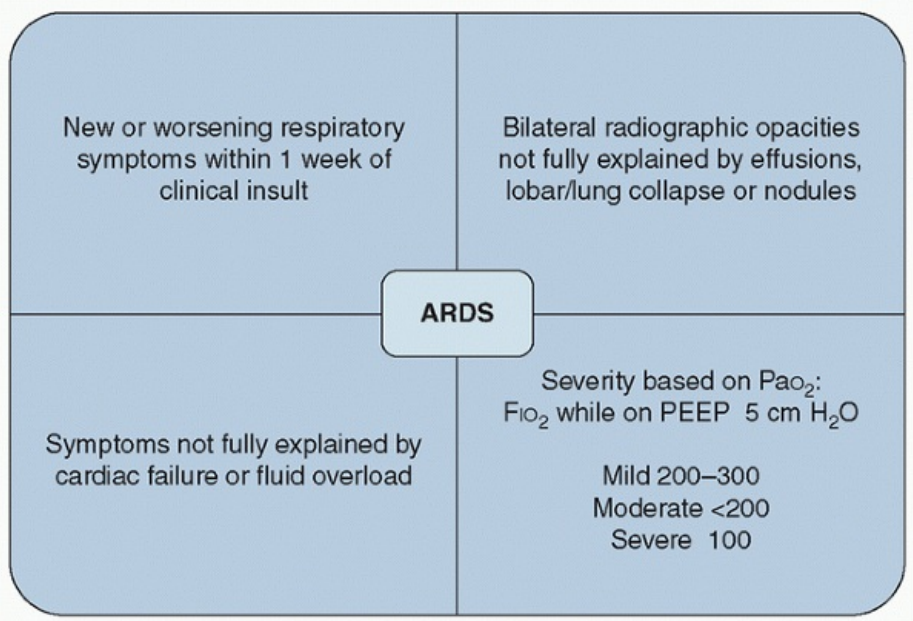


FIGURE 3.4 Definition of the acute respiratory distress syndrome (ARDS). FIO_2, fraction of inspired oxygen; PaO_2, partial pressure of oxygen; PEEP, positive end-expiratory pressure. (Adapted from Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307[23]:2526-2533.)

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D.2. Explain the pathophysiology of ARDS.

In ARDS, the alveoli are flooded with a neutrophilic protein-rich edema fluid (Fig. 3.5). Dysfunction of the alveolar epithelium and pulmonary capillary endothelium lead to noncardiogenic pulmonary edema. A depletion of functioning surfactant leads to alveolar collapse. The pathophysiologic cascade is incited at the molecular level. Pathogen microbial products (PAMPs) or endogenous damage-associated molecular pattern molecules (DAMPs) activate pattern recognition receptors such as the Toll-like receptors. This activation of innate immunity recruits inflammatory cells to the lung. The regulation of pulmonary inflammation plays a crucial role in both the control of pathogens and lung injury.

ARDS progresses through distinct clinical, pathologic, and radiologic phases. The acute exudative phase of ARDS is characterized by severe hypoxemia that is refractory to supplemental

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oxygenation and often requires invasive mechanical ventilation. Hypoxemia in this early phase is due to increased shunt fraction. Acute right-sided heart failure is common due to a marked elevation in pulmonary vascular resistance. Hypoxic and hypercapnic pulmonary vasoconstriction, regional atelectasis, and hyperinflation due to mechanical ventilation all contribute to the rise in pulmonary resistance. Radiologically, there are bilateral alveolar infiltrates. CT imaging demonstrates bilateral patchy opacities and dependent consolidation. Pleural effusions are common. ARDS caused by direct lung injury maybe more responsive to higher PEEP strategies. ARDS caused by systemic inflammatory states is associated with more pronounced shock and multisystem organ dysfunction.

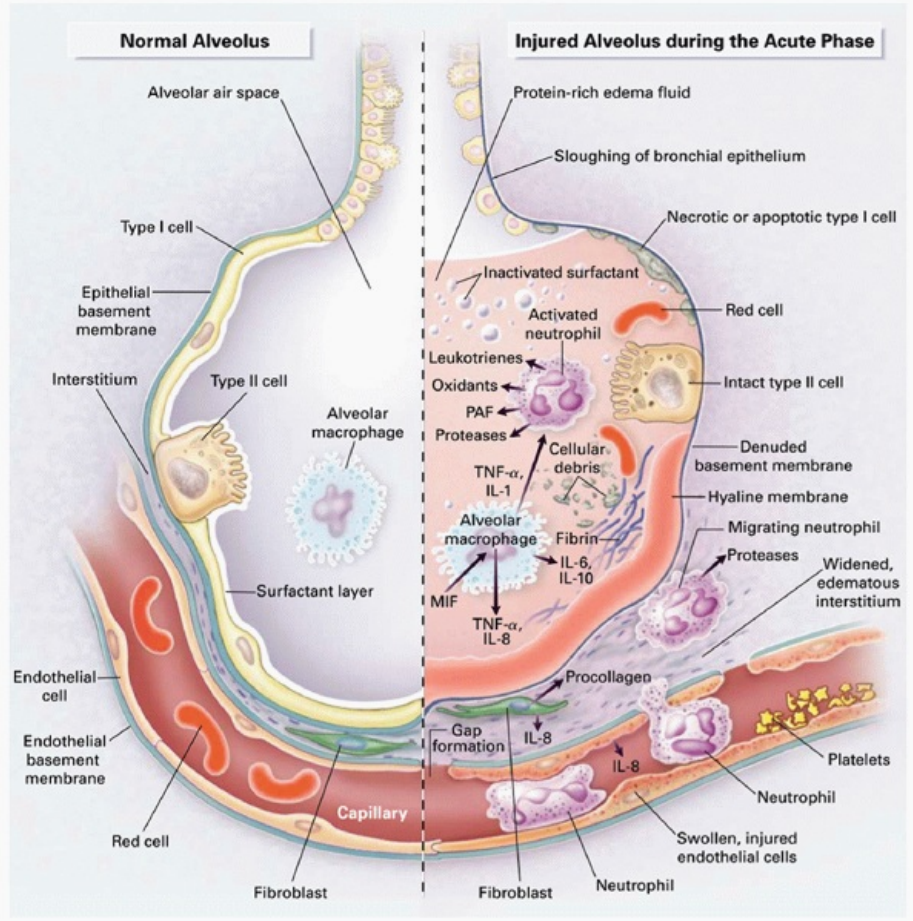


FIGURE 3.5 The pathogenesis of acute respiratory distress syndrome. IL, interleukin; MIF, macrophage inhibition factor; PAF, platelet-activating factor; TNF-*α*, tumor necrosis factor alpha. (Reused from Ware LB, Matthay MA. The acute respiratory distress syndrome. *N Engl J Med*. 2000;342[18]:1334-1349.)

The acute exudative phase of ARDS may progress to fibrosing alveolitis, which can appear as linear opacities on chest x-ray. The fibrosis reduces pulmonary compliance and increases dead space. Patients who recover from ARDS may have normal lung function or chronic fibrotic lung disease.

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D.3. What role does ventilator-induced lung injury (VILI) play in ARDS?

Mechanical ventilation injures the lungs through complex pathophysiologic processes. A variety of illnesses, particularly ARDS, increase the lung's susceptibility. Rarely, VILI leads to air leaks from the lung into the pleura or mediastinum. However, microscopic injury is a more common problem. The complications of VILI extend beyond the lungs. Excessive

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alveolar stretch in ARDS increases circulating inflammatory cytokines and injures small bowel and renal epithelial cells. These processes have been linked to progressive multisystem organ failure, which is the most common cause of death in ARDS.

VILI is due to excessive distention of some lung regions and repetitive collapse with shearing of others. “Volutrauma” is the name for the damage caused by excessive lung stretch with large amount of air. Despite its importance, it is difficult to measure the amount of air distending the lungs on mechanical ventilation. This is because ventilators only display the tidal volume—the amount of air delivered or exhaled. Ventilators do not measure the volume of air remaining in the lungs at end expiration (the functional residual capacity). The total lung volume that distends the lungs is the tidal volume plus the functional residual capacity. Because it is not possible to measure this volume, clinicians use the airway pressure at end inspiration as a surrogate marker for the lung's maximum distention by the ventilator. To measure this pressure, the clinician must pause the ventilator cycle momentarily at the end of inspiration to minimize the effect of resistance to airflow. This pause also allows time for the ventilator circuit to better equilibrate with the lungs. The plateau pressure is the pressure in the ventilator circuit during this pause.

The plateau pressure is an imperfect surrogate for the distending pressure of the lung. It is a composite of the force in the airway that distends the lung and the forces adjacent to the lung that may distend or oppose lung inflation. For example, a patient's inspiratory effort distends the lungs yet tends to lower plateau pressure on volume-controlled ventilation. Conversely, positive pleural pressure from intra-abdominal hypertension and gravitational effects from obesity tend to raise plateau pressure without increasing lung distention. In sum, clinicians should consider both tidal volume and plateau pressure to evaluate the risk of overdistention.

ARDS creates a heterogeneous disease process throughout the lungs. This varies the response to pressure applied by mechanical ventilation. Fluid-filled alveolar spaces with poor surfactant function remain atelectatic for most of the respiratory cycle, only opening during the late stages of a tidal breath. The large amount of force required to inflate these diseased

areas subjects the more normal lung units to excessive shear forces. Cyclical collapse, high distending pressure, and large tidal volume all increase alveolar capillary permeability and ongoing lung injury.

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E. Management of Mechanical Ventilation

E.1. Which mode of mechanical ventilation will you choose? Describe the features of that mode.

There is no proof that any mode of ventilation is superior in any clinical situation. Aside from avoiding purely assisted modes for passive patients, the choice of mode is largely dictated by physician preference. Choosing appropriate settings for a given mode of mechanical ventilation is more important than the choice of the mode. Therefore, it is essential for clinicians to have a detailed understanding of the settings for the mode they are using.

With traditional controlled mechanical ventilation, the patient had no control over any aspect of the respiratory cycle. Modern controlled ventilation modes can “assist” patients' respiratory efforts. In assisted modes, the ventilator recognizes

the patient's inspiratory effort by a negative pressure deflection in the ventilator circuit. The ventilator then cycles to inspiration and forces gas into the circuit's inspiratory limb. Gas is delivered until it reaches a set target of either pressure or volume.

Assist/control with volume targeting is the most commonly used mode in intensive care units worldwide. Inspiration begins when the ventilator recognizes the patient's inspiratory effort or at a minimum frequency set by a clinician. The ventilator compresses the air sufficiently to deliver a set tidal volume. In general, assist/control volume targeting allows the best assessment of respiratory mechanics. The mode also guarantees the delivery of a minimum minute volume. It also limits tidal volume, which can help avoid alveolar overdistention. However, assist/control with volume targeting may provide insufficient support for a patient with a strong respiratory drive. The tidal volume, duration of inspiration, and inspiratory flow rate are all set by the clinician. The ventilator cannot meet the patient's demand for an increased tidal volume or faster inspiratory gas flow. Patients with a strong respiratory drive may develop severe dyssynchrony and perform substantial work of breathing on this mode. Dyssynchrony is common with assist/control volume targeting and is usually due to double or ineffective triggering of inspiration.

With assist/control pressure targeting, the ventilator delivers gas until the pressure reaches a specified target. The volume and rate of gas delivered varies with patient effort and respiratory mechanics. Clinicians must set some criteria of timing of the inspiratory and expiratory cycles (either the inspiratory time or the ratio of the duration of inspiration and exhalation). The usual time of inspiration to prevent dyssynchrony is 0.8 to 1.2 seconds. A virtue of assist/control pressure targeting is that the inspiratory pressure will not exceed the upper limit. Moreover, the patient with high ventilator demand can increase the volume and rate of gas delivery by making stronger inspiratory efforts. However, the ventilator does not guarantee a minimum tidal volume.

Assisted ventilation with pressure targeting is called pressure support. Patients have the most control with this mode because the rate and duration of inspiratory airflow depend on patient effort. This mode is inappropriate for passive apneic patients. Like all pressure-targeted

modes, it provides increasing support to match increased patient inspiratory demand. In fact, oversupport is a common cause of dyssynchrony with this mode. In this situation, the patient's strong inspiratory drive causes the ventilator to deliver excessive airflow. This can lead to dynamic hyperinflation if the patient has insufficient time to exhale. Dynamic hyperinflation can lead to ineffective triggering and wasted ventilator effort. In this situation, dyssynchrony may improve with decreasing the inspiratory pressure target. Unlike assist/control-pressure targeting, pressure support lacks a set ventilator rate. It also has different criteria for cycling from inspiration to exhalation. The inspiratory flow rate decreases as the patient's effort wanes during inspiration. The ventilator cycles to exhalation when inspiratory flow decreases below a set threshold.

Synchronized intermittent mandatory ventilation (SIMV) is another popular mode. SIMV is a mixed mode; therefore, it shares the virtues and problems with its constituent modes. It is a combination of assist/control with spontaneous breaths. If the patient does make sufficient respiratory effort, the ventilator delivers controlled ventilation (either volume or pressure targeted). If the ventilator recognizes patient effort, it allows spontaneous ventilation. Spontaneous ventilation may provide improved distribution of gas flow compared with more supported breaths. Moreover, spontaneous breathing mitigates the hemodynamic effects of positive pressure. If there is PEEP, the breaths are CPAP. However, it is difficult for the patient to respond to alternating levels of support by modulating their effort on a breath-to-breath basis. Therefore, patient effort increases on controlled breaths. Many clinicians add pressure support to the spontaneous breaths. This will diminish the effects of spontaneous ventilation on SIMV.

A number of alternative modes are available. Many have refinements so that the ventilator adjusts flow during a breath or on subsequent breaths. Adaptive support ventilation, pressure-regulated volume control, and volume support are some of the options. Neurally adjusted ventilation assist (NAVA) uses a novel strategy; a tube placed from the nose/mouth into the esophagus provides electromyographic analysis of diaphragmatic effort. The ventilator synchronizes respiratory cycling and the magnitude of pressure support to the patient's diaphragmatic contraction. NAVA can improve ventilator patient synchrony because air leaks and dynamic hyperinflation do not obscure the patient's inspiratory efforts. Highfrequency oscillating ventilation (HFOV) is an alternative mode that requires a special ventilator. The principle of HFOV is the maintenance of a high mean airway pressure with extremely brief cycling above and below the mean. The ventilator targets pressure alternating between 70 cm H_2O and 0 cm H_2O at frequency around 4 to 12 Hz. Because the duration of the respiratory cycle is so brief, there is insufficient time for the lungs to equilibrate with the ventilator airway pressure. This results in 1 to 2 mL per kg breaths at a rate of 4 to 12 times per second. These breaths are smaller than the airway's dead space; therefore, HFOV exchanges gas via alternative mechanisms. The increased hemodynamic instability found in the HFOV trial is likely due to the continuously elevated airway pressure. In particular, right ventricular failure commonly

complicates HFOV for ARDS. A well-designed randomized controlled trial found that HFOV increased mortality compared with a lung protective ventilation strategy when used as a treatment for adults with ARDS. It is possible that a different HFOV protocol (such as one that targets a lower mean airway pressure) would have a benefit.

At present, there is no proven benefit for any of these alternative modes. In general, pressure-targeted modes create less dyssynchrony than volume-targeted modes when the respiratory drive is strong. However, the settings on the mode affect dyssynchrony more than the choice of mode. For the patient in ARDS, unconventional modes are acceptable as long as they are employed as part of a lung protective strategy described in the following text.

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E.2. How should you set the fraction of inspired oxygen (FIO_2)?

The FIO_2 is set to maintain sufficient arterial oxygenation. Given the poor solubility of oxygen, the oxygen saturation of hemoglobin rather than the PaO_2 is the more important determinant of arterial oxygen content. For example, a patient without anemia and hemoglobin that is 97% saturated with oxygen will carry 200 mL O_2 in every liter of blood (in hemoglobin). The same patient will have a PaO_2 90 mm Hg and just 2.7 mL O_2 dissolved in every liter of blood (in the plasma). In ARDS, it is acceptable to target an oxygen saturation of hemoglobin >88%. The FIO_2 should be limited as low as possible to avoid oxygen toxicity. The oxygen saturation target should be higher in situations such as intracranial hypertension, right ventricular failure, and systemic vasodilation.

Brower RG, Matthay MA, Morris A, et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342(18):1301-1308.

E.3. How should you set the positive end-expiratory pressure (PEEP)?

PEEP can recruit atelectatic alveoli, prevent cyclical alveolar closure, and decrease shunt fraction (Fig. 3.6). There is a theoretical benefit of higher levels of PEEP in severe ARDS. However, high levels of PEEP can decrease venous return and cardiac output. Excessive PEEP also overdistends alveoli leading to VILI and increased pulmonary vascular resistance. The ideal dose of PEEP would maximize respiratory system compliance, gas exchange, patient comfort, and hemodynamics. Unfortunately, the best method to select PEEP for individual patients remains controversial. The trial that established the current standard of care for ventilation in ARDS used a table to determine PEEP based on FIO_2 requirement. Multiple trials have failed to demonstrate a better method of PEEP determination than this table. Some clinicians use decremental PEEP trials by serially reducing PEEP after a recruitment maneuver. Other protocols set PEEP according to pressure-volume curves or measurement of transpulmonary gradients by esophageal probes. However, there is currently no evidence that physiologic methods effectively determine the PEEP that recruits lungs in ARDS. Some protocols emphasize hemodynamic effects such as limiting PEEP based on Doppler analysis of pulmonary artery flow. The average PEEP used for ARDS in clinical settings is around 8 cm H_2O. It is unclear whether or not this is the ideal practice.

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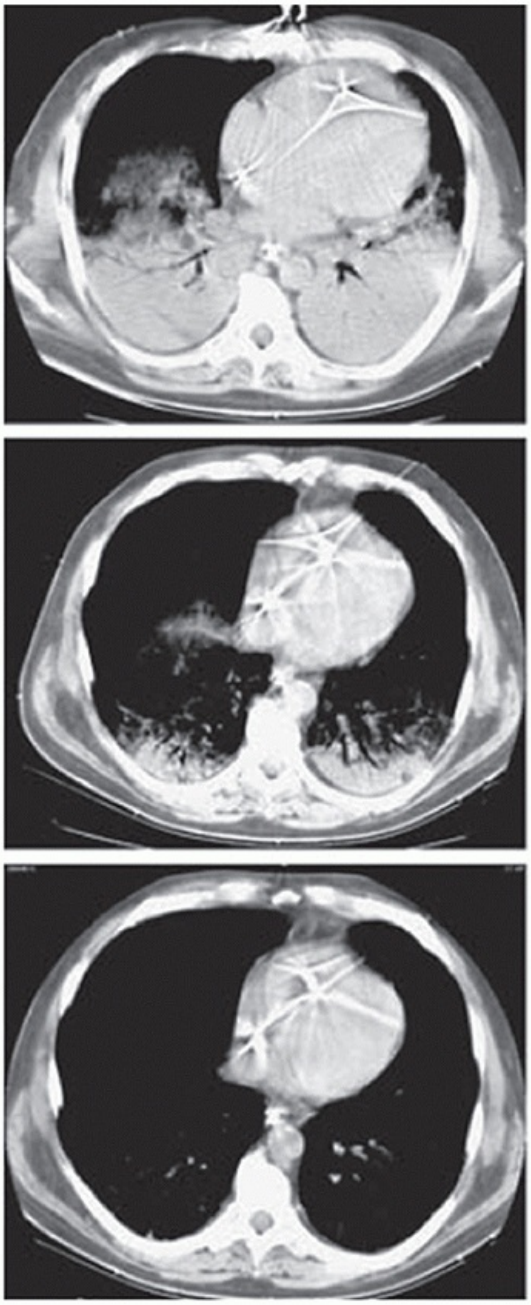


FIGURE 3.6 Lung recruitment in acute respiratory distress syndrome with progressive increase in positive end-expiratory pressure. (Reused from Borges JB, Okamoto VN, Matos GF, et al. Reversibility of lung collapse and hypoxemia in early acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 2006;174[3]:268-278.)

TABLE 3.4 Low-Stretch Lung Protective Ventilator Strategy for Acute Respiratory Distress Syndrome

	Allowable combinations of PEEP and Fio2			
Ventilator mode: assist/control volume **Initial tidal volume 6 mL/kg predicted body weight** **Plateau pressure ≤30 cm H_2O**	**FIO_2**	**PEEP cm H_2O**	**FIO_2**	**PEEP cm H_2O**
Respiratory rate 6-35 breaths/min set to achieve pH 7.3-7.45	0.3	5	0.7	14

Ratio of inspiration to expiration 1:1-1:1.3 Oxygenation goal PaO_2 55-80 mm Hg or SpO_2 88%-95%	0.4	5	0.8	14
	0.4	8	0.9	14
	0.5	8	0.9	16
	0.5	10	0.9	18
	0.6	10	1.0	18
	0.7	10	1.0	20
	0.7	12	1.0	22
	0.7	14	1.0	24

FIO_2, fraction of inspired oxygen; PEEP, positive end-expiratory pressure.

From Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med*. 2000;342(18):1301-1308.

E.4. What tidal volume and inspiratory pressure target should you set?

The approach of limiting tidal volume and plateau pressure has been validated in a landmark randomized controlled trial in patients with ARDS. This technique, called low tidal volume ventilation, significantly reduced organ failure and mortality. Although low tidal volume ventilation initially worsens gas exchange, it ultimately limits lung and extrapulmonary injury. Therefore, the initial tidal volume or inspiratory pressure should be set to keep the tidal volume <8 mL/kg/IBW and the plateau pressure <30 cm H_2O. Tidal volume and pressure should be incrementally lowered to target 6 mL/kg/IBW while monitoring the patient for dyssynchrony and worsening gas exchange (Table 3.4). Low tidal volume ventilation may reduce alveolar ventilation and worsen hypercapnia. Increasing respiratory rate is often insufficient to maintain alveolar ventilation. In fact, the low tidal volume approach may necessitate permitting hypercapnia. Although it may be well tolerated, hypercapnia can constrict pulmonary arterioles and dilate systemic and cerebral arterioles. Tidal volume restriction and hypercapnia can worsen ventilator patient dyssynchrony and double triggering of the ventilator. In this setting, the delivered tidal volumes are much larger than the clinician sets on the ventilator. Moreover, a patient's strong inspiratory effort can overdistend the lungs. On pressure-controlled ventilation, the tidal volumes may be excessive, whereas on volume-controlled ventilation, the plateau pressure may underestimate the distending pressure.

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F. Management of Refractory Respiratory Failure

The patient remains hypoxemic on FIO_2 of 0.8.

F.1. What else can you promote additional lung recruitment?

Recruitment maneuvers rely on the principle that it requires more pressure to inflate an atelectatic lung to a given volume than it does to maintain that volume after exhaling from maximum inflation. To perform a recruitment maneuver, the clinician sets a high level of CPAP for a short time interval (e.g., 40 cm H_2O for 40 seconds). Alternatively, for passively ventilated patients, the extrinsic PEEP can be increased on the ventilator for a short duration. Recruitment maneuvers may prevent or treat derecruitment related to disconnection of the ventilator circuit for suctioning.

Ideally, lung recruitment will reduce the amount of atelectatic lung and decrease shunt fraction. The hallmark of success is an improvement in the ratio of PaO_2 to FIO_2. Recruitment maneuvers share the deleterious effects of all treatments that raise airway pressure. The high level of airway pressure may be sufficient to obstruct venous return and reduce cardiac output as well as cause barotrauma. The benefit of recruitment maneuvers for patients depends on the inherent recruitability of their lungs. Given the physiologic rationale and benefits on gas exchange, clinicians should consider using recruitment maneuvers on a case-by-case basis.

Pronation is a recruitment strategy that avoids the deleterious effects of increased positive airway pressure. There are a number of mechanisms by which pronation may exert its benefit. Prone ventilation decreases the volume of lung that is compressed by the heart in the supine position. Pronation also displaces the diaphragm caudally and homogenizes the distribution of the pleural pressure. In ARDS, these mechanisms may recruit lung and decrease alveolar hyperinflation. Pronation may also have multiple effects on hemodynamics. By reducing the airway pressures clinicians set on mechanical ventilation, pronation may improve venous return and lower pulmonary vascular resistance. A large randomized trial demonstrated a survival advantage from prone positioning in severe ARDS. The patients had PaO_2:FIO_2 ratios <150 mm Hg and were treated early in their illness for at least 16 hours per day. A study-level meta-analysis has also demonstrated a survival advantage in severe ARDS.

Providing mechanical ventilation to patients while they sit in a chair or walk is the ideal therapy to recruit lung. Exercise improves cardiac output, lowers pulmonary vascular resistance, and avoids sedation. Similarly, avoidance of deep sedation and neuromuscular blockade can improve recruitment.

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F.2. What rescue strategies can you use for refractory ARDS?

Inhaled nitric oxide (NO) can improve ventilation-perfusion matching in the heterogeneous lungs of ARDS. Inhaled NO distributes to better ventilated lung units where it relieves reflexive hypoxic and hypercapnic vasoconstriction. This effect

can improve hypoxia and reduce pulmonary vascular resistance. NO has multiple other effects which may explain the absence of a demonstrable mortality benefit in ARDS. Therefore, the role of inhaled NO, if any, in ARDS should be restricted to refractory hypoxemia.

A number of ventilator strategies have been employed to rescue patients with refractory hypoxemia. A common feature is their use of high mean airway pressure to recruit lung. HFOV, airway pressure release ventilation (APRV), and inverse ratio ventilation all employ a brief expiratory phase. This prevents exhalation and maintains high intrathoracic pressure throughout the respiratory cycle. With HFOV and APRV, the goal is to create auto-PEEP. It is unclear if any of these ventilator strategies offer any advantage over setting a high level of extrinsic PEEP on a conventional mode of ventilation.

Extracorporeal gas exchange is also being evaluated as a rescue strategy for refractory ARDS. One approach is extracorporeal CO_2 removal, which requires relatively low blood flow rates. CO_2 removal can theoretically increase the gas tension available for oxygen in the alveoli and allow a reduction in tidal volume. A more aggressive strategy is venovenous extracorporeal membrane oxygenation (VV ECMO). It requires high blood flow rates and can reduce the CO_2 content and raise the O_2 content of mixed venous blood. VV ECMO can improve hemodynamics in ARDS by reducing hypoxic/hypercapnic pulmonary vasoconstriction and the magnitude of positive airway pressure required from mechanical ventilation. A randomized trial done at multiple centers in England demonstrated a survival advantage for patients with severe ARDS who were transferred to an ECMO center. There was also better than expected survival for patients with severe ARDS due to influenza when treated with ECMO. Bleeding and vascular complications are its main side effects.

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G. Adjunctive Management of Respiratory Failure

Since intubation, the patient has become hypotensive.

G.1. What is the cause and treatment of the hemodynamic instability associated with mechanical ventilation?

Hemodynamic instability is a common complication of emergency airway management and the institution of mechanical ventilation. Positive pressure ventilation can decrease the pressure gradient for venous return to the heart, thereby reducing cardiac output. Normally, circulatory reflexes will constrict the veins to restore venous return. However, sedatives and narcotics used to facilitate endotracheal intubation can blunt the autonomic response. Even low levels of positive pressure ventilation can reduce cardiac output in anesthetized postoperative patients, particularly if they have normal or reduced circulating blood volume. Fluid resuscitation and catecholamine vasopressors can raise the venous pressure and restore the pressure gradient for venous return and cardiac output. Many patients with ARDS require a positive fluid balance during the first 48 hours of mechanical ventilation to counteract the hemodynamic effects of PEEP and sedatives/narcotics.

Although diminished venous return is the most likely cause of hemodynamic instability, it is essential to consider acute cor pulmonale as an alternative explanation. The hypoxia, hypercarbia, and regional atelectasis associated with ARDS all raise pulmonary vascular resistance. Mechanical ventilation in ARDS may lead to areas of hyperinflation of the more normal lung regions. Hyperinflation raises pulmonary vascular resistance by compression of the capillaries in the alveolar septa. The severe rise of pulmonary vascular resistance can lead to right ventricular failure, particularly if the patient has had significant intravascular fluid resuscitation. The pressure rises in the right ventricle because it is unable to efficiently pump blood through the pulmonary vasculature. The incidence of acute cor pulmonale is as high as 50% in patients on mechanical ventilation for ARDS. The use of low-stretch ventilation and limitation of PEEP can lower this risk. The presence of markedly elevated central venous pressure as well as echocardiographic evidence of dilated right ventricular

interventricular septum suggests the diagnosis of acute cor pulmonale. Respirophasic variation in pulse pressure or inferior vena cava diameter does not predict an increase in cardiac output with fluid resuscitation when right-sided heart failure is present. In acute cor pulmonale, vasopressors can raise the systemic blood pressure to maintain the coronary perfusion to the right ventricular myocardium. Diuresis can help optimize right ventricular preload. The ventilator should be adjusted to prevent extremes of lung hyperinflation and sufficient PEEP to recruit poorly ventilated lung regions. Pulmonary vasodilators may be needed.

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G.2. What is the adjunctive medical therapy for ARDS?

After the initial resuscitation phase, many patients with ARDS require a different approach to fluid balance. The Fluids and Catheters Treatment Trial (FACTT) evaluated two fluid strategies instituted after the first 48 hours. With the “restrictive fluid” approach, patients received diuretics if they had oliguria and adequate perfusion. The “restricted fluid” approach group had better gas exchange and a shorter duration of mechanical ventilation than the “liberal fluid” group. There was no increase in hemodynamic instability or renal failure with a restrictive fluid approach. FACTT had a two-by-two factorial design and simultaneously demonstrated that routine use of pulmonary artery catheterization did not improve outcomes in ARDS. Therefore, clinicians should target even or slightly negative net fluid balance once patients have achieved hemodynamic stability and to avoid routine use of pulmonary artery catheters.

Severe anemia can diminish oxygen delivery. However, red blood cell transfusions are linked to a wide range of complications including nosocomial pneumonia. Moreover, red blood cell transfusions have a limited capacity to improve

oxygen consumption in critically ill patients. Although there is no specific randomized trial data in ARDS, it is reasonable to limit red blood cell transfusions in adequately perfused patients with isovolemic anemia unless the hemoglobin concentration is less than 7 g per dL.

Numerous trials have evaluated the ability of medications to modulate the natural history of ARDS. The support for systemic corticosteroids has waxed and waned for decades. The largest and highest quality randomized controlled trial found that corticosteroids offered no benefit and increased mortality if started after the first 2 weeks of ARDS. Currently, the preponderance of evidence does not support the use of corticosteroids for ARDS.

A number of other disease-modifying agents have been studied in ARDS. Rosuvastatin, a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (statin) had no benefit in a much anticipated trial. Recombinant activated protein C and ω-3 fatty acids also had no benefit. Theoretically, inhaled β-agonists would decrease lung edema and lung inflammation. However, no randomized trial has shown a benefit. Their use should be restricted to

treating bronchospasm. Mesenchymal stem cell therapy is currently the most promising therapy entering clinical trials.

One pharmacologic therapy that did have a benefit in clinical trials is cisatracurium besylate. A randomized placebo-controlled trial included patients with early ARDS and severe hypoxemia. The intervention arm received cisatracurium for 48 hours. These patients had improved gas exchange, less barotrauma, and decreased mortality compared with placebo-treated patients. Neuromuscular blockade can eradicate both the patient contribution to the lung distention and double triggering of the ventilator. In a sense, neuromuscular blockade is a technique to enforce low tidal volume ventilation. The risks of neuromuscular blockade and deep sedation have blunted enthusiasm for this approach. Surprisingly, a meta-analysis of three trials of neuromuscular blockade for ARDS did not find an increase in neuromuscular weakness. The exact role for neuromuscular blockade in ARDS remains unclear. The benefit is likely a class effect of neuromuscular blocking agents, although cisatracurium is attractive in critical illness because renal and hepatic insufficiencies have little effect on its clearance.

Ironically, the data in support of neuromuscular blockade has come at the same time a strong parallel literature supports limiting sedative use in patients on mechanical ventilation. In the absence of a compelling need for sedatives (e.g., status epilepticus), clinicians should interrupt continuous sedatives and neuromuscular-blocking agents at least daily. This approach is associated with a marked reduction in duration of mechanical ventilation. Reassuringly, this approach is also associated with improved long-term neuropsychiatric function among survivors of respiratory failure. Another strategy uses a detailed sedation protocol to avoid oversedation. Sedatives can contribute to delirium and disuse muscle atrophy. Moreover, clinicians may fail to recognize that their deeply sedated patients may be able to breathe without ventilator support. Sedation is not restorative sleep. Narcotics are still necessary for pain and dyspnea, and neuroleptics can be used for agitated delirium. Deeper sedation could be reserved for situations when severe agitation occurs or pronation is required. Treatment plans that limit sedative use require clinicians to provide calming, reassurance, repositioning, and ventilator adjustment to assure patient comfort. The study that validated the avoidance of routine sedatives for patients on mechanical ventilation used one-to-one bedside nursing and continuous presence of an intensivist in the intensive care unit.

Limiting sedation allows physical therapy. Patients may perform full physical therapy including walking while breathing through an endotracheal tube and a portable ventilator. The theoretical benefit of this approach is to decrease muscular atrophy, sedative requirements, and delirium.

The evolving treatment paradigm is to use deep sedation, narcotics, and neuromuscular blockade early in the course of severe ARDS in patients with excessive ventilator demands and ventilator dyssynchrony. Patients may require pronation during this phase. Clinicians should switch to the opposite approach of limited sedation as soon as there is stabilization. This includes limited or no sedation (aside from opiates for relief of pain or dyspnea) and physical therapy. This approach should also be used when the ARDS is less severe.

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H. Liberation of the Patient from Mechanical Ventilation

The patient slowly recovers over the next 3 days.

H.1. Explain the importance of the decision to extubate the patient or continue mechanical ventilation.

Unnecessarily prolonged mechanical ventilation can lead to pneumonia, delirium, and neuromuscular weakness. Unfortunately, clinicians may not recognize that a substantial number of their mechanically ventilated patients are capable of breathing without ventilator support. Conversely, the mortality rate associated with reintubation is extremely high. Intensive care unit patients fail extubation at rates of 15% to 20%. The risk is substantially higher in patients with chronic

illnesses. Patients who suffer extubation failure are seven times more likely to die, and the survivors are much more likely to require long-term care. Reintubation is associated with nosocomial pneumonia, although it is unknown whether the pneumonia is the cause or effect of reintubation. Therefore, the decision of whether or not to extubate a patient is one of the most important challenges facing anesthesiologists. There is an extensive literature and great controversy surrounding the topic and the strategies employed to liberate patients from mechanical ventilation vary widely.

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H.2. How will you prepare the patient for liberation from the ventilator?

The most important aspect of liberation from mechanical ventilation is the general care of the patient and the reversal of the cause of the patient's respiratory failure. Early in the course of an acute illness, the patient must be resuscitated out of shock. Generally in later stages, volume overload and hypertension must be avoided. This is especially important during the switch to negative pressure ventilation, which increases cardiac preload and left ventricular wall tension. Adequate protection against the development of coronary ischemia should be ensured in patients with significant coronary artery disease. The neurologic status should be optimized with the goal of maintaining airway protection and patency as well as adequate respiratory drive and strength. Sedation should be limited and reversed at least daily. Delirium should be avoided and treated.

Clinicians should aggressively reduce the FIO_2 and PEEP to the minimum acceptable level. Derecruitment happens quickly after reducing PEEP, so lengthy weaning may be unnecessary.

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H.3. How will you recognize when the patient is ready for extubation?

Traditionally, once FIO_2 and PEEP were at minimal settings, clinicians would assess patients for their ability to undergo a weaning trial. Tests of weaning readiness were used to identify patients in whom it is safe to reduce ventilator support. These tests included objective measures such as the negative inspiratory force, vital capacity, and the rapid shallow breathing index (RSBI). The research literature makes a clear distinction between these tests of weaning readiness and tests of extubation readiness (such as a prolonged T-tube trial as discussed in the following text). The best validated test to predict readiness for weaning is the RSBI. This test was performed by switching patients from assist control ventilation to a T-tube. A spirometer attached to the end of the endotracheal tube measured the tidal volume, and the respiratory rate was counted. Patients with ratios of <105 could safely go on to a test of extubation readiness with a T-tube trial lasting up to 2 hours. However, there is no clear advantage to performing a test of weaning readiness (such as the RSBI calculation) prior to initiating a test of extubation readiness. Instead, clinicians can perform daily clinical screening of patients on mechanical ventilation to assess them for extubation readiness (Table 3.5).

The purpose of clinical screening is to determine a pretest probability of extubation success. The pretest probability of success will be extremely low in the presence of clinical signs that clearly predict extubation failure. These signs include shock, severe intracranial hypertension, requirement of high FIO_2 or PEEP, and the absence of protective airway reflexes or spontaneous inspiratory efforts. If the pretest probability of extubation success is extremely low, there is no additional test that would be able to raise the posttest probability of success sufficiently to allow extubation. In these situations, the clinician should continue mechanical ventilation, treat the cause of the respiratory failure, and repeat the screening at least daily. Similarly, clinicians also should not perform tests of extubation readiness in situations where the pretest probability of extubation success is very high. These situations include patients who had been intubated for a brief and uncomplicated

procedure as well as those intubated for a sedative overdose that has resolved. When clinicians calculate a very high pretest probability of extubation success, they can proceed directly to extubation without testing.

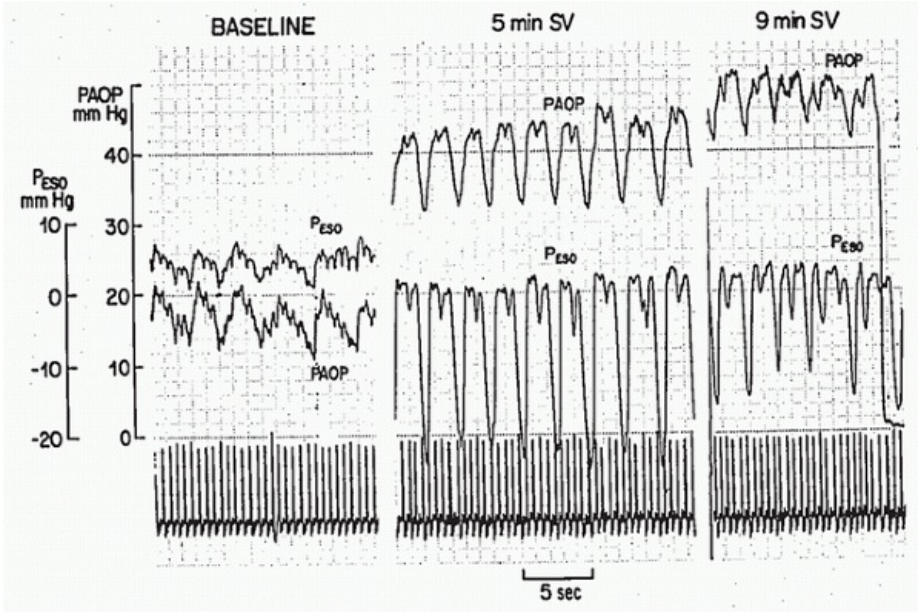
When there is an intermediate pretest probability for extubation success, clinicians should consider performing tests of extubation readiness. These tests simulate the conditions of spontaneous breathing after extubation. The most common tests are T-tube, CPAP, pressure support ventilation, and flow-by ventilation. The appearance of tachypnea, hemodynamic instability, diaphoresis, anxiety, or agitation signifies failure of the test. If the patient tolerates it, the trial continues for 30 to 120 minutes. Both durations are equivalent in clinical trials. Clinicians should consider extubation if the patient passes the trial. No study has proven the superiority of one test of extubation readiness over another. Perhaps, this is because the vast majority of critically ill patients who undergo these tests are able to sustain spontaneous breathing after extubation. There are, however, important physiologic differences between the methods. Given the varied causes of extubation failure, the utility of the different tests may vary in different situations. For example, in patients with significant heart disease, it is important to predict the consequences of switching from positive to negative pressure ventilation that occurs with extubation. Because positive pressure ventilation decreases cardiac preload and left ventricular afterload, extubation readiness testing performed with CPAP or minimal pressure support may not be predictive of success. Tests using T-tube or “flow-by”

ventilation (with pressure support and PEEP set to 0 cm H_2O) better simulate the hemodynamic stressors of breathing after extubation (Fig. 3.7). There are concerns about T-tubes imposing an unfair resistive load due to its narrow diameter. In one series, T-tube trials failed to identify a number of patients capable of successfully breathing after extubation. However, T-piece trials using size 7 to 8.5 endotracheal tubes accurately predict the work of breathing after extubation in critically ill patients. T-tube trials add the expense of the humidification and tubing attachments to the oxygen source. Moreover, the T-piece trials do not benefit from ventilator alarms.

TABLE 3.5 Clinical Screening Criteria for Extubation Readiness

Adequate level of alertness
PaO_2/FIO_2 ≥150 or SpO_2 ≥90% on FIO_2 ≤0.4
PEEP ≤5 cm H_2O
Cause of respiratory failure improving
Able to initiate an inspiratory effort
Hemodynamic stability
Absence of refractory acidemia

FIO_2, fraction of inspired oxygen; PaO_2, partial pressure of oxygen; PEEP, positive end-expiratory pressure; SpO_2, peripheral capillary oxygen saturation.



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FIGURE 3.7 Ventricular failure and pulmonary edema precipitated by spontaneous ventilation. At baseline **(left)**, the patient is on positive pressure ventilation. During spontaneous ventilation (SV), the esophageal pressure (P_{ESO}) is negative during inspiration and the pulmonary artery occlusion pressure (PAOP) rises. By 9 minutes, the PAOP is catastrophically elevated and respiratory muscle fatigue decreases the amplitude of P_{ESO}. (Reused from Lemaire F, Teboul JL, Cinotti L, et al. Acute left ventricular dysfunction during unsuccessful weaning from mechanical ventilation. *Anesthesiology*. 1988;69(2):171-179, with permission.)

Trials with pressure support theoretically overcome the resistance imposed by the ventilator circuit. However, the amount of pressure support required is unclear. These trials may underestimate the work of breathing after extubation. The opposite phenomenon is also important. Pressure support may create dyssynchrony on mechanical ventilation. In particular, oversupport may induce tachypnea. Clinicians may misinterpret tachypnea to mean that the patient cannot be extubated. This may lead to needlessly prolonged mechanical ventilation. Automatic tube compensation software is designed to improve the application of minimal pressure support during tests of extubation readiness. However, at present, there is no proof of advantage for this approach in clinical trials.

In place of tests of readiness for extubation, some clinicians prefer to gradually wean ventilator support. Pressure support can be incrementally reduced or the number of controlled breaths reduced on SIMV. However, there is no proof that any ventilator strategy or weaning process trains and strengthens respiratory muscles. Moreover, in clinical trials, these methods prolong the time to extubation. The importance of liberation as opposed to weaning from mechanical ventilation is illustrated by a clinical trial which showed that pairing a once daily awakening from sedatives with a trial of spontaneous ventilation reduces mortality.

A final step prior to extubation is to consider the risk of postextubation stridor. The cuff leak test is an imperfect predictor. Clinicians should only consider using it when there are risk

factors for laryngeal edema such as prolonged intubation, large endotracheal tube, asthma, traumatic intubation, and ventilator patient dyssynchrony.

In situations such as COPD or congestive heart failure, extubation directly to prophylactic NIPPV may reduce the need for reintubation. However, these patients must be carefully reevaluated to make sure they are not dependent on NIPPV for excessive periods of time, preventing effective nutrition and physical therapy.

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Chapter 4
Lung Transplantation

Jennifer Dietrich

Charles W. Hogue Jr.

A 52-year-old woman with progressively worsening dyspnea on exertion, limited daily activity despite supplemental oxygen, and radiographic and spirometric evidence of severe obstructive pulmonary disease was scheduled for bilateral sequential lung transplantation. History was remarkable for 30 pack-years history of smoking (although none for 10 years), mild hypertension (145/86 mm Hg), normal left ventricular ejection fraction, and osteoarthritis.

A. Medical Disease and Differential Diagnosis

1. What were the expected manifestations of severe obstructive pulmonary disease in this patient, and why was she a transplant candidate?
2. What other end-stage lung diseases can also be treated with transplantation?
3. How many lung transplantations have been performed?
4. What are the selection criteria for recipients?
5. How is the decision made to transplant one or both lungs, and does this influence preoperative management?
6. How does a single-lung transplantation (SLT) differ technically from a bilaterallung transplantation (BLT)?

B. Preoperative Evaluation and Preparation

1. What preoperative evaluation is desirable?
2. Would you premedicate this patient? If so, how?
3. What vascular access is appropriate?
4. Is preoperative epidural catheter placement advantageous?

C. Intraoperative Management

1. What special equipment is necessary?
2. How would you monitor this patient?
3. How would you induce anesthesia in this patient?
4. How would you ventilate this patient? What kind of endotracheal tube would you use?
5. How does the physiology of single-lung ventilation influence the procedure?
6. How does single-lung ventilation affect cardiopulmonary function? What are the problems of single-lung ventilation in this patient? How would you treat them?
7. What problems are associated with the lateral position?
8. Should volatile anesthetics be avoided during single-lung ventilation?
9. At what specific points in the procedure are problems anticipated?
10. How would you deal with problems related to clamping of the pulmonary artery (PA)?
11. What hemodynamic alterations would you expect during graft implantation and reperfusion? How would you correct them?

12. When is cardiopulmonary bypass (CPB) necessary for lung transplantation?

13. Should fluid administration be restricted, and are blood products commonly required?
14. Would you extubate the patient upon conclusion of the procedure?

D. Postoperative Management

1. What are the major complications after lung transplantation?
2. How is postoperative ventilation managed, and for how long is it required?
3. What special precautions should be taken when a lung transplant recipient requires general anesthesia for subsequent nonpulmonary surgery?
4. What are the long-term outcomes of lung transplantation?
5. Are there surgical alternatives to lung transplantation?

A. Medical Disease and Differential Diagnosis

A.1. What were the expected manifestations of severe obstructive pulmonary disease in this patient, and why was she a transplant candidate?

Severe obstructive pulmonary disease results in increased airway resistance, reduced expiratory flow rates, and high residual lung volumes. There is a point at which the expiratory airway obstruction and lung hyperinflation become so severe that the chest wall cannot physically expand to accommodate a normal tidal volume, resulting in restrictive physiology superimposed on obstructive disease. This condition is usually refractory to medical management and substantially limits daily activity. This patient's age and lack of other significant systemic illness allowed her to be considered a transplant candidate.

Chronic obstructive pulmonary disease (COPD) (36%), idiopathic pulmonary fibrosis (21%), emphysema secondary to α_1-antitrypsin deficiency (7%), and cystic fibrosis (16%) are the most common obstructive disorders in adults undergoing lung transplantation. At one time, concerns about mediastinal displacement and profound ventilation/perfusion mismatch secondary to hyperinflation of the remaining native lung prevented surgeons from attempting SLT for emphysema. However, clinical experience has demonstrated that many emphysemic patients can be successfully treated by SLT. Due to the severe shortage of organs for transplant, single-lung procedures have been advocated as a means to increase the number of recipients. However, with 5-year survival rates after SLT approaching only 50% and increasing experience suggesting that bilateral lung transplantation (BLT) for COPD is associated with improved functional outcomes and improved long-term survival, BLT emerged as a formidable (alternative) approach to treat this patient population. The improved survival with BLT may possibly be due to the later development of bronchiolitis obliterans syndrome (BOS) as well as a trend for higher quality of life score compared with SLT. Nonetheless, although transplantation may improve the quality of life for patients with severe COPD, the decision for SLT or BLT remains controversial and is based on the individual situation taking into account regional organ allocation policies, individual center experience, and organ availability.

Christie JS, Edwards LB, Aurora P, et al. The registry of the International Society for the Heart and Lung Transplantation: twenty-sixth official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant*. 2009;28:1031-1049.

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A.2. What other end-stage lung diseases can also be treated with transplantation?

The first successful (i.e., the patient left the hospital) SLTs were performed in 1983 for idiopathic pulmonary fibrosis. Since

that time, the procedure has been applied to patients suffering from various end-stage pulmonary diseases (Table 4.1). In general, the underlying

disease processes produce lung dysfunction that can be broadly characterized as obstructive, restrictive, infectious (e.g., cystic fibrosis and bronchiectasis), or vascular. As of 2008, most SLTs have been performed for obstructive lung disease, followed by idiopathic pulmonary fibrosis. The most common indications for BLT are cystic fibrosis and obstructive lung disease.

TABLE 4.1 Lung Transplants Categorized by Disease

END-STAGE LUNG DISEASE	SINGLE-LUNG TRANSPLANT (% OF TOTAL)	BILATERAL/DOUBLE-LUNG TRANSPLANT (% OF TOTAL)
Cystic fibrosis	1.5	24.9
Retransplant	3.4	2.3
Idiopathic pulmonary arterial hypertension	0.6	4.4
α_1-Antitrypsin deficiency	5.0	5.9
Sarcoidosis	1.8	2.9
Interstitial lung disease	34.9	18.2
Emphysema/chronic obstructive pulmonary disease	43.0	26.6
Miscellaneous	4.5	5.9

Reflecting a loss of lung parenchymal elasticity and compliance, *end-stage restrictive disease* is characterized by profoundly reduced lung volumes and diffusing capacity but relative preservation of ventilatory flow rates. Comparison of flow-volume loops representing obstructive and restrictive diseases is shown in Figure 4.1. The underlying disease process also tends to obliterate pulmonary microvasculature, thereby chronically increasing vascular resistance, producing pulmonary hypertension, and predisposing to cor pulmonale. Most patients with restrictive disease are good candidates for an SLT because the stiff, vasoconstricted native lung will receive relatively little ventilation and perfusion and can therefore usually be left without compromising the transplanted lung.

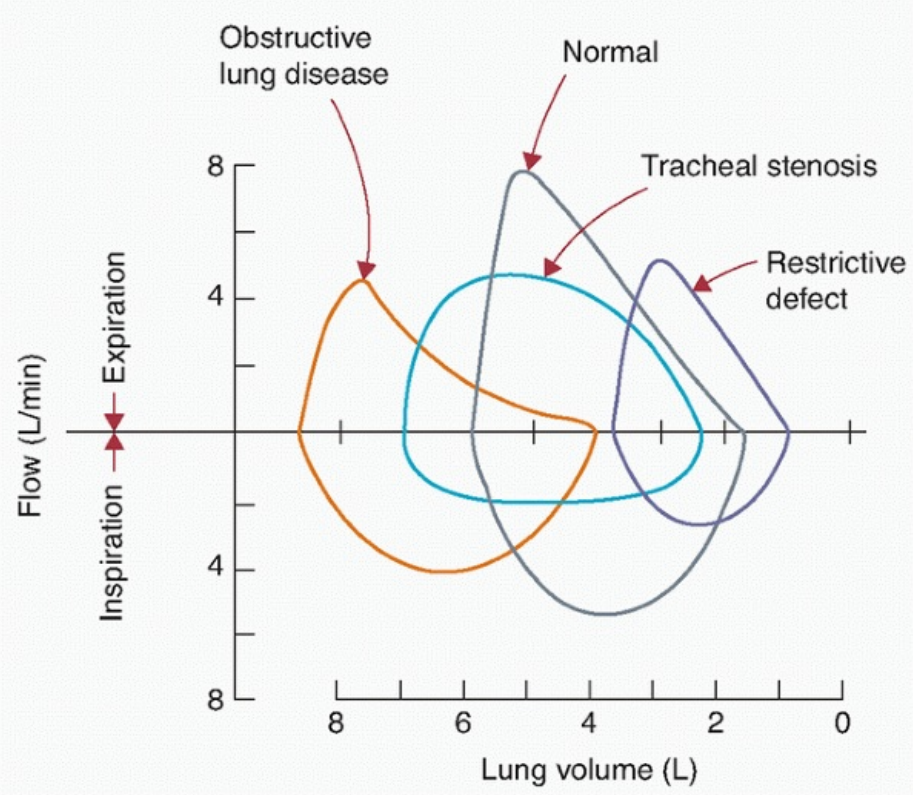


FIGURE 4.1 Representative tracings of flow-volume loops from a healthy individual, a patient with parenchymal obstructive disease, a patient with tracheal stenosis, and a patient with restrictive disease from parenchymal fibrosis. (Modified from Goudsouzian N, Karamanian A. *Physiology for the Anesthesiologist*. 2nd ed. Norwalk, CT: Appleton-Century-Crofts; 1984:213, with permission.)

Infectious lung disease such as cystic fibrosis is the most frequent indication for lung transplantation in patients younger than 18 years. Characterized by chronic infection and the production of copious purulent secretions, patients with cystic fibrosis primarily exhibit obstructive functional abnormalities with increased airway reactivity. Under most circumstances, residual lung volumes and functional residual capacity are increased and bronchodilators have little effect on expiratory flow rates. Because of potential infectious cross-contamination of the transplanted lung, chronic infectious disease represents a contraindication to SLT. However, SLT with contralateral pneumonectomy has been performed as an alternative solution.

Pulmonary vascular disease with severe pulmonary hypertension and right ventricular dysfunction has also emerged as an indication for transplantation. Pathologically, severe PA hypertension can result from idiopathic proximal vascular processes such as persistent pulmonary hypertension (PPH) or secondary to chronically increased pulmonary blood flow (e.g., left-to-right intracardiac shunt, leading to Eisenmenger syndrome) or pulmonary venous hypertension from left-sided heart diseases. Pulmonary hypertension may precipitate chronic hypoxemia via an intracardiac defect that allows for development of a right-to-left shunt. Improved medical therapy for PPH, particularly with continuous long-term intravenous prostacyclin infusions or sildenafil, has affected the numbers of patients undergoing lung transplantation for this disease.

Controversy exists with respect to choice of SLT versus BLT for patients with idiopathic pulmonary arterial hypertension (IPAH). Because a native lung can usually be left intact without compromising a transplanted lung (which will receive most of blood flow), some patients with pulmonary arterial vascular disease may be reasonable candidates for SLT, *with concurrent repair of any cardiac anomalies*. Early reports indicated poorer functional recovery and higher mortality after SLT versus BLT for PPH. Some reports suggest the earlier manifestation of BOS in patients after SLT versus BLT, and although survival curves diverge 3 years after transplantation, controversy remains whether or not procedure type is the main cause. Some centers have adopted BLT as the mainstay of treatment for patients presenting with IPAH.

Christie JS, Edwards LB, Aurora P, et al. The registry of the International Society for the Heart and Lung Transplantation: twenty-sixth official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant*. 2009;28:1031-1049.

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Yusen RD, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first adult lung and heart-lung transplant report—2014; focus theme: retransplantation. *J Heart Lung Transplant*. 2014;33:1009-1024.

A.3. How many lung transplantations have been performed?

Although the first human lung allograft was performed in 1963, transplantation of one or both lungs did not emerge as a viable therapeutic option for patients with end-stage lung disease until the 1980s. The ultimate emergence of this procedure can be largely attributed to advances in the prevention and treatment of airway complications, infections, and rejection. Since initiation of an international registry for lung transplantation in the mid-1980s, the number of procedures reported yearly rose sharply, until beginning to slow in 1993. To date, the highest yearly total was 3,725 in 2011. Despite this volume, the number of patients awaiting lung transplantation continues to exceed the limited donor supply. As of the 2014 international registry, 47,647 lung transplantations had been reported worldwide.

Christie JS, Edwards LB, Aurora P, et al. The registry of the International Society for the Heart and Lung Transplantation: twenty-sixth official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant*. 2009;28:1031-1049.

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A.4. What are the selection criteria for recipients?

In general, patients with severe end-stage lung disease are considered candidates for transplantation when their life expectancy is less than 2 to 3 years. They have minimal disease of other organ systems, and they are mentally and psychologically capable of following strict regimens for rehabilitation and immunosuppressive therapy. These criteria contribute to a high (>80%) likelihood of surviving the lung transplantation for at least 90 days and 5-year posttransplant survival from a general medical standpoint. Specific criteria, including age, are dependent on the type of lung disease and whether the planned procedure is SLT or BLT. Recent data reveal that the age of lung transplant recipients is increasing with approximately 35% now 60 years of age and older compared to 15% in 1998. The average age of the recipient is 35.5 years. In contrast to inclusion criteria formulated when lung transplantation was in its infancy, concomitant steroid therapy, previous intrathoracic surgery, mechanical ventilation, and right ventricular failure are no longer considered absolute contraindications.

Bigham M, Dickstein ML, Hogue CW Jr. Cardiac and lung transplantation. In: Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia: Principles and Clinical Practice*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:637-662.

Christie JS, Edwards LB, Aurora P, et al. The registry of the International Society for the Heart and Lung Transplantation: twenty-sixth official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant*. 2009;28:1031-1049.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia, PA: Elsevier Science; 2003:295-314.

Weill D, Benden C, Corris PA, et al. A consensus document for the selection of lung transplant candidates: 2014—an update from the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant*. 2015;34:1-15.

Yusen RD, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first adult lung and heart-lung transplant report—2014; focus theme: retransplantation. *J Heart Lung Transplant*. 2014;33:1009-1024.

A.5. How is the decision made to transplant one or both lungs, and does this influence preoperative management?

SLT is often preferred because of the extreme shortage of donor organs; however, as experience increases with BLT and the improvement in outcomes compared with SLT, many centers are performing BLT more frequently than SLT. The only absolute contraindication to SLT is infectious lung disease (e.g., cystic fibrosis and bronchiectasis) because leaving the native lung could endanger the long-term viability of the transplanted lung. As noted earlier, severe emphysema was once thought of as a contraindication to SLT because of the probability of mediastinal shift and marked ventilation mismatch between the highly distensible native lung and the graft. This is only rarely of clinical significance, and it is now accepted that SLT can be successfully performed in patients with obstructive disease. Although SLT is technically easier and advocated for more difficult recipients, such as those with prior thoracic surgery or coexisting illnesses, functional improvements are often better with BLT. In addition, the status of the donor lungs further influences the decision of whether to perform a single or bilateral procedure. Finally, transplantation of two lobes from two living related donors for patients with inflammatory disease who are unlikely to survive the wait for a cadaver donor is gaining acceptance. From a practical standpoint, the decision to perform an SLT or a BLT has little impact on preoperative management because both procedures necessitate the same level of preparation.

Date H, Tanimoto Y, Goto K, et al. A new treatment strategy for advanced idiopathic interstitial pneumonia: living-donor lobar lung transplantation. *Chest*. 2005;128(3):1364-1370.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia, PA: Elsevier Science; 2003:295-314.

Sundaresan RS, Shiraishi Y, Trulock EP, et al. Single or bilateral lung transplantation for emphysema? *J Thorac Cardiovasc Surg*. 1996;112:1485-1494.

A.6. How does a single-lung transplantation (SLT) differ technically from a bilateral-lung transplantation (BLT)?

It is extremely important that anesthesiologists be broadly familiar with the surgical methods because manipulation of the heart and lungs at specific points during the transplantation can produce marked cardiopulmonary disturbances. Ideally, the anesthesiologist should anticipate these changes and adapt the anesthetic management accordingly.

SLT is usually performed in the lateral decubitus position through a thoracotomy incision, often with the upper leg and pelvis angled to allow groin exposure for potential femoral cannulation and CPB. In contrast, bilateral sequential lung transplantation is usually performed with the patient supine through a “clamshell” incision (bilateral anterior thoracotomies with or without transverse sternotomy). For both SLT and BLT, intermittent single-lung ventilation is required during dissection of the native lung to be removed and implantation of the graft. Once stable single-lung ventilation is established, dissection of the lung to be transplanted is initiated with isolation of the PA. To assess the cardiopulmonary response to diverting the entire cardiac output through one lung, progressive temporary occlusion of the vessel is first performed manually; if well tolerated, the vessel is then clamped and stapled. After ligation of the PA, the pneumonectomy is completed. Implantation of the graft begins with anastomosis of the airway. In the past, the bronchial anastomosis was wrapped with an omental pedicle, mobilized through a small abdominal incision in an effort to improve blood supply to the airway and promote healing. However, the use of a “telescoping” bronchial anastomosis has now largely obviated the need for omental wrapping. The PA branch is then attached to the graft, followed by anastomosis of a cuff of the left atrium containing the pulmonary veins. The implanted lung is then partially inflated, the left atrial cuff and pulmonary veins de-

aired, and circulation to the organ restored. If the attempt to establish adequate hemodynamics and oxygenation after reperfusion of the transplanted lung is unsuccessful, this is the time to consider using extracorporeal membrane oxygenation (ECMO) or CPB. In a sequential BLT, this is often the point in the case where the decision may be made to place the patient on extracorporeal support prior to attempting to transplant the second lung. The use of extracorporeal support for BLT often varies by institutional and patient factors. If an en bloc technique for BLT is used, CPB is required. Additional surgical technique for BLT is described in the following text.

Patients presenting for SLT with chronic PPH of primary or secondary etiology often exhibit severe compromise of the right ventricular function. To avoid additional right ventricular compromise, many institutions choose to institute partial normothermic CPB during SLT for PPH or in patients with severe pulmonary hypertension and right ventricular dysfunction secondary to restrictive or obstructive disease. Cannulation is typically through the femoral artery and the right atrium unless simultaneous correction of an intracardiac defect is planned. In such patients, conventional aortic and single- or double-stage atrial cannulation are performed. Implantation of the lung is otherwise performed in the same manner as described earlier.

BLT was first described by the Toronto Lung Transplant Group in the mid-1980s as en bloc implantation of both lungs simultaneously. The procedure is performed through a median sternotomy using hypothermic CPB, cardioplegic cardiac arrest, and single tracheal (or double bronchial) anastomosis of the trachea and main PA. Although the procedure initially produced encouraging results, considerable limitations related to technical complexity, morbidity, mortality, and application to many patients with end-stage lung disease soon became apparent. Not surprisingly, use of the procedure declined sharply and has now been largely replaced by the bilateral sequential implantation technique, which does not uniformly require hypothermic CPB. Introduced in 1990, bilateral sequential (or bilateral single) lung transplantation has become the surgical procedure of choice when replacement of both lungs is necessary. According to the 2014 international registry, approximately 75% of the transplants performed in 2012 were BLTs. As noted earlier, in contrast to SLT, bilateral sequential lung transplantation procedures are performed in the supine position. In general, the procedure can be regarded as having two phases. First, the most severely compromised lung (as determined by preoperative ventilation/perfusion lung scanning) is removed during ventilation of the “good” contralateral lung. Implantation is achieved through a bronchial anastomosis as with an SLT. The second lung is then removed and transplanted during ventilation of the new lung alone. As noted

earlier, if there is hemodynamic or ventilatory instability during ventilation of the new lung alone, extracorporeal support may be instituted prior to implanting the second lung.

Aigner C, Klepetko W. Bilateral lung transplantation. *Operative Tech Thorac Cardiovasc Surg.* 2012;17(3):181-193.

Davis RD. Bilateral sequential lung transplantation. *Operative Tech Thorac Cardiovasc Surg*. 2007;12(1):57-72.

Flye MW, ed. *Atlas of Organ Transplantation*. Philadelphia, PA: WB Saunders; 1995:296-312.

Hayanga JW, D'Cunha J. The surgical technique of bilateral sequential lung transplantation. *J Thorac Dis*. 2014;6(8):1063-1069.

Nagendran M, Maruthappu M, Sugand K. Should double lung transplant be performed with or without cardiopulmonary bypass? *Interact Cardiovasc Thorac Surg.* 2011;12(5):799-804.

Pasque MK, Cooper JD, Kaiser LR, et al. Improved technique for bilateral lung transplantation: rationale and initial clinical experience. *Ann Thorac Surg*. 1990;49:785-791.

Yusen RD, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first adult lung and heart-lung transplant report—2014; focus theme: retransplantation. *J Heart Lung Transplant*. 2014;33:1009-1024.

B. Preoperative Evaluation and Preparation

B.1. What preoperative evaluation is desirable?

At most centers, an extensive physical examination, psychological evaluation, and numerous tests of cardiopulmonary function are performed before acceptance into the transplant program. This facilitates the preanesthetic evaluation that ideally is performed when the patient is first accepted into the transplant program. Familiarity with pulmonary function tests, ventilation/perfusion lung scan results, heart catheterization, echocardiographic data (including evidence of intracardiac shunts), exercise tolerance, oxygen use, and dependence on continuous pulmonary vasodilator infusion (i.e., prostacyclin) are beneficial for formulating an anesthetic plan. Although many of these parameters are regularly reassessed, the interval between evaluation and transplantation necessitates that a careful history and physical examination be repeated before the procedure, focusing on signs of pulmonary hypertension and cardiac dysfunction.

Bigham M, Dickstein ML, Hogue CW Jr. Cardiac and lung transplantation. In: Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia: Principles and Clinical Practice*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:637-662.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia, PA: Elsevier Science; 2003:295-314.

B.2. Would you premedicate this patient? If so, how?

As with all critically ill patients, considerations regarding preoperative sedation are governed primarily by the functional limitations imposed by the underlying disease and the potential consequences of hypercarbia and hypoxemia as a result of the sedation. Special consideration must also be given to the possibility that the donor lungs will be deemed unacceptable at final inspection, and therefore, the procedure is canceled. When indicated, parenteral sedation is usually chosen because of insufficient time to effectively administer oral anxiolytics. Midazolam alone or with diphenhydramine (potentially protecting the lung against drug-induced histamine release) is often sufficient. Clinically, most patients with end-stage restrictive, obstructive, or infectious lung disease are tachypneic while breathing room air and cannot tolerate aggressive sedation. Also, patients with pulmonary hypertension and significant right-to-left intracardiac shunting (i.e., Eisenmenger physiology) are often cyanotic despite oxygen supplementation and may not tolerate sedation well. In contrast, patients with PPH and no intracardiac defect often appear reasonably normal and will benefit from sedation because of the potential for stress-related increases in pulmonary vascular resistance. In addition to sedative premedication, consideration needs be given to immunosuppression protocols, and, in appropriate patients, supplemental bronchodilator therapy.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15(1):143-157.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia, PA: Elsevier Science; 2003:295-314.

B.3. What vascular access is appropriate?

Typically, a large-bore intravenous catheter and central venous access for PA catheter placement are secured before surgery. In many centers, additional central venous cannulation is performed with a multiple-lumen catheter to provide intraoperative and postoperative venous access. For patients with chronic infectious lung disease or a history of previous intrathoracic procedures, a second large-bore intravenous catheter is often obtained because of the potential for brisk blood loss during dissection of pleural adhesions. Meticulous removal of air from venous infusion lines should be performed, particularly in patents with known or suspected right-to-left shunts. At many institutions, cannulation of a femoral artery, instead of the radial artery, is performed under local anesthesia in the operating room, because radial arterial pressures may become damped during the procedure secondary to vasoactive medication infusion or positioning of the arms.

Flye MW, ed. *Atlas of Organ Transplantation.* Philadelphia, PA: WB Saunders; 1995:313-318.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15(1):143-157.

B.4. Is preoperative epidural catheter placement advantageous?

Pain control after lung transplantation can be critical in facilitating tracheal extubation and rehabilitation. Both lumbar and thoracic epidural catheters have been used for postoperative pain management. Epidural catheters may be placed immediately before the procedure or postoperatively prior to extubation. If placed before the procedure, there must be consideration that there is the possibility of anticoagulation and CPB during the transplantation procedure. The practice of placing preoperative epidurals is supported by data indicating no adverse sequelae to preoperatively placed epidural catheters, including patients who required emergent heparinization and CPB. Obvious exceptions to this approach are patients who are anticoagulated preoperatively or those in whom CPB is planned. Delaying placement of the epidural catheter until the postoperative period may also be a possibility.

Feltracco P, Barbieri S, Milevoj M, et al. Thoracic epidural analgesia in lung transplantation. *Transplant Proc*. 2010;42:1265-1269.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15(1):143-157.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia, PA: Elsevier Science; 2003:295-314.

C. Intraoperative Management

C.1. What special equipment is necessary?

Necessary items for lung transplantation include an anesthesia ventilator capable of delivering a wide range of inspiratory/expiratory (I:E) ratios, varying inspired oxygen concentrations, and ventilatory modes as well as efficacy at higher airway pressures. Apparatus to deliver continuous positive airway pressure (CPAP) should be readily available, as should a fiberoptic bronchoscope to confirm double-lumen tube or bronchial blocker/device positioning, to provide guided airway suctioning, and for inspection of the anastomosis. Access to transesophageal echocardiography (TEE) is often beneficial, and a CPB machine should always be immediately available for lung transplantation. An inhaled nitric oxide (iNO) delivery system is highly desirable during lung transplantation. Vasopressors, inotropes, and selective pulmonary vasodilators may also be needed during these cases.

C.2. How would you monitor this patient?

Intraoperatively, hemodynamic, and respiratory changes are often acute and profound, so extensive monitoring is imperative. In addition to the electrocardiogram, arterial blood pressure, and peripheral arterial oxygen saturation, PA catheter placement is routine for lung transplantation at most institutions because of the profound changes in pulmonary and systemic hemodynamics that often occur. During SLT, PA catheters often migrate to the

operative side after the patient has been laterally positioned even when radiographically confirmed to be in the nonoperative lung. Therefore, the surgeon should be reminded to palpate the PA and withdraw the catheter if necessary before cross-clamping the vessel. PA catheters capable of measuring mixed venous oxygen saturation have become widely used. TEE is often employed during lung transplantation to evaluate vascular anastomoses and right ventricular function, particularly during clamping of the PA, as well as to assess for intracardiac shunts and adequacy of de-airing maneuvers.

Bigham M, Dickstein ML, Hogue CW Jr. Cardiac and lung transplantation. In: Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia: Principles and Clinical Practice*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:637-662.

Miyaji K, Matsubara H, Nakamura K, et al. Equivalence of flow velocities through bilateral pulmonary vein anastomoses in bilateral living-donor lobar lung transplantation. *J Heart Lung Transplant*. 2005;24(7):860-864.

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Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia, PA: Elsevier Science; 2003:295-314.

Schenk P, Globits S, Koller J, et al. Accuracy of echocardiographic right ventricular parameters in patients with different end-stage lung diseases prior to lung transplantation. *J Heart Lung Transplant*. 2000;19(2):145-154.

C.3. How would you induce anesthesia in this patient?

As with induction of anesthesia in any critically ill patient, multiple techniques have been safely used for patients undergoing lung transplantation. The only general rule is that induction be relatively gradual because abrupt withdrawal of sympathetic tone in these patients with high sympathetic activity can result in marked cardiovascular compromise, particularly during the transition from spontaneous to mechanical ventilation. For this reason, injecting an epidural catheter with local anesthetic before induction of anesthesia can be problematic. Effective alveolar ventilation and nitrogen washout are poor in the patient with severe obstructive lung disease and high residual volumes; therefore, prolonged (i.e., 15 to 20 minutes) preoxygenation is worthwhile, followed by a rapid-acting induction agent to shorten the excitement stage, expedite airway management, and prevent opiate-induced truncal rigidity. Thiopental, etomidate, propofol, and ketamine have all been used safely, but specific properties of each drug in the setting of the patient's underlying disease should be considered. Thiopental, for example, may not be desirable for patients with bronchospasm or pulmonary hypertension because of a propensity for histamine release. Alternatively, the sympathomimetic properties of ketamine may preclude use in the presence of pulmonary hypertension, whereas its bronchodilating effects may be beneficial in the setting of bronchospasm. After administration of the hypnotic, either fentanyl, 10 to 15 μg per kg, or sufentanil, 1 to 2 μg per kg, has been commonly used with succinylcholine or a nondepolarizing muscle relaxant to complete induction. Benzodiazepines, scopolamine, and/or volatile anesthetic agents are frequently administered after induction to promote amnesia and in the case of volatile agents to promote bronchodilation.

Bigham M, Dickstein ML, Hogue CW Jr. Cardiac and lung transplantation. In: Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia: Principles and Clinical Practice*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:637-662.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15(1):143-157.

C.4. How would you ventilate this patient? What kind of endotracheal tube would you use?

After induction, the trachea is usually intubated with a left endobronchial double-lumen tube for both SLT and BLT. Use of a single-lumen endotracheal tube with either an external or an internal bronchial blocking catheter has been described but does not appear to be clearly superior to the left double-lumen tube for most procedures. Furthermore, an endobronchial double-lumen tube allows for differential lung ventilation if required postoperatively. One exception to this approach has been in patients with cystic fibrosis who exhibit thick tenacious secretions that are difficult to suction through the small-lumen suction catheters necessary for double-lumen tubes. In these patients, it is often helpful to first place a large single-lumen tube and perform extensive bronchoscopic-directed bronchial lavage and suctioning before placement of the double-lumen tube.

The transition from spontaneous to mechanical ventilation invariably produces hemodynamic alterations resulting from acute changes in intrathoracic pressure and chest wall compliance. With obstructive lung disease, mechanical ventilation magnifies air-trapping, leading to “pulmonary tamponade.” Varying degrees of this phenomenon should be expected during anesthesia induction. The treatment consists of intermittent apnea with an open ventilator circuit, adjustment of the ventilatory pattern to an I:E ratio of 1:5 or less with moderate tidal volumes, and administration of bronchodilating drugs. Prompt restoration of blood pressure usually ensues. If hypotension persists, other causes of circulatory compromise must be excluded including pneumothorax. With restrictive disease, higher inflation pressures and positive end-expiratory pressure (PEEP) are often required. In both obstructive and restrictive disease, optimal balance of ventilation with hemodynamic stability often necessitates tolerating a degree of hypercapnia. In pulmonary hypertensive patients,

mechanical ventilation usually produces less cardiovascular disturbance if caution is exercised not to increase pulmonary vascular resistance (e.g., from hypoxia, hypercarbia, or lung hyperinflation).

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15(1):143-157.

Triantafillou AN, Heerdt PM, Patterson GA. Lung transplantation. In: Youngberg JA, Lake CA, Roizen MF, et al, eds. *Cardiac, Vascular, and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:703.

Weir EK, Reeves JT, eds. *Pulmonary Vascular Physiology and Pathophysiology.* New York: Marcel Dekker; 1989:241-290.

C.5. How does the physiology of single-lung ventilation influence the procedure?

In laterally positioned patients, gravity helps redistribute blood away from the nonventilated lung during single-lung ventilation and lessen intrapulmonary shunt. In supine patients, this benefit is obviously lost and single-lung ventilation may not be well tolerated. In general, because of large residual lung volumes that will become filled with a high concentration of oxygen during the initial stages of the procedure, lung recipients with severe obstructive lung disease may maintain oxygenation for the first 10 to 15 minutes of single-lung ventilation. However, rapid arterial desaturation may then occur once a substantial portion of the residual volume is absorbed. Alternatively, patients with restrictive lung disease and a low functional residual capacity may rapidly exhibit both hypoxia and hypercarbia if not ventilated. Multiple steps can be taken to improve oxygenation including insufflation of oxygen or CPAP to the nonventilated lung, bronchoscopic-guided suctioning of the ventilated lung, careful manipulation of the ventilatory pattern, and PEEP to the ventilated lung. Differential PEEP/CPAP should be done cautiously, however, because increased airway pressure in the ventilated lung can divert blood toward the nonventilated side. In some patients, intermittent ventilation of the operative lung may have to be performed before pneumonectomy. In general, oxygenation improves after the clamping of the PA supplying the nonventilated lung. For desaturation not responding to the usual maneuvers, tourniquets can be placed around the PA by the surgeon as a temporizing step until dissection permits proper stapling of this vessel.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia, PA: Elsevier Science; 2003:295-314.

Triantafillou AN, Heerdt PM, Patterson GA. Lung transplantation. In: Youngberg JA, Lake CA, Roizen MF, et al, eds. *Cardiac, Vascular, and Thoracic Anesthesia.* New York: Churchill Livingstone; 2000:703.

C.6. How does single-lung ventilation affect cardiopulmonary function? What are the problems of single-lung ventilation in this patient? How would you treat them?

Isolated ventilation of the dependent lung is often accompanied by a marked acute increase in peak inspiratory pressure and a subsequent gradual progressive rise in PA pressure. As noted earlier, because of the beneficial effect of gravity on redistributing blood away from the nondependent nonventilated lung, single-lung ventilation is often tolerated better from a respiratory standpoint by patients undergoing SLT in the lateral position than those undergoing BLT in the supine position. Close monitoring of right ventricular performance during

conversion to single-lung ventilation is extremely important because of the increase in afterload produced by hypoxic vasoconstriction and redistribution of blood flow. Although unusual, if the right ventricle becomes hypokinetic and distended (TEE imaging) or the central venous pressure (CVP) increases disproportionally to the raise in PA pressure, and if the left ventricular ejection fraction decreases, ventilation may have to be altered to minimize the increase in PA pressure.

Triantafillou AN, Pasque MK, Huddleston CB, et al. Predictors, frequency, and indications for cardiopulmonary bypass during lung transplantation in adults. *Ann Thorac Surg*. 1994;57:1248-1251.

C.7. What problems are associated with the lateral position?

SLT is usually performed in the lateral decubitus position, often with the upper leg and pelvis angled to allow groin exposure for potential femoral cannulation and CPB. Not surprisingly, position-related changes in venous return, coupled with compression of the dependent lung by the mediastinum and diaphragm, may promote systemic hypotension and ventilation/perfusion mismatch. Furthermore, PA pressure usually tends to rise after lateral positioning, probably because of gravity-induced shifts in pulmonary blood flow distribution, vascular congestion, and increased vascular resistance.

Triantafillou AN, Heerdt PM, Patterson GA. Lung transplantation. In: Youngberg JA, Lake CA, Roizen MF, et al, eds. *Cardiac, Vascular, and Thoracic Anesthesia.* New York: Churchill Livingstone; 2000:703.

C.8. Should volatile anesthetics be avoided during single-lung ventilation?

Because of experimental evidence demonstrating inhibition of hypoxic pulmonary vasoconstriction (HPV) by the volatile anesthetic agents, some authors have suggested that these drugs be avoided in the anesthetic management of patients with end-stage lung disease requiring single-lung ventilation. However, true clinical significance of these experimental observations remains somewhat controversial. From a clinical standpoint, commonly used doses of isoflurane (e.g., end-tidal concentrations of 1.0% or less) have not been empirically associated with worsening of intrapulmonary shunt and hypoxia. Therefore, isoflurane remains widely used in these patients and may actually benefit some lung recipients because of its bronchodilating properties (also see Chapter 2, section C.13).

Benumof JL. Anesthesia for one-lung ventilation [reply]. *Anesthesiology*. 1988;69:631.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15(1):143-157.

Lumb AB, Slinger P. Hypoxic pulmonary vasoconstriction: physiology and anesthetic implications. *Anesthesiol*. 2015;122:932-946.

Marshall BE. Anesthesia for one-lung ventilation [letter]. *Anesthesiology*. 1988;69:630-631.

C.9. At what specific points in the procedure are problems anticipated?

- Anesthesia induction
- Lateral positioning
- Single-lung ventilation
- Clamping of the PA
- Graft implantation
- Graft reperfusion

C.10. How would you deal with problems related to clamping of the pulmonary artery (PA)?

To assess the cardiopulmonary response to diverting the entire cardiac output through one lung, progressive occlusion of the vessel is first performed manually (Fig. 4.2). Careful assessment of right ventricular function is performed with the TEE looking for evidence of right ventricular distension or hypokinesis. If well tolerated, the vessel is then clamped and stapled. If occlusion is poorly tolerated, the vessel is unclamped and a pulmonary vasodilator such as prostaglandin E_1 or iNO and/or positive inotropic infusion begun. If severe respiratory or cardiovascular derangement persists after reclamping of the vessel despite

pharmacologic intervention, heparin is administered and CPB instituted to avoid profound hypoxia or right ventricular

failure. However, for most patients undergoing SLT, hypoxemia during single-lung ventilation and after PA clamping is rarely a problem and right ventricular performance is adequately maintained.

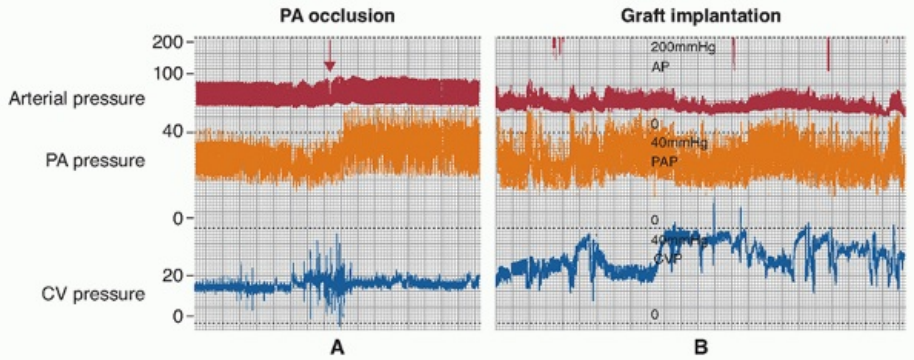


FIGURE 4.2 Tracings of femoral arterial blood pressure, along with pulmonary artery (PA) and central venous (CV) pressures, before and after occlusion of the left PA **(A)** and during implantation of a left lung graft **(B)**. All pressures are in millimeters of mercury. AP, arterial pressure; CVP, central venous pressure; PAP, pulmonary artery pressure.

Triantafillou AN, Heerdt PM, Patterson GA. Lung transplantation. In: Youngberg JA, Lake CA, Roizen MF, et al, eds. *Cardiac, Vascular, and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:703.

C.11. What hemodynamic alterations would you expect during graft implantation and reperfusion? How would you correct them?

During the process of performing the vascular and bronchial anastomoses, major disturbances on cardiac filling and rhythm can be produced (Fig. 4.2). Although often transient, systemic hypotension and pulmonary hypertension can ensue. Transient hypotension may follow the introduction of the vasodilator-containing lung graft preservatives into the systemic circulation. Incomplete de-airing of the lung can lead to coronary artery air embolism, leading to transient myocardial ischemia. The latter is manifested by ST-segment elevation and regional wall motion abnormalities on TEE. This condition is typically responsive to maintaining perfusion pressures with pressors. After reperfusion and subsequent ventilation of the new lung, PA pressures and arterial blood gases should be closely followed. PA pressure usually falls after reperfusion of the donor organ. If a substantial decrease is not observed, potential causes include anastomotic problems with the atrial cuff or the PA. When pulmonary anastomotic problems are suspected, the surgeon should palpate to assess whether the PA catheter is located proximal or distal to the anastomosis. If a proximal location is confirmed, direct measurement of PA pressures should be performed with a needle connected to pressure tubing handed off the operative field. Assessment of the PA and venous flow pattern by TEE can sometimes be of benefit in evaluating adequacy of the anastomoses. Early graft dysfunction can manifest shortly after reperfusion of the first lung and may be the result of various insults. Occurring in 15% to 50% of cases, early graft dysfunction ranges in severity from modest chest radiograph abnormalities and increased inspired oxygen requirements to fulminant pulmonary edema with hypoxia and cardiovascular compromise. Immediate treatment includes adjustment of ventilation, addition of PEEP, and pulmonary vasodilators. iNO may be effective for improving oxygenation and reducing PA pressures, and some clinicians advocate “prophylactic” iNO administration although benefit of this intervention has not been validated. Should graft dysfunction become evident after implantation of the first lung, but before completion of the second lung transplantation, consideration should be given to initiating CPB. When severe hypoxemia persists after lung transplantation despite maximal medical

therapy including the use of iNO, ECMO may be indicated because primary graft dysfunction is the most frequent cause of perioperative mortality following lung transplantation.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia, PA: Elsevier Science; 2003:295-314.

Perrin G, Roch A, Michelet P, et al. Inhaled nitric oxide does not prevent pulmonary edema after lung transplantation measured by lung water content: a randomized clinical study. *Chest*. 2006;129(4):1024-1030.

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Pilcher DV, Snell GI, Scheinkestel CD, et al. High donor age, low donor oxygenation, and high recipient inotrope requirements predict early graft dysfunction in lung transplant recipients. *J Heart Lung Transplant*. 2005;24:1814-1820.

Prekker ME, Herrington CS, Hertz MI, et al. Early trends in PaO2/fraction of inspired oxygen ratio predict outcome in lung transplant recipients with severe primary graft dysfunction. *Chest*. 2007;132:991-997.

C.12. When is cardiopulmonary bypass (CPB) necessary for lung transplantation?

CPB may be used electively for patients with severe PA hypertension, in whom double-lumen endobronchial tubes cannot be placed, or when visualization of hilar structures is poor. However, in the absence of intraoperative complications, CPB is not always used because it may increase bleeding and blood product usage. It has also been suggested that CPB may aggravate postoperative lung dysfunction, although this has not been evident in cases where lung transplant was performed in conjunction with cardiac surgery. Nonetheless, the use of CPB has been associated with longer duration of mechanical ventilation and hospitalization, although it is difficult to differentiate whether the latter results directly from CPB or is the result of a complicated procedure that resulted in the need for CPB. Indications for CPB include right ventricular dysfunction not responding to medical therapy, early graft dysfunction occurring during or prior to implantation of the second lung during bilateral procedures, and surgical misadventures. Unplanned CPB is reported to occur in 12% to 46% of lung transplantation procedures, but predicting which patients may require this intervention is extremely difficult. Some report that CPB is more likely to be necessary for restrictive lung diseases than obstructive diseases. Based on a 2010 review of published lung transplant articles regarding patient outcomes and the use of CPB, there was weak evidence to support using CPB electively, but that using it for clinically indicated cases is appropriate. Essentially, either approach may be clinically appropriate. As noted in an earlier section, the use of CPB may vary based on institution and patient factors.

In attempt to derive the benefits of CPB while reducing complications, some centers advocate the use of heparin-bound ECMO systems. This approach allows for pulmonary support both during and after the procedure with minimal systemic anticoagulation.

Dalibon N, Geffroy AN, Moutafis M, et al. Use of cardiopulmonary bypass for lung transplantation: a 10-year experience. *J Cardiothorac Vasc Anesth*. 2006;20:668-672.

Lau CL, Hoganson DM, Meyers BF, et al. Use of an apical heart suction device for exposure in lung transplantation. *Ann Thorac Surg*. 2006;81(4):1524-1525.

Nagendran M, Maruthappu M, Sugand K. Should double lung transplant be performed with or without cardiopulmonary bypass? *Interact Cardiovasc Thorac Surg*. 2011;12(5):799-804.

Parekh K, Meyers BF, Patterson GA, et al. Outcome of lung transplantation for patients requiring concomitant cardiac surgery. *J Thorac Cardiovasc Surg*. 2005;130(3):859-863.

Triantafillou AN, Pasque MK, Huddleston CB, et al. Predictors, frequency, and indications for cardiopulmonary bypass during lung transplantation in adults. *Ann Thorac Surg*. 1994;57:1248-1251.

C.13. Should fluid administration be restricted, and are blood products commonly required?

The amount of crystalloid that can be safely administered intraoperatively without adversely affecting the graft appears to be widely variable. Although efforts should be made to minimize fluid infusion intraoperatively, many patients undergoing lung transplantation require large amounts to maintain hemodynamic stability. Not uncommonly, central venous and pulmonary capillary wedge pressures of 3 to 5 mm Hg immediately after a transplantation are evident despite infusion of large amounts of crystalloid and colloid as well as only moderate blood loss. The transplanted lung is at risk for pulmonary

edema due to lack of lymphatic drainage and inflammatory insults, direct pulmonary trauma, and inflammatory cytokine release associated with reperfusion and organ harvest. The incidence of postoperative reperfusion pulmonary edema is described as 10% to 35%. Some reports suggest the practice of

fluid restriction and low CVPs. In one study, CVPs greater than 7 mm Hg are correlated with longer intensive care unit stays and higher mortality.

Before the development of the BLT procedure without CPB, patients with a history of surgery involving the lung or pleura or chronic infectious lung diseases were not deemed acceptable candidates for lung transplantation because of the anticipated excessive bleeding associated with dissecting a scarred lung after anticoagulation for CPB. Now, without the uniform requirement for heparinization, such patients are generally regarded as operative candidates. As with other surgical procedures in which hemorrhage is anticipated, continuous infusion of an antifibrinolytic has been proposed to reduce intraoperative bleeding in patients with cystic fibrosis or a history of previous intrathoracic surgery. Variables reported to increase the need for blood product usage include the use of CPB, double-lung procedures, and patients with cystic fibrosis. Transfusion therapy should remain a team decision and warrants a discussion between members of both the anesthesiology and surgical staff. If blood products are to be administered, the anesthesiologist must know whether the patient has antibodies to cytomegalovirus (CMV) and must closely check blood products to confirm they coincide with the patient's status.

Bigham M, Dickstein ML, Hogue CW Jr. Cardiac and lung transplantation. In: Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia: Principles and Clinical Practice*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:637-662.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia, PA: Elsevier Science; 2003:295-314.

Pilcher DV, Scheinkestel CD, Snell GI, et al. High central venous pressure is associated with prolonged mechanical ventilation and increased mortality after lung transplantation. *J Thorac Cardiovasc Surg*. 2005;129:912-918.

Wang Y, Kurichi JE, Blumenthal NP, et al. Multiple variables affecting blood usage in lung transplantation. *J Heart Lung Transplant*. 2006;25(5):533-538.

C.14. Would you extubate the patient upon conclusion of the procedure?

A few studies have shown with proper selection of patients after SLT or BLT that early or immediate tracheal extubation is possible and can be successful. However, because of the frequent use of CPB and the resulting insult often associated with the procedure, the large postoperative volume shifts, hypothermia, and the frequent need for postoperative bronchoscopy, the trachea of lung transplant recipients is not generally extubated immediately after the procedure. Accordingly, unless intraoperative events (e.g., hyperinflation of the remaining intact lung) suggest that postoperative differential lung ventilation will be required, or functional issues such as profound oropharyngeal edema or difficult intubation are present, the double-lumen endotracheal tube is exchanged for a single-lumen tube. In many patients, the endotracheal tube change can be facilitated by use of an exchange catheter. However, great care should be taken to not advance the catheter too far and damage the graft. It is often beneficial to perform fiberoptic bronchoscopy to examine bronchial anastomoses and aggressively suction secretions or blood after replacement of the double-lumen tube with a singlelumen endotracheal tube. As with many procedures, careful inspection of the upper airway for edema should be performed by laryngoscopy before the endotracheal tube is exchanged.

Coccia C, Rocca GD, Costa MG, et al. Very early extubation after lung transplantation. *Eur J Anaesthesiol*. 2002;19:25.

Hansen LN, Ravn JB, Yndgaard S. Early extubation after single-lung transplantation: analysis of the first 106 cases. *J Cardiothorac Vasc Anesth*. 2003;17:36-39.

Rocca GD, Coccia C, Costa GM, et al. Is very early extubation after lung transplantation feasible? *J Cardiothorac Vasc Anesth*. 2003;17:29-35.

D. Postoperative Management

D.1. What are the major complications after lung transplantation?

Early graft dysfunction, episodes of rejection, infection, and airway complication are the major early complications of lung transplantation. Early graft dysfunction varies in severity from mild shunting and chest radiograph infiltrates to gross pulmonary edema with reduced lung

compliance and intrapulmonary shunting. Management includes fluid restriction, diuretics, PEEP, iNO, and ECMO for severe cases. Immunosuppression is usually initiated before surgery, and the induction phase of therapy is continued for 5 to 10 days. The exact regimen varies between institutions but typically includes azathioprine, steroids, cyclosporine, and polyclonal antilymphocyte/antithymocyte globulins or interleukin-2 receptor antagonists. Acute rejection episodes are usually treated with *intense* steroid therapy and optimization of other immunosuppressant dosages. A challenge arises in differentiating acute rejection from infection as a source of shunting and chest radiograph infiltrates. Transbronchial biopsy is often necessary to make the distinction from histologic specimens. Bacterial pneumonia is the most frequent infection in the first 2 weeks. Although unusual in the first 2 weeks after transplantation, CMV is the second most common source of infectious pneumonitis. Broad-spectrum antibiotics are given perioperatively, and the regimen is adjusted based on the results of donor and recipient cultures. Antibiotic therapy for patients with cystic fibrosis is challenging, and the drug chosen is dictated by the patient's cultures and prior history of the organisms colonizing his or her lungs. Prophylactic acyclovir appears to be effective in reducing infections caused by herpes simplex, and trimethoprim-sulfamethoxazole is given to prevent infections from *Pneumocystis carinii*.

Christie JS, Edwards LB, Aurora P, et al. The registry of the International Society for the Heart and Lung Transplantation: twenty-sixth official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant*. 2009;28:1031-1049.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia, PA: Elsevier Science; 2003:295-314.

D.2. How is postoperative ventilation managed, and for how long is it required?

After most procedures, the FIO_2 can be rapidly reduced, and weaning from the ventilator can be initiated as soon as the patient is warm and stable. An exception to this approach is the patient who has undergone SLT for pulmonary hypertension. Because of a propensity for episodes of cardiopulmonary instability during the first 24 to 48 hours postoperatively, it is advantageous to keep these patients mechanically ventilated during this period, although increasing experience is revealing the positive effects of rapid weaning protocols in those patients that tolerate it.

Postoperatively, ventilation/perfusion mismatch and intrapulmonary shunt are often more pronounced after SLT than BLT. Not surprisingly, patients with restrictive disease usually display the best pulmonary function after SLT because the graft receives the majority of both ventilation and perfusion. Alternatively, after SLT in emphysemic patients, the remaining native lung often receives a substantial portion of the tidal volume, whereas in pulmonary hypertensive patients, the native lung continues to be ventilated but receives very little blood flow. On rare occasions, differential ventilation of the transplanted and native lung is needed after SLT for obstructive lung disease. In these situations, the double-lumen endobronchial tube is left in place and two ventilators are employed. The native lung is ventilated with low tidal volume (2 to 3 mL per kg) and rate, or even just connected to CPAP without intermittent mandatory ventilation. Nonetheless, the condition usually resolves rapidly with return of spontaneous ventilation. Postural changes in arterial oxygen saturation are often prominent in SLT recipients. In general, patients who received a single lung for pulmonary hypertension or emphysema display better postoperative pulmonary function with the “transplant side up,” whereas the opposite may be true in certain patients with restrictive lung disease. The precise etiology of this response is unclear but probably reflects positional variation in ventilation/perfusion matching.

Bigham M, Dickstein ML, Hogue CW Jr. Cardiac and lung transplantation. In: Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia: Principles and Clinical Practice*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:637-662.

Triantafillou AN, Heerdt PM, Patterson GA. Lung transplantation. In: Youngberg JA, Lake CA, Roizen MF, et al, eds. *Cardiac, Vascular, and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:703.

D.3. What special precautions should be taken when a lung transplant recipient requires general anesthesia for subsequent nonpulmonary surgery?

In general, after lung transplantation, the patient can be treated like any other fragile immunocompromised patient. Recipients have subsequently undergone various surgical procedures unrelated to their pulmonary disease after lung transplantation and have few anesthetic

problems. Not surprisingly, differences in the compliance and expiratory flow rates of a native and transplanted lung after SLT for emphysema can result in alterations in intraoperative capnography. This phenomenon has been described as producing a biphasic pattern of carbon dioxide exhalation, with the first peak reflecting exhalation from the transplanted lung and the second peak exhalation from the native lung. In addition, the transplanted lung is denervated so the cough reflex is present only in the proximal native airway and mucociliary function is impaired. In contrast, HPV is intact after lung transplantation and central respiratory control is unaffected. However, a blunted response to carbon dioxide may persist for patients with preoperative hypercapnia. The major factor limiting long-term survival from lung transplantation is BOS. This progressive condition characterized by progressive narrowing of small airways must be considered in patients with prior lung transplantation presenting for surgery and anesthesia after the initial recovery phase. Other perioperative considerations for the patient with a prior lung transplant undergoing subsequent surgery are based on whether the patient was the recipient of one versus two lungs. In the former case, ventilation and perfusion of the remaining “diseased” native lung is influenced by the functional status of the transplanted lung. For patients with obstructive lung disease, overinflation of the native lung and resultant mediastinal shift with associated ventilation and hemodynamic consequences, although rare, must be considered when employing positive pressure ventilation.

Although these patients should be assessed with the vigilance applied to patients without a history of transplantation, some points are noteworthy. Patients should be thoroughly evaluated to rule out the presence of an infection. Other preoperative workup should assess presence of renal dysfunction due to immunosuppressive therapy, presence of upper gastrointestinal bleeding due to gastritis and/or peptic ulcer disease, and hepatobiliary and/or pancreatic dysfunction, because these are common in patients after transplantation. Perioperative medications may also include a variety of antibiotic regimens, “stress-dose” steroids, and β-agonists because these patients may be more apt to bronchoconstriction. Aspiration precautions should also be implemented.

Bigham M, Dickstein ML, Hogue CW Jr. Cardiac and lung transplantation. In: Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia: Principles and Clinical Practice*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:637-662.

Kostopanagiotou G, Smyrniotis V, Arkadopoulos N, et al. Anesthetic and perioperative management of adult transplant recipients in nontransplant surgery. *Anesth Analg*. 1999;89:613-622.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia, PA: Elsevier Science; 2003:295-314.

D.4. What are the long-term outcomes of lung transplantation?

Increased experience and improved techniques have made lung transplantation a realistic option for many patients. However, the procedure is not without substantial risk, and a favorable outcome is by no means ensured. There is data to suggest that survival after lung transplant is better in patients with cystic fibrosis, IPAH, sarcoidosis, and α_1-antitrypsin (AAT) deficiency compared with COPD and idiopathic pulmonary fibrosis (IPF). This may be due to the fact that COPD and IPF patients are older and have more comorbidities. As of 2012, 3-month, 1-, 3-, 5-, and 10-year survival rates after lung transplantation are 88%, 80%, 65%, 53%, and 32%, respectively. According to the registry data, the improvement in survival can be attributed to improvements in 1-year survival. Most patients who underwent BLT demonstrated better survival compared with SLT in all disease categories. Interestingly, malignancies (lymphomas early and then skin

malignancies later) accounted for 12% of all deaths between 5 and 10 years after transplant. The major cause of early mortality is graft dysfunction and non-CMV infection, and the major causes of late mortality are non-CMV infection, BOS, and rejection. Survival rates differed significantly by age with lower short- and long-term survival in age groups greater than 50 years of age.

Yusen RD, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first adult lung and heart-lung transplant report—2014; focus theme: retransplantation. *J Heart Lung Transplant*. 2014;33:1009-1024.

D.5. Are there surgical alternatives to lung transplantation?

Some patients with severe emphysema who are not deemed transplant candidates may benefit from lung volume reduction surgery (LVRS) or “reduction pneumoplasty.” Performed either through a median sternotomy or through a bilateral thoracoscopy, the goal of LVRS is to remove up to 30% of the patient's most severely compromised lung tissue. Postoperatively, this allows the previously hyperexpanded chest and depressed diaphragm to resume a more normal shape, therefore improving chest wall mechanics and eventually pulmonary function. However, beneficial effects of the procedure are not immediately evident, usually requiring 1 to 2 months. Furthermore, whether the improvement in pulmonary function is sufficient to warrant the risk of the procedure remains controversial. Nonetheless, recent data indicate that for many patients, LVRS represents a viable alternative to transplantation.

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Tutic M, Lardinois D, Imfeld S, et al. Lung-volume reduction surgery as an alternative or bridging procedure to lung transplantation. *Ann Thorac Surg*. 2006;82(1):208-213.

Chapter 5

Ischemic Heart Disease and Coronary Artery Bypass Grafting

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A 57-year-old man with triple-vessel coronary artery disease (CAD) was scheduled for coronary artery bypass grafting (CABG). He had a myocardial infarction (MI) 7 months ago. He was taking nitroglycerin, digoxin, metoprolol, isosorbide dinitrate (Isordil), and nifedipine. His blood pressure (BP) was 120/80 mm Hg, and his heart rate (HR) was 60 beats per minute.

A. Medical Disease and Differential Diagnosis

1. What is triple-vessel CAD? Name the branches of the coronary arteries.
2. What are the indications for CABG?
3. What is percutaneous coronary intervention (PCI)? Discuss its indications, contraindications, and results.
4. What are the results of CABG?

B. Preoperative Evaluation and Preparation

1. Which preoperative tests would you order?
2. How would you evaluate the patient's left ventricular function?
3. What are the three major determinants of myocardial oxygen consumption? How are they measured clinically?
4. Which factors determine myocardial oxygen supply?
5. Would you discontinue digoxin? Why? What is its half-life?
6. Would you discontinue the β-blocker (metoprolol)? Why? What is its half-life? What is the role of β-adrenergic blockers in treating congestive heart failure (CHF)?
7. If the patient who is on metoprolol develops hypotension intraoperatively, how would you manage it?
8. What is nifedipine? How does it work?

C. Intraoperative Management

C.I. Before Cardiopulmonary Bypass

- How do you monitor the patient?
- What is the Allen's test?
- Should you monitor temperature from multiple sites?

- How do you know that the tip of the pulmonary artery (PA) catheter is in the right ventricle (RV) or the PA?
- What is normal pulmonary artery occlusion pressure (PAOP)?
- Is it necessary to monitor PA pressure for coronary artery operations?
- What are the complications of PA catheterization?
- What are the hemodynamic consequences of myocardial ischemia? How can you detect myocardial ischemia? Is PAOP a sensitive indicator of myocardial ischemia?
- How would you monitor electrocardiogram (ECG)? Why V_5? If you do not have precordial leads in your ECG machine, how can you monitor the left ventricle (LV)?
- Discuss the principles and clinical applications of intraoperative transesophageal two-dimensional echocardiography.
- How would you induce anesthesia?
- How would you maintain anesthesia?
- What is the better anesthetic agent for this operation—an inhalation or intravenous (IV) agent?
- What are the cardiovascular effects of isoflurane, desflurane, sevoflurane, morphine, and fentanyl?
- Is isoflurane dangerous for the patient with CAD?
- What is the cardiovascular effect of nitrous oxide (N_2O)?
- What kind of neuromuscular blocker (NMB) would you use? Why?
- If ST-segment depression is seen during surgery, how would you treat it? What is the relation between perioperative myocardial ischemia and postoperative MI?
- Would you use prophylactic nitroglycerin during CABG to prevent intraoperative myocardial ischemia or perioperative MI?
- How would you correct hypertension?

- How would you treat hypotension?
- What are the indications for IV metoprolol, labetalol, or esmolol during surgery? How much would you give? What are the relative contraindications?
- How would you correct increased PAOP?
- What should you do during sternotomy?
- Would you monitor PAOP continuously? Why?
- Discuss autologous transfusion and blood conservation for cardiac surgery.

C.II. During Cardiopulmonary Bypass

- What anticoagulant would you give before cardiopulmonary bypass (CPB)? How much would you give? What is its mechanism?
- What is the half-life of heparin? How is it eliminated?
- How do you monitor heparin dosage? What is the activated coagulation time (ACT) test?
- What is total CPB? What is partial bypass?
- What is the purpose of venting the LV? How can it be done?
- How many types of oxygenators are there? What are the advantages of each type?
- What kind of priming solution would you use? How much priming solution would you use? When would you prime with blood? Why?
- What are the advantages and disadvantages of hemodilution?
- What kinds of pumps are used in CPB? Are they pulsatile or not?
- How do you monitor the patient during CPB?
- How much BP would you keep during CPB? Why?
- How would you treat hypotension during CPB?

- How would you treat hypertension (a mean arterial pressure [MAP] of over 100 mm Hg)?
- How do you prepare an IV infusion of sodium nitroprusside, nicardipine, and nitroglycerin? What are the usual doses? Which do you prefer to use?
- How much pump flow would you maintain during CPB?
- How would you adjust the pump flow during hypothermia?
- How would you adjust the pump flow during hemodilution?
- What are the advantages of hypothermia? Does hypothermia offer neuroprotection?
- How does blood viscosity change during hypothermia and hemodilution?
- What are the main causes of death associated with accidental hypothermia?
- Would you give anesthesia during CPB? Why?
- Would you give muscle relaxants during CPB? How is the action of muscle relaxant affected during CPB?
- How do you know the patient is well perfused during CPB?
- How much gas flow would you use for the oxygenator? What kind of gas would you use? Why?
- What are the disadvantages of hypocapnia during CPB?
- The arterial blood gases and electrolytes during CPB are as follows: pH, 7.36; $PaCO_2$, 42 mm Hg; PaO_2, 449 mm Hg; CO_2 content, 24 mEq per L; sodium (Na), 128 mEq per L; potassium (K), 5.8 mEq per L; and hematocrit (Hct), 20%. The patient's temperature is 27°C (80.6°F). At what temperature are blood gases measured? How would you correct the blood gases according to patient's body temperature? Would you treat the arterial blood gases at 37°C (98.6°F) or at patient's body temperature?
- If the blood level of the venous reservoir is low, what would you replace it with? Blood or balanced salt solution?
- How do you estimate the fluid balance during CPB?
- How would you preserve the myocardium during CPB?
- What is the cardioplegic solution? How much would you use?
- For how long a period can the aorta be cross-clamped?
- Why would urine become pink in some cases of CPB? What is the renal threshold for plasma hemoglobin?
- At what temperature can the patient be weaned from CPB?
- Why does it take longer to rewarm than to cool the patient by the pump oxygenator?
- How would you defibrillate the heart internally during CPB?
- Why is calcium chloride usually administered right before the patient comes off the pump?
- If the HR is 40 beats per minute, what should you do?
- How does the blood sugar level change during CPB? Why? What is optimal glucose control intraoperatively? Does hyperglycemia increase neurologic complications during CPB?
- What are the effects of CPB on platelet and coagulation factors?
- How would you prepare for termination of CPB?

- How would you decide the need for inotropic support?

C.III. After Cardiopulmonary Bypass

- How would you reverse heparin? How much protamine would you use? What are the other drugs used to neutralize heparin?
- What is the action mechanism of protamine?
- What are the complications of too much protamine?

- Why did the patient develop hypotension after protamine was administered? How do you treat and prevent this condition?
- What are the indications for intra-aortic balloon pump (IABP)?
- What are the principles of IABP?
- What are the complications of IABP?
- Can PAOP represent left ventricular end-diastolic volume (LVEDV) after CABG?

D. Postoperative Management

1. What are the postoperative complications?
2. Would you reverse the muscle relaxants? Why?
3. When will you wean the patient from the respirator?
4. What criteria would you use in deciding when to wean the patient from the respirator?

A. Medical Disease and Differential Diagnosis

A.1. What is triple-vessel CAD? Name the branches of the coronary arteries.

Triple-vessel CAD involves progressive atherosclerosis of the major branches of the coronary arteries with eventual luminal obstruction and myocardial injury. The intimal disease is typically segmental but can be diffuse in severe cases. The coronary arteries are the following:

- The right coronary artery (RCA)
- The left anterior descending (LAD) branch of the left main coronary artery (LMCA)
- The left circumflex (CX) branch of the LMCA

The branches of coronary arteries are shown in Figure 5.1. The LAD and CX arise from the LMCA. The sinus node is supplied by the RCA in approximately 50% to 60% of people and by the CX artery in the remaining 40% to 50%. The atrioventricular (AV) node is supplied

by the RCA in 85% to 90% of people and by the left CX artery in the remaining 10% to 15%; therefore, the RCA is dominant in 85% to 90% of patients. The most common “targets” for coronary bypass grafting are LAD, obtuse marginal (branch of CX), and posterior descending (branch of RCA) arteries.

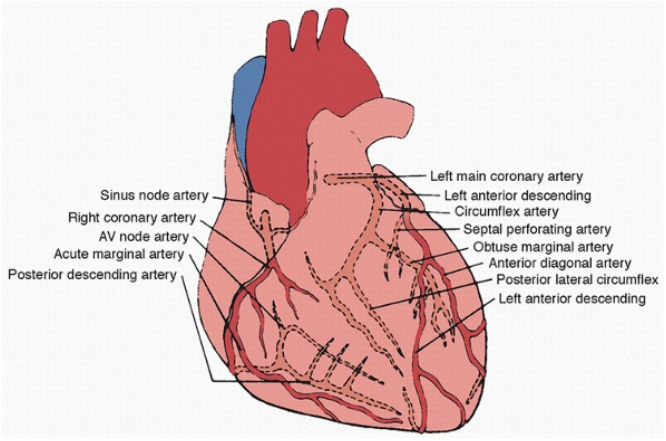


FIGURE 5.1 Branches of the coronary arteries. AV, atrioventricular.

Bonow RO, Mann DL, Zipes DP, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 9th ed. Philadelphia, PA: Saunders Elsevier; 2012:465.

A.2. What are the indications for CABG?

Patients whose angina is not controlled by medical treatment or who have unacceptable side effects with such management should be considered for coronary revascularization. The indications for CABG are as follows:

- Acute myocardial infarction if a nonsurgical intervention failed or there is ischemia at rest or hemodynamic instability/cardiogenic shock or complications, such as ventricular septal defect or ruptured papillary muscle and mitral

regurgitation

- Life-threatening ventricular arrhythmia in the presence of significant left main (>50%) or coronary artery (>70%) obstruction
- At the same time with other cardiac surgical procedures

Bonow RO, Mann DL, Zipes DP, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 9th ed. Philadelphia, PA: Saunders Elsevier; 2012:1353.

Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2011;124:e652-e735.

A.3. What is percutaneous coronary intervention (PCI)? Discuss its indications, contraindications, and results.

PCI has developed rapidly since its introduction in 1977. It is now an acceptable method of treating selected patients who have angina pectoris. This technique involves the passage of a small (3 French) catheter into the involved coronary artery and through the stenosis. With the balloon portion of the catheter straddling the stenosis, inflations are performed that result in enlargement of the stenotic lumen and a controlled injury involving, to a varying degree, plaque compression, intimal fissures, and medial stretching. Following the dilation, coronary stents are introduced to maintain long-term patency. The stents are either baremetal (cobalt-chromium alloy) or drug-eluting stents (DES).

PCI has redefined who is candidate for elective surgical myocardial revascularization. With the current available technology, PCI is considered a therapeutic option in any individual with disabling ischemic symptoms despite good medical therapy and focal obstructive coronary disease regardless of cause. The indications for PCI are as follows:

- Isolated discrete proximal single- or double-vessel disease
- Post-CABG with new stenotic lesions or stenosis at distal anastomosis
- Restenosis following PCI
- Contraindications to CABG
- Coronary stenosis following cardiac transplantation
- Occluded vessels within the last 6 months and less than 15 mm in length
- Post-streptokinase therapy for revascularization

PCI is contraindicated in the following:

- Left main CAD in which the distal coronary vessels are not protected by at least one completely patent large collateral vessel
- Multivessel severe diffuse disease
- Absence of a discrete obstructing lesion

The primary success rate of PCI is approximately 90%, but restenosis occurs at a rate of approximately 30%, 6 months postprocedure. Dilatation can be repeated with a 90% success rate. The artery tends to remain patent after the second angioplasty. With the introduction of

coronary stents, which act as a metal scaffold, the restenosis rate after PCI has been decreasing, and fewer patients require subsequent revascularization: 10% to 15% after stenting versus 25% to 35% after PCI alone. The decrease in luminal diameter following stent placement is evident within the first 6 to 9 months after stent placement and is the result of proliferative neointimal tissue growth in response to the associated injury and inflammation. The stent scaffold is coupled with polymers that elute or slowly release pharmacologic agents (sirolimus, an immunosuppressant, and paclitaxel, an antineoplastic) which inhibit the neointimal growth. The DES have reduced the need for repeat revascularization to an even lower rate, 4% to 6%.

However, the PCI is a different therapeutic approach than CABG. PCI is targeting the area of lesion only, whereas CABG bypasses these lesion areas. This may be the reason that, at least in the intermediate term, CABG is considered to be superior for patients with multivessel disease.

Diegeler et al. showed that, for isolated high-grade lesions of the LAD, CABG through a left anterior thoracotomy is as effective as PCI with stent placement. Although stenting provided excellent short-term results with fewer periprocedural adverse events, CABG was superior with regard to the need for repeated intervention in the target vessel and freedom from angina at 6 months of follow-up. Further, Serruys et al. compared outcomes between PCI with stent and CABG surgery and found that at 5 years, there was no difference in mortality between stenting and surgery for multivessel disease. Importantly, the incidence of stroke or MI was not significantly different between the two groups. However, the rate of major adverse cardiac and cerebrovascular events was higher in the stent group, driven by the increased need for repeat revascularization. A recent report on 10-year outcomes also showed that for the treatment of unprotected LMCA disease, PCI with stent implantation showed similar long-term mortality and rates of death, Q-wave MI, or stroke. However, stenting, even with DES, was associated with higher rates of repeat revascularization than was CABG. Lastly, a recent comparison between stenting and CABG in patients with previously untreated three-vessel disease or LMCA disease concluded that CABG remains the standard of care for patients with three-vessel or LMCA disease because the use of CABG, as compared with PCI, resulted in lower rates of the combined end point of major adverse cardiac or cerebrovascular events at 1 year.

Bonow RO, Mann DL, Zipes DP, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 9th ed. Philadelphia, PA: Saunders Elsevier; 2012:1301.

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left anterior descending coronary artery. *N Engl J Med*. 2002;347:561-566.

Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2011;124:e652-e735.

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Park DW, Kim YH, Yun SC, et al. Long-term outcomes after stenting versus coronary artery bypass grafting for unprotected LMCA disease: 10-year results of bare-metal stents and 5-year results of drug-eluting stents from the ASAN-MAIN (ASAN Medical Center-Left MAIN Revascularization) Registry. *J Am Coll Cardiol*. 2010;56(17):1366-1375.

Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360:961-972.

Serruys PW, Ong AT, van Herwerden LA, et al. Five-year outcomes after coronary stenting versus bypass surgery for the treatment of multivessel disease. *J Am Coll Cardiol*. 2005;46:575-581.

A.4. What are the results of CABG?

Kuan et al. reported a perioperative MI rate of 4% to 6%. The overall operative mortality rate of CABG at major medical centers is approximately 1%. Reoperation is associated with a higher operative mortality, approximately 2% to 3%. Rahimtoola et al. studied the status of patients who underwent CABG for unstable angina over a 10-year period. The 1-month mortality rate was 1.8%. The 5-year survival rate was 92%, and the 10-year survival rate was 83%. CABG was repeated at a rate of 1% to 2% per year; 81% of patients were anginafree or had only mild angina. Cameron et al. found observationally that the 16-year survival rate among the group receiving the internal mammary artery (IMA) graft, as compared with

the group receiving the vein grafts conveyed a greater survival benefit over time. Goldman et al. described a 10-year serial follow-up of patients operated on in the 1980s comparing saphenous vein grafts (SVG) to IMA grafts. They found that the 10-year patency rate for SVG was 61% versus 85% in IMA grafts. Overtime, SVG patency decreased from 95% at 1 week to 61% at 10 years versus 99% to 85% for IMA grafts.

A systematic overview of the seven randomized trials that compared coronary bypass surgery with medical therapy between 1972 and 1984 yielded 2,649 patients. Patients undergoing CABG had a significantly lower mortality at 5, 7, and 10 years, but by 10 years, 41% of the patients initially randomized to medical therapy had undergone CABG. Therefore, coronary bypass surgery prolongs survival in patients with significant left main CAD (irrespective of symptoms) and in patients with three-vessel disease that includes the proximal LAD coronary artery (irrespective of left ventricular function). Surgical therapy also prolongs life expectancy in patients with two-vessel disease and left ventricular dysfunction, particularly in those with a critical stenosis of the proximal LAD coronary artery. Although no study has documented a survival benefit with surgical treatment in patients with single-vessel disease, there is evidence of poor long-term survival rate with medical therapy alone in patients with impaired left ventricular function.

Hannan et al. studied prospectively 37,212 patients who underwent CABG and 22,102 patients who underwent stenting; CABG was associated with a significantly higher likelihood of survival (hazard ratios for death 0.75 for two-vessel CAD and 0.64 for three-vessel CAD, compared with stenting). The CABG patients had significantly lower ejection fractions, were more likely to have had an MI in the week before the procedure, had a significantly higher prevalence of comorbidities, and were significantly more likely to have three-vessel disease.

Magovern et al. reported that use of perioperative statin therapy significantly reduces mortality in high-risk patients undergoing CABG surgery.

Bonow RO, Mann DL, Zipes DP, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 9th ed. Philadelphia, PA: Saunders Elsevier; 2012:1301.

Cameron A, Davis KB, Green G, et al. Coronary bypass surgery with internal-thoracic-artery grafts—effects on survival over a 15-year period. *N Engl J Med*. 1996;334:216-219.

Collard CD, Body SC, Shernan SK, et al. Preoperative statin therapy is associated with reduced cardiac mortality after coronary artery bypass graft surgery. *J Thorac Cardiovasc Surg*. 2006;132(2):392-400.

Goldman S, Zadina K, Moritz T, et al. Long-term patency of saphenous vein and left internal mammary artery grafts after coronary artery bypass surgery: results from a Department of Veterans Affairs Cooperative Study. *J Am Coll Cardiol*. 2004;44(11):2149-2156.

Haase J, Jung T, Störger H, et al. Long-term outcome after implantation of bare metal stents for the treatment of coronary artery disease: rationale for the clinical use of antiproliferative stent coatings. *J Interv Cardiol*. 2003;16(6):469-473.

Hannan EL, Racz MJ, Walford G, et al. Long-term outcomes of coronary-artery bypass grafting versus stent implantation. *N Engl J Med*. 2005;352:2174-2183.

Kandzari DE, Leon MB, Popma JJ, et al. Comparison of zotarolimus-eluting and sirolimus-eluting stents in patients with native coronary artery disease: a randomized controlled trial. *J Am Coll Cardiol*. 2006;48(12):2440-2447. Kuan P, Bernstein SB, Ellestad MH. Coronary artery bypass surgery morbidity. *J Am Coll Cardiol*. 1984;3:1391.

Magovern JA, Moraca RJ, Bailey SH, et al. Preoperative statin is associated with decreased operative mortality in high risk coronary artery bypass patients. *J Cardiothorac Surg.* 2010;5:8.

Rahimtoola SH, Nunley D, Grunkemeier G, et al. Ten-year survival after coronary bypass surgery for unstable angina. *N Engl J Med.* 1983;308:676-681.

B. Preoperative Evaluation and Preparation

B.1. Which preoperative tests would you order?

In addition to the routine systemic examinations of all organ systems, special attention should be paid to the cardiovascular status.

- Renal function—urinalysis, blood urea nitrogen, creatinine
- The routine evaluation of the hepatic function is not any more the standard, unless specifically indicated, that is, previous history of hepatitis or jaundice or the patient is drug abuser.

- Pulmonary function—chest x-ray film (absolutely indicated in reoperated sternotomies to investigate the proximity of the sternum to the anterior surface of the heart), baseline arterial blood gases, and spirometry if indicated
- Hematologic function—complete blood count, prothrombin time, partial thromboplastin time, platelets (platelet function if available and/or indicated; namely, for those patients previously receiving antiplatelet therapy)
- Metabolism—electrolytes and blood sugar
- Cardiovascular function—resting and exercise ECG (if a stress test was performed preoperatively), cardiac catheterization and coronary angiography, location and severity of coronary occlusion, echocardiography, and left ventricular function (from catheterization, magnetic resonance imaging, enhanced multidetector CT, and/or echocardiography)

B.2. How would you evaluate the patient's left ventricular function?

- Medical history: history of MI and presence or absence of angina
- Symptoms and clinical signs of left ventricular failure (dyspnea at rest or exercise, nocturnal orthopnea) and/or right heart failure (ascites, pitting edema, jugular vein distention)
- Cardiac catheterization, angiography, and echocardiography
- Ejection fraction (normally ~65%)
- LVEDP or PAOP: normal 6 to 15 mm Hg
- Left ventricular wall motion (by echocardiography)—normal (wall thickening of >30%), hypokinesis (wall thickening of 10% to 30%), akinesia (wall thickening of <10%), or dyskinesia (outward motion during systole) (Fig. 5.2)

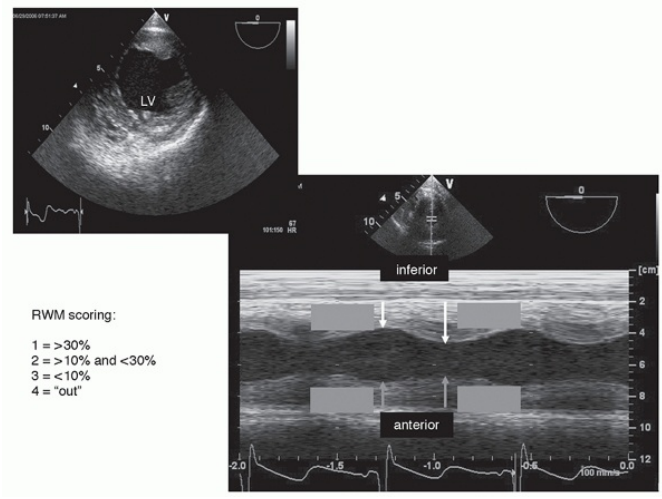


FIGURE 5.2 Echocardiographic evaluation of the left ventricle (LV). The transgastric midpapillary shortaxis view of the left ventricle is shown in left. By placing a cursor line across the middle of the inferior (top of the image) and anterior (bottom of the image) segments of the left ventricular myocardium, the motion of the segments over time is shown in the right image. The percentage of wall thickening can be either visually estimated, or measured, between diastole and systole. RWM, regional wall motion.

- Cardiac index (normal >2.2 L/min/m^2)
- Myocardial viability studies (contrast echocardiography or positron emission tomography study)

Abnormal regional wall motion (RWM) is the result of CAD; the interruption of perfusion results in abnormal motion in the related myocardial segments. There is a gradation of wall motion abnormality that consists progressively of hypokinesis, akinesis, and, subsequently, dyskinesis in which a wall moves away from the center of the ventricle. Wall thickening and

endocardial motion are intrinsically tied, and all regional wall motion abnormalities (RWMA) are expected initially to be associated with abnormalities of thickening as well as endocardial motion (see also Chapter 7, section A.3).

Bonow RO, Mann DL, Zipes DP, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 9th ed. Philadelphia, PA: Saunders Elsevier; 2012:245.

Pagel PS. Cardiac physiology. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:98-131.

Schuleri KH, Centola M, George RT, et al. Characterization of peri-infarct zone heterogeneity by contrastenhanced multidetector computed tomography: a comparison with magnetic resonance imaging. *J Am Coll Cardiol*. 2009;53(18):1699-1707.

B.3. What are the three major determinants of myocardial oxygen consumption? How are they measured clinically?

The three major determinants of myocardial oxygen consumption are myocardial wall tension, contractility, and HR.

Myocardial wall tension is estimated by the following:

- The Laplace equation states that the myocardial wall tension (T) is analogous to the diameter of the ventricle (R, radius) and the intracavitary pressure (P) and inversely proportional to the myocardial wall thickness (Th): T = P × R ÷ 2Th
- Diastolic wall tension is related to the diastolic radius (R) of the ventricle, which is considered a surrogate of preload or LVEDV; the latter is assessed by the PAOP (because neither LVEDP or left atrial pressure can be directly measured).
- Afterload is approximated via the systolic BP, which equals systolic ventricular pressure if there is no aortic stenosis.

Contractility is evaluated by:

- *Invasive techniques.* Maximal velocity of contraction (Vmax), dP/dt (pressure time indices of ventricle: how fast [dt] the intraventricular pressure [dP] develops), or left ventricular end-systolic pressure/volume ratio
- *Noninvasive technique*. Pre-ejection period/left ventricular ejection time, and global and regional ventricular wall motion by echocardiography (Fig. 5.3)

Bonow RO, Mann DL, Zipes DP, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 9th ed. Philadelphia, PA: Saunders Elsevier; 2012:1278.

O'Brien ERM, Nathan HJ. Coronary physiology and atherosclerosis. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:132-156.

B.4. Which factors determine myocardial oxygen supply?

Myocardial oxygen (O_2) supply = coronary blood flow × arterial O_2 content

The coronary blood flow depends on the following:

- Diastolic aortic pressure (DAP)
- LVEDP
- Patency of coronary arteries
- Coronary vascular tone

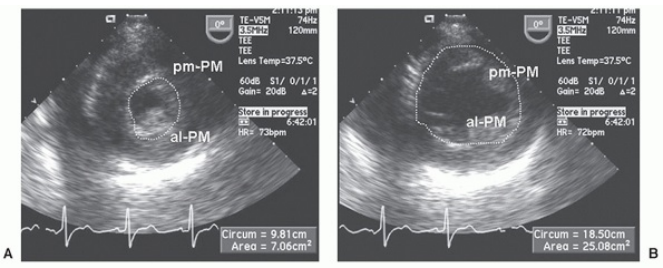


FIGURE 5.3 Echocardiographic evaluation of the systolic function of the left ventricle. The transgastric midpapillary short-axis view of the left ventricle is shown in systole **(A)** and diastole **(B)**. The endocardial border is traced (without including the endocardium of the two papillary muscles), and the end-systolic (ESA) and enddiastolic (EDA) areas are calculated. The percentage area change (fractional area change [FAC]) is calculated as: FAC = (EDA - ESA) / EDA. The FAC correlates with but does not substitute the percentage ejection fraction. al-PM, anterolateral papillary muscle; pm-PM, posteromedial papillary muscle.

And it can be determined by the formula:

Coronary blood flow = coronary perfusion pressure ÷ myocardial vascular resistance, or, Coronary blood flow = (DAP -

LVEDP) ÷ myocardial vascular resistance

The arterial O_2 content (CaO_2) is determined by the following equation:

CaO_2 = 1.34 (mL/g) × hemoglobin concentration (g/dL) × O_2 saturation (%) + (0.0031 × PaO_2)

O'Brien ERM, Nathan HJ. Coronary physiology and atherosclerosis. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:132-156.

B.5. Would you discontinue digoxin? Why? What is its half-life?

In order to prevent digitalis intoxication after CPB, digitalis preparations are usually discontinued one half-life (1.5 to 1.7 days for digoxin, 5 to 7 days for digitoxin) before surgery. Digitalis intoxication is quite possible, especially after CPB when acid-base and electrolytes are abnormal. If a digitalis-dependent patient is in CHF, digitalis is continued until the night before surgery. However, the predisposing factors to digitalis intoxication, especially hypopotassemia and hypercalcemia, have to be prevented.

Royster RL, Butterworth J, Groban L, et al. Cardiovascular pharmacology. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:239-297.

B.6. Would you discontinue the β-blocker (metoprolol)? Why? What is its half-life? What is the role of β-adrenergic blockers in treating congestive heart failure (CHF)?

The *β*-blocker (metoprolol) should be continued not only up until surgery but also throughout the perioperative period. In patients with unstable angina, sudden withdrawal of *β*-blocker may produce an exacerbation of symptoms and may precipitate acute MI. The dose of *β*-blocker does not need to be reduced before surgery for fear of bradycardia, hypotension, or difficulty in weaning from CPB. The half-life of oral propranolol is 3.4 to 6 hours and of metoprolol 3 hours. Both propranolol and metoprolol are metabolized in the liver.

Propranolol disappears from the plasma and atria within 24 to 48 hours after discontinuing doses of 30 to 240 mg per day. It has been shown that with a 0.5-mg dose of propranolol IV, blood levels as high as 50 ng per mL are obtained but rapidly drop off to immeasurable levels within 5 to 10 minutes. No myocardial depression has been seen with these small IV doses. Current advanced cardiac life support guidelines suggest a 5-mg bolus of metoprolol at 5-minute intervals, and a 0.1 mg per kg bolus dose of propranolol divided into three equal doses at 2- to 3-minute intervals.

Reductions in HR with a *β*-blocker (propranolol or metoprolol) occur at lower serum levels than depression of myocardial contractility. Accordingly, as drug levels decrease after discontinuation of therapy, reductions in chronotropic response last longer than reductions in inotropy. This is an important concept in treating tachycardias in patients with significant ventricular dysfunction and CHF: a small dose is appropriate and indicated, whereas a large dose may suppress even further the inotropic state.

Numerous studies have confirmed improvements in cardiac function, exercise capacity, and long-term survival in patients with heart failure resulting from MI, hypertrophic cardiomyopathy, or idiopathic dilated cardiomyopathy with *β*-antagonists. *β*-Antagonists may also be of benefit in patients with diastolic dysfunction, secondary to hypertension.

Potential benefits of *β*-adrenergic blockade in heart failure include decreased HR and normalization of *β*-receptor function. Slower HRs improve diastolic function by increasing the diastolic filling time and myocardial perfusion and by decreasing the myocardial oxygen consumption. *β*-Adrenergic receptors are downregulated in heart failure, but their response is normalized by long-term *β*-blockade. Partial *β*-agonists may provide baseline sympathetic drive but act as antagonists against excessive sympathetic stimulation.

Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2011;124:e652-e735.

Royster RL, Butterworth J, Groban L, et al. Cardiovascular pharmacology. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:239-297.

B.7. If the patient who is on metoprolol develops hypotension intraoperatively, how would you manage it?

The more common causes of intraoperative hypotension, such as hypovolemia, deep anesthesia, and surgical manipulation, should be corrected first. There are no specific antagonists for metoprolol. In rare instances, it is necessary to administer atropine for bradycardia or epinephrine, isoproterenol, glucagon, calcium, or digitalis to counteract the negative inotropic state associated with *β*-blockade. Cardiogenic hypotension is usually associated with high PAOP and low BP.

Royster RL, Butterworth J, Groban L, et al. Cardiovascular pharmacology. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:239-297.

B.8. What is nifedipine? How does it work?

Nifedipine is a calcium channel blocker. At present, verapamil (a phenylalkylamine); diltiazem (a benzothiazepine); nicardipine, nifedipine, isradipine, amlodipine, felodipine, nimodipine, and clevidipine (dihydropyridines); and bepridil (a diarylaminopropylamine ether) are approved for clinical use in the United States. Calcium channel blockers inhibit excitation-contraction coupling of myocardial and smooth muscle by blocking the calcium influx at cellular membranes. This results in decreased myocardial contractility and vasodilation, respectively, and as a consequence, decreased

myocardial oxygen consumption. Calcium channel blockers are effective for the treatment of variant angina (Prinzmetal angina), angina pectoris, and possibly acute MI.

Calcium also plays a key role in cardiac electrical activity. The electrical activity of the sinoatrial (SA) and AV nodal cells are especially dependent on the calcium or “slow” current, whereas the remaining of the specialized conduction system is more dependent on the sodium or “fast” current. Verapamil has a more profound influence on the calcium current of the SA and AV nodes. This drug has been most useful in the treatment of supraventricular tachyarrhythmias, which are often caused by reentry through the AV node. In contrast,

nifedipine and nicardipine have less influence on the SA node and no effect on AV conduction time. Therefore, nifedipine and nicardipine might be used when further suppression of AV conduction is undesirable. The relative cardiovascular effects of calcium channel blockers are shown in Table 5.1. Verapamil was found to profoundly depress the cardiovascular system during high concentrations of halothane or isoflurane anesthesia. However, because of a tendency for increased incidence of sinus arrest and bradycardia and more hemodynamic depression during enflurane anesthesia, Rogers et al. concluded that IV verapamil is better tolerated during low-dose isoflurane and halothane anesthesia.

TABLE 5.1 Relative Cardiovascular Effects of Oral Calcium Channel Blockers

	VERAPAMIL	DILTIAZEM	NIFEDIPINE
Antiarrhythmic	+++	++	-
Cardiac depression	++	+	+
Vasodilation	+	++	+++
Tachycardia	-	-	++

-, No effect; +, mild effect; ++ moderate effect; +++ marked effect.

Curran MP, Robinson DM, Keating GM. Intravenous nicardipine: its use in the short-term treatment of hypertension and various other indications. *Drugs*. 2006;66(13):1755-1782.

Gradman AH, Vivas Y. New drugs for hypertension: what do they offer? *Curr Hypertens Rep*. 2006;8(5):425-432.

Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:239-297.

Rogers K, Hysing ES, Merin RG, et al. Cardiovascular effects of/and interaction between calcium-blocking drugs and anesthetics in chronically instrumented dogs, II: verapamil, enflurane and isoflurane. *Anesthesiology*. 1986;64:568-575.

C. Intraoperative Management

C.I. Before Cardiopulmonary Bypass

C.I-1. How do you monitor the patient?

- ECG—simultaneous leads V_5 and II, multiple-lead ST-segment analysis
- Arterial line for BP and arterial blood gases
- PA catheter—pulmonary and central venous pressures (CVP), hemodynamic parameters (cardiac output, stroke volume, systemic and pulmonary vascular resistance)
- CVP line only—if the patient has good left ventricular function and no problems are expected
- Urine output
- Temperature—esophageal (or PA) and bladder (or rectal, tympanic, or nasopharyngeal)
- Laboratory—arterial blood gases, electrolytes, Hct, ACT, and oxygen saturation of the mixed venous blood (SVO_2)
- Airway pressures and respiratory gases analyzer
- End-tidal carbon dioxide (CO_2) analyzer
- Pulse oximeter for plethysmography (adequacy of peripheral pulse, pulse rate) and arterial oxygenation
- Transesophageal echocardiography (TEE) if not contraindicated. Absolute contraindications are esophagectomy or esophagogastrectomy, active upper gastroesophageal bleeding, or recent surgery, oropharyngeal trauma, and presence of esophageal pathology (tracheoesophageal fistula, stricture, trauma, tumor, scleroderma, Mallory-Weiss tear, and diverticulum). However, the anticipated benefits should be weighed against potential risks in every patient, prior to deciding whether to insert a TEE probe.
- Cerebral oximeter especially for patients with high risk of postoperative neurologic outcomes, such as those undergoing hypothermic circulatory arrest

- Bispectral index to ensure adequate level of unconsciousness and eliminate the risk of intraoperative awareness

C.I-2. What is the Allen's test?

The Allen's test is used to detect the presence of adequate collateral ulnar arterial circulation. The radial and ulnar arteries are occluded by the examiner's fingers, and the patient is then asked to make a tight fist repeatedly until the palmar skin is blanched (to empty the blood from the hand). If the patient is under anesthesia, the blood in the hand may be drained by a third person squeezing the hand. The hand is held above the heart level to help venous drainage. Then, the fist is opened slowly and put down to the heart level. Only the ulnar compression is released, and the flush of the palmar skin is watched. The Allen's test is:

- Normal—if the flush appears in less than 7 seconds (presence of adequate collateral connections between the superficial [ulnar] and deep [radial] palmar arches)
- Borderline—7 to 15 seconds
- Abnormal—greater than 15 seconds

A modified Allen's test may be done with a Doppler detector or a pulse oximeter. The results of Allen's test are abnormal in approximately 3% of young healthy individuals. However, Slogoff et al. studied the complications following radial artery cannulation in 1,699 cardiovascular surgical patients. They concluded that in the absence of peripheral vascular disease, Allen's test is not a predictor of ischemia of the hand during or after radial artery cannulation, and that radial artery cannulation is a low-risk, high-benefit monitoring technique that deserves wide clinical use. However, in the current litigious setting and in the face of some evidence to the contrary, it is probably prudent to continue to perform Allen's test and document the results. Some authorities still consider the use of Allen's test as the standard of care.

Alastruey J, Parker KH, Peiró J, et al. Can the modified Allen's test always detect sufficient collateral flow in the hand? A computational study. *Comput Methods Biomech Biomed Engin*. 2006;9(6):353-361.

Barbeau GR, Arsenault F, Dugas L, et al. Evaluation of the ulnopalmar arterial arches with pulse oximetry and plethysmography: comparison with the Allen's test in 1010 patients. *Am Heart J*. 2004;147(3):489-493.

Brzezinski M, Luisetti T, London MJ. Radial artery cannulation: a comprehensive review of recent anatomic and physiologic investigations. *Anesth Analg*. 2009;109(6):1763-1781.

Cederholm I, Sørensen J, Carlsson C. Thrombosis following percutaneous radial artery cannulation. *Acta Anaesthesiol Scand*. 1986;30:227-230.

Hildick-Smith D. Use of the Allen's test and transradial catheterization. *J Am Coll Cardiol*. 2006;48(6):1287.

Reich DL, Mittnacht A, London M, et al. Monitoring of the heart and vascular system. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:416-451.

Slogoff S, Keats AS, Arlund C. On the safety of radial artery cannulation. *Anesthesiology*. 1983;59:42-47.

C.I-3. Should you monitor temperature from multiple sites?

In many cardiac surgery centers, temperature is measured from two or more sites in order to estimate the accurate core temperature and achieve even distribution of body heat during cooling and rewarming by extracorporeal circulation (ECC). Esophageal, nasopharyngeal, bladder, or tympanic sites measure core temperature; the axillary and rectal sites measure peripheral temperature. Urinary bladder temperature monitoring through a urinary catheter is quite convenient and popular and reflects a body temperature between core and periphery. During cooling and rewarming by ECC, the core temperature changes rapidly, whereas the peripheral temperature changes slowly. The opposite changes are witnessed during surface cooling or warming.

Temperatures are measured during cooling on ECC to ensure that the organs most susceptible to potential hypoperfusion, such as the brain, actually receive the protective effect of the desired hypothermia. In this regard, nasopharyngeal or tympanic membrane temperatures are the monitoring sites, although they, at times, overestimate or underestimate the actual brain temperature. During rewarming, cerebral hyperthermia should be avoided (by maintaining a gradient of 5°C between the arterial blood and brain, with the brain having the lower temperature) and should be corrected immediately because hyperthermia increases the cerebral oxygen consumption and may exacerbate postoperative neuropsychological dysfunction.

Bar-Yosef S, Mathew JP, Newman MF, et al. Prevention of cerebral hyperthermia during cardiac surgery by limiting on-bypass rewarming in combination with post-bypass body surface warming: a feasibility study. *Anesth Analg*. 2004;99:641-646.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:567-568.

Grocott HP, Stafford-Smith M, Mora Mangano CT. Cardiopulmonary bypass management and organ protection. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:838-887.

C.I-4. How do you know that the tip of the pulmonary artery (PA) catheter is in the right ventricle (RV) or the PA?

There are three main differences in the pressure tracings, as shown in Figure 5.4.

Diastolic pressure is higher in PA than in RV because the closed pulmonary valve maintains a diastolic gradient between the PA and the RV.

- PA pressure: 20 to 25/5 to 10 mm Hg
- RV pressure: 20 to 25/0 to 5 mm Hg

Pressure contour

- PA pressure tracing has a dicrotic notch, which is created by the closure of pulmonary valve, and the diastolic part is descending (decreasing).
- RV pressure tracing has a sharp drop and a plateau in early diastole, and the diastolic part is ascending (increasing).

Ventricular filling

- In the late diastolic phase, PA pressure is decreasing because of diastolic runoff in the pulmonary circulation, whereas the RV pressure is increasing because of ventricular filling.

C.I-5. What is normal pulmonary artery occlusion pressure (PAOP)?

- Normal—4 to 12 mm Hg
- Borderline—13 to 17 mm Hg
- Heart failure—over 18 mm Hg

Barash PG, Cullen BF, Stoelting RK, et al. eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013.

C.I-6. Is it necessary to monitor PA pressure for coronary artery operations?

The indication to monitor PA pressure includes the following:

Diagnostic

- Diagnosis of shock states
- Differentiation of high- versus low-pressure pulmonary edema
- Diagnosis of primary pulmonary hypertension

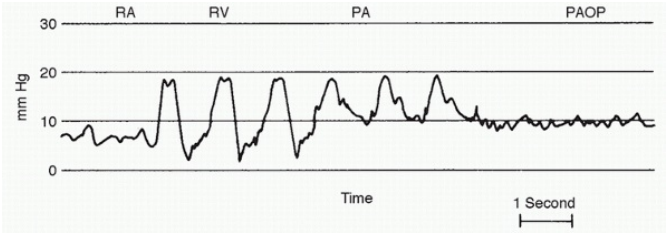


FIGURE 5.4 Pressure tracings of right atrium (RA), right ventricle (RV), pulmonary artery (PA), and pulmonary artery occlusion pressure (PAOP).

- Diagnosis of valvular disease, intracardiac shunts, cardiac tamponade, and pulmonary embolus
- Monitoring and management of complicated acute MI
- Assessing hemodynamic response to therapies
- Management of multiorgan system failure and/or severe burns
- Management of hemodynamic instability after cardiac surgery
- Assessment of response to treatment in patients with primary pulmonary hypertension

Therapeutic: Aspiration of Air Emboli

The indication to monitor PA pressure depends on the ventricular function. For patients who have good left ventricular function (ejection fraction >50% and normal ventricular wall motion), the CVP is considered to correlate well with the PAOP; therefore, PA pressure monitoring may not be necessary for this group of patients. On the other hand, for patients with poor left ventricular function (ejection fractions <40% or prominent wall motion abnormalities), PA pressure monitoring is indicated. Other indications for monitoring PA pressure include the presence of pulmonary hypertension, combined coronary stenosis and valvular disease, and complex cardiac lesions.

However, results of several studies in recent past involving critically ill patients have consistently demonstrated that use of PA catheter was either associated with increased mortality and morbidity or no difference in fatal and nonfatal outcomes as compared to use of CVP alone or other noninvasive monitoring. Much debate exists regarding this topic, and it is

unlikely that there ever will be a resolution. Nevertheless, there has been substantive reduction in the use of the PA catheter both in surgical and medical settings.

Binanay C, Califf RM, Hasselblad V, et al. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *JAMA*. 2005;294(13):1625-1633.

Djaiani G, Karski J, Yudin M, et al. Clinical outcomes in patients undergoing elective coronary artery bypass graft surgery with and without utilization of pulmonary artery catheter-generated data. *J Cardiothorac Vasc Anesth*. 2006;20(3):307-310.

Harvey S, Harrison DA, Singer M, et al. Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): a randomised controlled trial. *Lancet*. 2005;366(9484):472-477.

Harvey S, Young D, Brampton W, et al. Pulmonary artery catheters for adult patients in intensive care. *Cochrane Database Syst Rev*. 2006;(3):CD003408.

Hessel EA, Apostolidou I. Pulmonary artery catheter for coronary artery bypass graft: does it harm our patients? Primum non nocere. *Anesth Analg*. 2011;113:987-989.

Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. *N Engl J Med*. 2003;348(1):5-14.

Schwann NM, Hillel Z, Hoeft A, et al. Lack of effectiveness of the pulmonary artery catheter in cardiac surgery. *Anesth Analg*. 2011;113:994-1002.

Shah MR, Hasselblad V, Stevenson LW, et al. Impact of the pulmonary artery catheter in critically ill patients: meta-analysis of randomized clinical trials. *JAMA*. 2005;294(13):1664-1670.

Vender JS. Pulmonary artery catheter utilization: the use, misuse, or abuse. *J Cardiothorac Vasc Anesth*. 2006;20:295-299.

C.I-7. What are the complications of PA catheterization?

From Venipuncture Sites (as for Central Venous Pressure) Common complications

- Infection—sepsis
- Hematoma
- Air embolism
- Thrombosis
- Catheter shearing and embolization

Subclavian approach

- Pneumothorax
- Hemothorax
- Hydrothorax

Internal jugular approach

- Pneumothorax
- Neck hematoma from puncture of carotid artery
- Possible vagus nerve injury and brachial plexus injury
- Thoracic duct perforation from left-side approach

The basilar or cephalic vein approach has fewer complications, but the failure rate is higher.

From Pulmonary Artery Catheter

Arrhythmias 1.5% to 11%, complete heart block, thromboembolism, pulmonary infarction from continuous wedging, massive hemorrhage from perforation of PA or right atrium (RA), failure to wedge, hemoptysis, intracardiac knotting, balloon rupture, endocardial thrombi, and tricuspid valve injury

Murphy GS, Vender JS. Monitoring the anesthetized patient. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:707-708.

Reich DL, Mittnacht A, London M, et al. Monitoring of the heart and vascular system. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:416-451.

C.I-8. What are the hemodynamic consequences of myocardial ischemia? How can you detect myocardial ischemia? Is PAOP a sensitive indicator of myocardial ischemia?

For four decades following classic observation on the effects of coronary occlusion on myocardial contraction, it was believed that transient severe ischemia caused either irreversible cardiac injury—that is, infarction—or prompt recovery. However, in the 1970s, it became clear that after a brief episode of severe ischemia, prolonged myocardial dysfunction with gradual return of contractile activity occurred, a condition termed *myocardial stunning*. Alternatively, severe chronic ischemia can result in diminished contractile performance manifested by chronic RWMA (*hibernation*).

Acute myocardial ischemia affects systolic and diastolic cardiac function. Diastolic dysfunction usually manifests before alterations in systolic function. The immediate impact on ventricular compliance is related to the etiology of the ischemic event. Decreased myocardial oxygen supply is initially accompanied by an increase in compliance. In contrast, increased myocardial oxygen demand is associated with an immediate loss of ventricular compliance (e.g., the ventricle becomes stiffer). Therefore, the ventricle requires a higher filling pressure (end-diastolic pressure) to maintain a given stroke volume. A cascade of events occurs, which may include wall motion abnormalities, dysrhythmias, and conduction block. An 80% reduction of coronary blood flow causes akinesis (<10% of radial systolic thickening), whereas a 95% decrease causes dyskinesis (thinning, instead of thickening, during systole). If the ischemia becomes severe, the continuously elevated LVEDP will lead to pulmonary edema (Fig. 5.5).

Although a number of sensitive techniques are available for detection of ischemia, such as magnetic resonance spectroscopy, radiolabeled lactate determinations, or direct measurement of end-diastolic pressure, but all are impractical intraoperatively. The most popularly recognized sign of ischemia is ECG ST-segment changes. The ECG criteria for ischemia are horizontal or down-sloping ST-segment depression at least 0.1 mV at 0.06 second from J-point, up-sloping ST-segment depression at least 0.2 mV at 0.08 second from J-point, and ST-segment elevation at least 0.15 mV (1 mV = 10 mm). Other ECG signs of ischemia include inverted T waves and a new onset of arrhythmias or conduction abnormalities.

RWMA, detected with two-dimensional echocardiography, have been shown to be the earliest and most sensitive sign of myocardial ischemia. RWMA appear with just 25% decrease in coronary blood flow in the absence of ECG changes, whereas ECG signs of ischemia are apparent with a 50% decrease in coronary blood flow. During exercise, patients with CAD develop RWMA after 30 seconds, whereas ECG changes do not occur until after 90 seconds. RWMA was four times more sensitive than ECG ST-segment change in detecting intraoperative ischemia. Moreover, ST-segment changes cannot be analyzed if the patient has conduction disturbances, such as bundle branch block or ventricular-paced rhythms. Worsening wall motion after CABG surgery should be considered a prognostic indicator of adverse cardiovascular outcome.

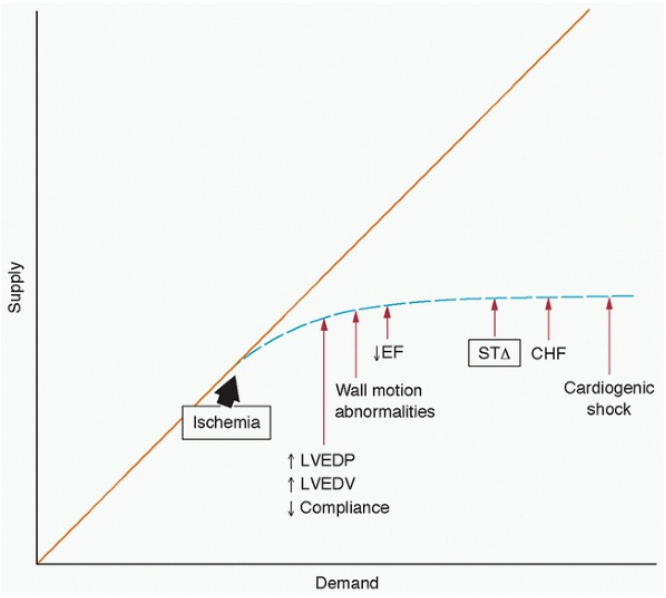


FIGURE 5.5 Hemodynamic consequences of myocardial ischemia. Ischemia occurs when demand exceeds supply. CHF, congestive heart failure; EF, ejection fraction; LVEDP, left ventricular end-diastolic pressure; LVEDV, left ventricular end-diastolic volume; STΔ, ST-segment changes. (From Barash PG. Monitoring myocardial oxygen balance: physiologic basis and clinical application. In: *ASA Refresher Courses in Anesthesiology* . 1985;13:24, with permission.)

Measurement of PAOP has been suggested as an early and sensitive indicator of ischemia to be used when the ECG is not diagnostic. Although acute increases in PAOP or development of V waves may reflect ischemia, the absence of a change in PAOP does not ensure the absence of ischemia. Häggmark et al. reported that the sensitivity, specificity, and predictive value (positive and negative) of PAOP abnormalities for ischemia ranged between 40% and 60%. Leung et al. found that 61% of TEE wall motion abnormalities in CABG patients occurred without significant changes in HR, systolic arterial pressure, or PA pressure. Only 10% of episodes were accompanied by 5 mm Hg or greater changes in PA pressure. These studies question the value of PA catheterization and monitoring for detection of intraoperative ischemia.

Häggmark S, Hohner P, Ostman M, et al. Comparison of hemodynamic, electrocardiographic, mechanical, and metabolic indicators of intraoperative myocardial ischemia in vascular surgical patients with coronary artery disease. *Anesthesiology*. 1989;70:19-25.

Leung JM, O'Kelly B, Browner WS, et al. Prognostic importance of postbypass regional wall-motion abnormalities in patients undergoing coronary artery bypass graft surgery. SPI Research Group. *Anesthesiology*. 1989;71:16-25.

Mantha S, Ochroch EA, Roizen MF, et al. Anesthesia for vascular surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:1108-1135.

Mittnacht AJC, Weiner M, London MJ, et al. Anesthesia for myocardial revascularization. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:522-569.

Swaminathan M, Morris RW, De Meyts DD, et al. Deterioration of regional wall motion immediately after coronary artery bypass graft surgery is associated with long-term major adverse cardiac events. *Anesthesiology*. 2007;107:739-745.

C.I-9. How would you monitor electrocardiogram (ECG)? Why V_5? If you do not have precordial leads in your ECG machine, how can you monitor the left ventricle (LV)?

Multiple-lead ECG monitoring provides the best clinically available method of detecting perioperative ischemia. Based primarily on results obtained from exercise treadmill testing, 96% of ischemic events can be detected by combining ECG leads II and V_5; therefore, leads II and V_5 are the optimal leads for intraoperative myocardial ischemia. However, London et al. found that the standard combination of leads II and V_5 was only 80% sensitive, whereas combining leads V_4 and V_5 increased sensitivity to 90% in patients with known or suspected CAD undergoing noncardiac surgery with general anesthesia. The sensitivity increased to 96% by combining leads II, V_4, and V_5. If only one lead can be displayed, V_5 should be used because lead V_5 has the greatest sensitivity: 75% intraoperatively and 89% during exercise treadmill testing. See also Chapter 14, section C.3.

London MJ, Hollenberg M, Wong MG, et al. Intraoperative myocardial ischemia: localization by continuous 12-lead electrocardiography. *Anesthesiology*. 1988;69:232-241.

C.I-10. Discuss the principles and clinical applications of intraoperative transesophageal two-dimensional echocardiography.

TEE is a well-established technique to visualize cardiac anatomy and function. Echocardiography is based on fundamental ultrasonic principles. Ultrasound is defined as sound above the upper threshold of human hearing (20,000 Hz). The ultrasound waves (1 to 7 MHz) are created by applying an alternating electric current of 500 to 1,500 pulses per second on a piezoelectric crystal. A short burst (pulse) of high-frequency, low-intensity sound is then emitted and directed through the human body to detect boundaries between structures of different acoustic impedance. The ultrasound wave is partially reflected at the boundary of media with different acoustic impedance, a property that is primarily determined by the slight difference in density between different tissues. The transmission of ultrasound through the heart, with detection of the returning echoes detailing the position and movement of cardiac structures, is termed *cardiac ultrasound* or *echocardiography*. Two-dimensional ultrasound reconstructs cardiac anatomy in shades of gray, from the time delay and decreased intensity of the reflected ultrasound. The ultrasound beam sweeps in an arc to give a panoramic view of the heart that results in cross-sectional images that are anatomically recognizable. With M-mode ultrasound, the ultrasonic beam is aimed in one direction only and therefore depicts only one dimension of the target structure in an image that does not resemble cardiac structure. See also Chapter 7, section A.6.

Doppler echocardiography blood flow is measured by applying Doppler frequency shift analysis to echoes reflected by a moving target (red blood cells or cardiac tissue). According to the Doppler principle, the frequency of the reflected ultrasound is different from the frequency of the emitted ultrasound. This change in frequency is proportional to the speed of the moving target. Color-coded Doppler flow imaging (color flow Doppler) simultaneously presents real-time images of intracardiac blood flow and moving cardiac structures in two dimensions. Color flow Doppler permits the evaluation of valvular function and intracardiac shunts.

The clinical applications of intraoperative echocardiography are as follows:

- *Monitoring ventricular volume and function*. When left ventricular short-axis cross section is monitored at the level of the midpapillary muscles, TEE provides the anesthesiologist with a direct, semiquantitative method to assess left ventricular preload and ejection in real time and guide the administration of fluids and inotropes.
- *Monitoring diastolic function*. Both Doppler assessment of transmitral and transpulmonary vein flow patterns can provide important information about diastolic dysfunction that may be prevalent in as many as 50% of patients presenting for open heart surgery, namely, those with history of hypertension, aortic stenosis, and hypertrophic cardiomyopathy. It is important to note that in patients with valvular disease, a component of LV dysfunction arises from abnormal diastolic function.
- *Ischemic heart disease*. RWMA, such as hypokinesia, akinesia, and dyskinesia, are the earliest signs of myocardial ischemia (Figs. 5.2 and 5.3), as discussed in section C.I-8.

Measurements of systolic wall thickening, another excellent sign of myocardial ischemia, are not reproducible because of a difficulty in delineating the epicardial border accurately in two-dimensional echocardiography. The impairment of the diastolic function can be qualitatively estimated, and the filling pressures can be estimated using a combination of spectral Doppler measurements of the blood flow through the pulmonary veins and the mitral valve.

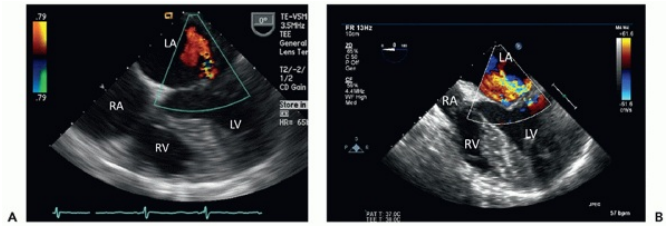


FIGURE 5.6 Color Doppler echocardiography. **A.** Superimposed on a two-dimensional image (here, the midesophageal view), the relative velocities of the red blood cells from a selected area *(triangle)* are visualized. Timed to the ECG (on the bottom of the sector image), normal or abnormal blood flows can be viewed as they cross orifices. In this case, a small regurgitant jet originating from the mitral valve during systole is seen. The color of the jet displays velocity and direction, according to the scale, on the left side of the figure. The mitral regurgitation jet is moving upward toward the left atrium (LA) and is colored red. **B.** In this midesophageal four-chamber view of the left ventricle (LV), a systolic mitral regurgitant jet is directed inside the left atrium. RA, right atrium; RV, right ventricle.

- *Air embolism*. In the left atrium, LV, and aorta, air embolism can be detected by TEE during open heart surgery. Therefore, TEE can be used to help the surgeon evacuate air bubbles from the left heart before the heart ejects blood and air into the systemic circulation.
- *Valvular regurgitation*. Valvular regurgitation can be determined intraoperatively by color Doppler echocardiography before and immediately after conservative valve repair (annuloplasty, commissurotomy) or valve replacement. The degree of valvular incompetency can be accurately measured using a combination of two-dimensional and Doppler techniques (Figs. 5.6 and 5.7), and the function of the repaired or replaced valve can be quantitatively evaluated.
- *Valvular stenosis*. Spectral Doppler echocardiography can be used intraoperatively to measure the pressure gradient across a valvular stenosis and calculate the area of the diseased valve.
- *Congenital heart disease*. TEE techniques allow a more aggressive approach to complex cardiac reconstructions because the surgeon has the ability to visualize the heart and evaluate adequacy of the surgical repair immediately after the operative procedure.
- *Thoracic aorta*. TEE can accurately diagnose thoracic aortic aneurysm, dissection, disruption, and atheroma. Epiaortic echocardiography is performed to examine the ascending aorta and arch if severe atheroma is found in the descending aorta or arch by TEE. Severe atheroma of thoracic aorta is an independent predictor of postoperative neurologic outcome. The atheroma is graded as follows: grade I, normal to mild intimal thickening; grade II, severe intimal thickening; grade III, atheroma protruding less than 5 mm into the lumen; grade IV, atheroma protruding greater than 5 mm; and grade V, atheroma with a mobile component (Fig. 5.8).
- *Cardiac tumors*. Atrial myxoma can be easily diagnosed by TEE. Preoperative and postoperative TEE with contrast can assess the presence and severity of mitral regurgitation secondary to valve damage from a ball-valve effect of the myxoma.

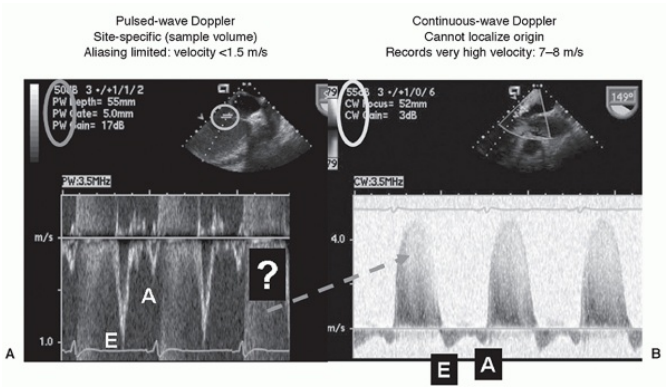


FIGURE 5.7 Doppler mode. **A.** A typical pulsed-wave (PW) Doppler velocity consists of a spectral recording of varying intensity, depending on the acoustic density of the reflected interface (the mass of blood cells). The most dense (or brightest) portion of the spectral tracing represents the velocity of most blood cells. The velocity is recorded from a specific site *(white circle)*, and the maximum velocity recorded is limited (usually <1.5 m per second). In this PW Doppler spectrum, *E* represents the diastolic early filling, and *A* the diastolic late (due to atrial contraction) velocity. During systole, there is a broad signal *(question mark)* representing systolic flow through the mitral valve (probably mitral regurgitation). However, neither the direction nor the peak velocity can be visualized. **B.** In contrast, continuous-wave (CW) Doppler records the velocities of all the red blood cells moving along the path of the sound beam. A CW Doppler recording always consists of a full spectral envelope with the outer border corresponding to the fastest moving blood cells. The site of origin of a high-velocity jet is inferred from the particular lesion that is being examined. The maximum velocity that can be recorded can be as high as 8 m per second. Here, the direction (from bottom to top, or from the left ventricle toward the left atrium) as well as the maximum systolic velocity (˜5 m per second) can be visualized, detailing the mitral regurgitation jet.

- *Other cardiac pathology*. Hypertrophic obstructive cardiomyopathy (HOCM) (idiopathic hypertrophic subaortic stenosis) can be identified by the combination of systolic anterior motion of the mitral valve and left ventricular outflow obstruction. Cardiac tamponade caused by a pericardial effusion or hematoma can be detected.
- *Neurosurgery*. TEE was found to be the most sensitive monitor to detect venous air embolism during neurosurgical operations in the sitting position. Patent foramen ovale and paradoxical air embolism can be detected by TEE.
- *Monitoring for noncardiac surgery*. Recent guidelines by Porter et al. suggest the utility of TEE in healthy patients who are acutely hemodynamically unstable during surgery, critically ill patients with significant respiratory and cardiac diseases undergoing noncardiac surgery, and patients undergoing high-risk noncardiac procedures, such as orthopedic surgery and kidney and liver transplants. TEE would be used as a hemodynamic diagnostic and monitoring tool to guide and evaluate effectiveness of therapeutic interventions.

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Kahn RA, Sherman SK, Konstadt SN. Intraoperative echocardiography. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: WB Saunders; 2011:315-382.

Kühl HP, Hanrath P. The impact of transesophageal echocardiography on daily clinical practice. *Eur J Echocardiogr*. 2004;5(6):455-468.

Mahmood F, Matyal R. A quantitative approach to the intraoperative echocardiographic assessment of the mitral valve for repair. *Anesth Analg*. 2015;121:34-58.

Porter TR, Shillcutt SK, Adams MS, et al. Guidelines for the use of echocardiography as a monitor for therapeutic intervention in adults: a report from the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2015;28(1):40-56.

Shapira Y, Vaturi M, Weisenberg DE, et al. Impact of intraoperative transesophageal echocardiography in patients undergoing valve replacement. *Ann Thorac Surg*. 2004;78(2):579-583.

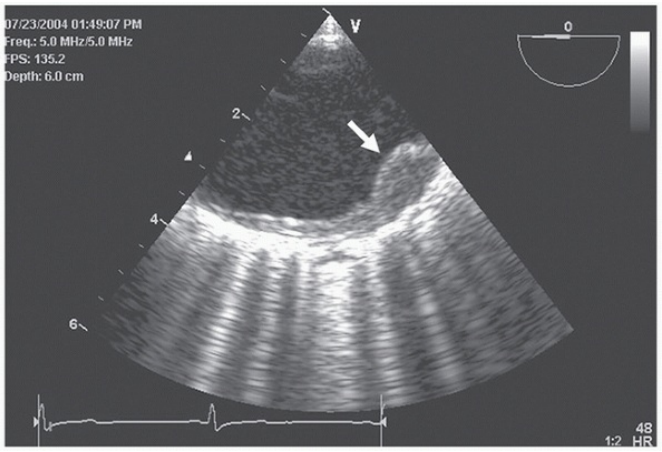


FIGURE 5.8. Atheromatous aortic disease. An echocardiographic picture of the short-axis view of the descending thoracic aorta is shown. The anterior aortic wall is irregularly thickened, and a large atheroma (8 mm) is present at 5 o'clock *(arrow)*. This is a grade IV atheroma.

C.I-11. How would you induce anesthesia?

Midazolam 1 to 2 mg is given as soon as the standard monitors are applied and prior to the arterial line is inserted (under local anesthesia). This is important in alleviating anxiety, which can exacerbate myocardial ischemia. A smooth induction is essential to prevent hypotension, hypertension, and tachycardia. Different techniques may be used to achieve a smooth induction. For patients with good left ventricular function, anesthesia is induced with fentanyl, 2 to 5 μg per kg, and propofol, 1 to 2 mg per kg. The patient is ventilated by mask with 100% oxygen. After administration of a nondepolarizing muscle relaxant (vecuronium, rocuronium), the trachea is intubated. The choice of nondepolarizing muscle relaxant varies extremely from center to among practitioners. Succinylcholine is used less frequently in cardiac surgery. If the patient has a history of hypertension or the initial systolic BP is over 150 mm Hg, lidocaine or a β-blocker (or a mixed α- and β-blocker) is administered. For patients with poor left ventricular function, potent inhalation agents such as isoflurane, sevoflurane, and desflurane should be used cautiously during induction of anesthesia because of their dose-dependent reduction in myocardial contractility and systemic arterial resistance. In lieu of the increasing incidence of delirium in the elderly postoperatively, benzodiazepines should be avoided in patients older than 70 years. Alternatively, etomidate 0.2 mg per kg may be administered for induction. However, it is more important to maintain stable hemodynamics than the choice of induction anesthetic agents. See also

Chapter 11, section C.6 for other measures to prevent tachycardia and hypertension at the time of intubation.

Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:522-569.

Mangusan RF, Hooper V, Denslow SA, et al. Outcomes associated with postoperative delirium after cardiac surgery. *Am J Crit Care*. 2015;24:156-163.

C.I-12. How would you maintain anesthesia?

Again, smooth anesthesia is essential to achieve a balance between myocardial oxygen demand and supply. Different agents and techniques may be used to accomplish the same goal. A combination of fentanyl (or another synthetic opioid) and isoflurane, sevoflurane, or desflurane (or propofol) is a popular choice. After the patient is intubated, a mixture of 60% air and 40% oxygen is administered to lessen the possibility of oxygen toxicity. Clearly, this ratio is subject to underlying pulmonary disease and ongoing intraoperative clinical conditions.

The depth of anesthesia must be titrated to meet the requirements of the varying intensities of surgical stimulation. Skin incision and sternal splitting are very painful. However, the strongest stimulation is usually from sternal retraction with the self-retaining retractor. Fentanyl, around 5 μg (0.1 mL) per kg (or another synthetic opioid), is given right before the skin incision, before sternotomy, and intermittently throughout surgery as needed to maintain adequate analgesia. Very high doses of fentanyl or sufentanil have been successfully used for cardiac anesthesia. There have been significant changes in practice over the past decade, whereby much lower doses of narcotic are administered to facilitate early extubation. Nowadays, maintenance of anesthetic is based on administration of volatile agents and smaller opioid dosages as was the practice in the 1980s and 1990s. Vasoactive agents are also used to regulate the hemodynamics (HR, systemic arterial pressure, and filling pressures).

Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:522-569.

C.I-13. What is the better anesthetic agent for this operation—an inhalation or intravenous (IV) agent?

Both inhalation, IV, and combined agents have been used successfully. Both have advantages and disadvantages. Understanding the cardiovascular effects of each anesthetic agent and careful titration of each drug will improve the balance between myocardial oxygen demand and supply. Early detection and appropriate control of the major determinants of myocardial oxygen consumption (BP, HR, PAOP) are mandatory if myocardial ischemia is to be avoided. Another consideration is the desirability of early extubation. High-dose narcotic and large doses of sedatives and muscle relaxants should be avoided if early extubation is planned.

Studies point toward a beneficial effect of volatile agents in preconditioning the myocardium against an ischemic injury. De Hert et al. reviewed various animal studies that demonstrate exposure of myocardium to volatile anesthetics before ischemia prevents ischemia-reperfusion injury, resulting in better recovery and cardiac function after ischemia. Although in two metaanalyses, Symons and Myles and Yu and Beattie reported that anesthetic choice did not affect incidence of perioperative morbidity and mortality, another two suggest that there is a benefit. In one of these, Landoni et al. performed a meta-analysis isolating studies comparing either desflurane or sevoflurane to total intravenous anesthesia (TIVA) and found that desflurane and sevoflurane significantly decreased the rate of MI and death in patients undergoing cardiac surgery as well as other end points of decreased cardiac biomarker release, MI, and postoperative use of inotropic drugs. Currently, there is significant variability in anesthetic technique during cardiac surgery and no consensus on which technique is superior for cardioprotection.

De Hert SG, Turani F, Mathur S, et al. Cardioprotection with volatile anesthetics: mechanisms and clinical implications. *Anesth Analg*. 2005;100:1584-1593.

De Hert S, Vlasselaers D, Barbé R, et al. A comparison of volatile and non volatile agents for cardioprotection during on-pump coronary surgery. *Anaesthesia*. 2009;64(9):953-960.

Guarracino F, Landoni G, Tritapepe L, et al. Myocardial damage prevented by volatile anesthetics: a multicenter randomized controlled study. *J Cardiothorac Vasc Anesth*. 2006;20(4):477-483.

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Mittnacht AJC, Weiner M, London MJ, et al. Anesthesia for myocardial revascularization. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:522-569.

Riess ML. The rocky road from bench to bedside: beta-blockers and anesthetic postconditioning. *Anesthesiology*. 2009;110:451-452.

Slogoff S, Keats AS, Dear WE, et al. Steal-prone coronary anatomy and myocardial ischemia associated with four primary anesthetic agents in humans. *Anesth Analg*. 1991;72:22-27.

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Symons JA, Myles PS. Myocardial protection with volatile anaesthetic agents during coronary artery bypass surgery:

a meta-analysis. *Br J Anaesth*. 2006;97:127-136.

Tuman KJ, McCarthy RJ, Spiess BD, et al. Does choice of anesthetic agent significantly affect outcome after coronary artery surgery? *Anesthesiology*. 1989;70:189-198.

Yu CH, Beattie WS. The effects of volatile anesthetics on cardiac ischemic complications and mortality in CABG: a meta-analysis. *Can J Anaesth*. 2006;53:906-918.

C.I-14. What are the cardiovascular effects of isoflurane, desflurane, sevoflurane, morphine, and fentanyl?

Isoflurane, desflurane, and sevoflurane all produce a dose-related depression in ventricular function and vascular tonus due to altered Ca_2+ entry and sarcoplasmic reticulum function in myocytes. Out of all the volatile anesthetics, isoflurane causes the most reduction in vascular tone and coronary vasodilation, suggesting the possibility of steal syndrome in patients with CAD. However, there is not conclusive evidence that isoflurane is more harmful than other anesthetics assuming that coronary perfusion pressure is maintained. Compared to the other volatile anesthetics, desflurane causes the most increase in HR. Isoflurane and desflurane may cause tachycardia if the inspiratory concentration is increased rapidly; the mechanism is due to increased sympathetic system outflow.

All of the potent drugs decrease arterial pressure in a dose-related manner. The mechanism of BP decrease includes vasodilation, myocardial depression and decreased cardiac output, and decreased sympathetic nervous system tone.

Narcotics such as morphine and fentanyl at their clinical dose have minimal cardiovascular effects. Both may cause bradycardia. Neither sensitizes the heart to catecholamines or depresses myocardial function. The cardiovascular effects of morphine depend on the dose used. Large doses of morphine sulfate have reportedly caused myocardial lactate production and reduction in coronary blood flow in animals. Sethna et al. found that morphine sulfate, 0.25 mg per kg IV, did not produce a global myocardial ischemia in patients with CAD. High doses of morphine, 1 mg per kg, produce a significant decrease in arterial BP and systemic vascular resistance accompanied by an average 750% increase in plasma histamine. On the other hand, high doses of fentanyl, 50 μg per kg, do not produce any significant changes in BP, vascular resistance, and plasma histamine levels.

Hemmings HC, Egan TD. *Pharmacology and Physiology for Anesthesia: Foundations and Clinical Application* . Philadelphia, PA: Elsevier Saunders; 2013.

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Mittnacht AJC, Weiner M, London MJ, et al. Anesthesia for myocardial revascularization. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:522-569.

Sethna DH, Moffitt EA, Gray RJ, et al. Cardiovascular effects of morphine in patients with coronary arterial disease. *Anesth Analg*. 1982;61:109-114.

Skubas N, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:916-919.

C.I-15. Is isoflurane dangerous for the patient with CAD?

In patients with CAD, the use of isoflurane is still controversial. Reiz et al. reported that 1% isoflurane induced coronary vasodilation that was not related to normal autoregulation

and that both decreased coronary perfusion pressure (systemic hypotension), and redistribution of myocardial blood flow (coronary steal) may contribute to development of regional myocardial ischemia. In Reiz and Ostman study, using 1.5 minimum alveolar concentration (MAC) isoflurane-N_2O anesthesia, concluded that isoflurane may cause coronary steal with myocardial ischemia in patients with CAD. However, Smith et al. reported that the substitution of 0.5% to 1.12% isoflurane for 85 μg per kg of fentanyl did not result in an increased incidence of myocardial ischemia, as seen by ST-segment or segmental wall motion changes in patients with CAD. Moreover, Tarnow et al. demonstrated that 0.5% isoflurane with 50% N_2O improved the tolerance to pacing-induced myocardial ischemia in patients with significant CAD.

Two large-scale prospective outcome studies by Slogoff et al. and Tuman et al. could find no evidence that the incidence of ischemia was increased by isoflurane in patients with CAD undergoing CABG surgery. Furthermore, this finding held true even for patients with steal-prone coronary anatomy in the studies by Slogoff et al., Pulley et al., and Leung et al.

Several animal studies further confused this issue. Priebe proved that isoflurane was a myocardial depressant and a potent coronary vasodilator in the dog. Sill et al. demonstrated that high concentrations of isoflurane (1.5% and 2.5%) dilated intramyocardial arterioles rather than epicardial coronary arteries in the intact dog. Buffington et al. reported that isoflurane (1.2% to 1.5%) produced a decrease in collateral flow and a decrement in collateral zone contraction while enhancing flow in the normally perfused zone. They concluded that isoflurane was an arteriolar vasodilator and hence produced coronary steal in dogs with chronic coronary occlusion. On the contrary, Cason et al. found that in the dog, isoflurane or halothane at 0.5% and 1.5 MAC had little effect on coronary vascular resistance, and ischemia was precipitated by tachycardia or hypotension rather than by coronary steal. Moreover, Davis and Frank demonstrated that isoflurane decreased myocardial infarct size after LAD coronary artery occlusion in dogs. In addition, Gilbert et al. reported greater coronary reserve in swine anesthetized with isoflurane versus halothane at 0.5 to 2.0 MAC. Recently, Hartman et al. demonstrated that adenosine, but not isoflurane, redistributed blood flow away from collateraldependent myocardium in the presence of a coronary steal-prone anatomy in the chronically instrumented dog. They further found that reductions in myocardial perfusion during isoflurane anesthesia depend on systemic arterial pressure and that isoflurane

did not produce coronary steal in this model of multivessel CAD. Furthermore, Cheng et al. found that neither isoflurane nor halothane as the sole anesthetic in clinical concentrations caused significant coronary vasodilation or coronary steal when the coronary perfusion pressure decreased from 55 to 30 mm Hg in a swine model of chronic coronary occlusion with collateral development.

On the basis of recent animal and recent clinical studies, isoflurane in clinical concentrations may be used safely in patients with CAD provided that hypotension and tachycardia are avoided.

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Sill JC, Bove AA, Nugent M, et al. Effects of isoflurane on coronary arteries and coronary arterioles in the intact dog. *Anesthesiology*. 1987;66(3):273-279.

Slogoff S, Keats AS, Dear WE, et al. Steal-prone coronary anatomy and myocardial ischemia associated with four primary anesthetic agents in humans. *Anesth Analg*. 1991;72:22-27.

Smith JS, Cahalan MK, Benefiel DJ, et al. Fentanyl versus fentanyl and isoflurane in patient with impaired left ventricular function. *Anesthesiology*. 1985;63:A18.

Tarnow J, Markschies-Hornung A, Schulte-Sasse U. Isoflurane improves the tolerance to pacing-induced myocardial ischemia. *Anesthesiology*. 1986;64:147-156.

Tuman KJ, McCarthy RJ, Spiess BD, et al. Does choice of anesthetic agent significantly affect outcome after coronary artery surgery? *Anesthesiology*. 1989;70:189-198.

C.I-16. What is the cardiovascular effect of nitrous oxide (N_2O)?

N_2O is a weak central nervous system depressant. It has been generally considered to have minimal effects on other organ systems. N_2O has significant cardiovascular effects that may be depressant or stimulatory, depending on the anesthetics with which it is combined. When high-dose fentanyl is used during coronary surgery, the effects of N_2O

depend on the patient's cardiac function. Following the administration of 50% N_2O, there are no significant changes in any of the hemodynamic parameters in patients with normal left ventricular function (LVEDP <15 mm Hg). On the contrary, there is a significant decrease in cardiac index and stroke volume index in patients with left ventricular dysfunction (LVEDP >15 mm Hg). When added to other inhalation anesthetics, N_2O increases arterial pressure and systemic vascular resistance, suggesting that it has a vasoconstrictive action. N_2O increases pulmonary vascular resistance in patients with mitral stenosis and pulmonary hypertension.

The pulmonary vascular effects of N_2O are also variable. Patients with elevated PA pressure may have further increases when N_2O is added. Konstadt et al. did not corroborate these findings in patients with mitral valvular disease. A study in infants failed to show further increases of pulmonary vascular resistance with the addition of N_2O.

The contribution of N_2O to myocardial ischemia is controversial. Philbin et al. suggested that addition of N_2O to anesthesia with high-dose fentanyl (100 μg per kg followed by 1 μg/kg/min), or sufentanil (30 μg per kg followed by 0.3 μg/kg/min), can produce clinically imperceptible regional myocardial ischemia in the areas supplied by stenotic coronary arteries of dogs. However, monitoring with two-dimensional TEE did not reveal myocardial ischemia in patients with CAD when N_2O was added to low-dose fentanyl (15 μg per kg followed by 0.2 μg/kg/min) or high-dose sufentanil (20 μg per kg).

Clinically, N_2O may be used before CPB if high-dose narcotics are not used and hypotension does not occur. However, after CPB, N_2O should be avoided because of the possibility of expanding any air bubbles remaining in the coronary and cerebral circulation.

In the current clinical practices across the country, N_2O is likely used in very few centers because the most common anesthetic scheme appears to be a balanced anesthetic with variable mixtures of oxygen in air, a potent volatile agent (amnesia), and low-dose fentanyl or sufentanil along with liberal use of vasoactive medications to regulate the hemodynamics.

Balasaraswathi K, Kumar P, Rao TL, et al. Left ventricular end-diastolic pressure (LVEDP) as an index for nitrous oxide use during coronary artery surgery. *Anesthesiology*. 1981;55:708-709.

Cahalan MK, Prakash O, Rulf EN, et al. Addition of nitrous oxide to fentanyl anesthesia does not induce myocardial ischemia in patients with ischemic heart disease. *Anesthesiology*. 1987;67:925-929.

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Messina AG, Yao FS, Canning H, et al. The effect of nitrous oxide on left ventricular pump performance and contractility in patients with coronary artery disease: effect of preoperative ejection fraction. *Anesth Analg*. 1993;77:954-962.

Philbin DM, Föex P, Drummond G, et al. Postsystolic shortening of canine left ventricle supplied by a stenotic coronary artery when nitrous oxide is added in the presence of narcotics. *Anesthesiology*. 1985;62:166-174.

C.I-17. What kind of neuromuscular blocker (NMB) would you use? Why?

Previously, use of pancuronium in cardiac surgery in the United States was popular. When full paralyzing doses are given in a bolus, pancuronium generally produces tachycardia and hypertension caused by vagolytic effect and norepinephrine released from cardiac sympathetic nerves. Pancuronium is an attractive agent to avoid hypotension and bradycardia (HR <50 beats per minute) when both the systolic BP and the HR are on the thresholds of normal. Theoretically, pancuronium may increase myocardial oxygen consumption caused by tachycardia and hypertension. In practice, most patients with CAD receive β-adrenergic blocking agents, which can counteract the vagolytic effects of pancuronium. Additionally, bradycardia associated with the popular narcotic-based anesthetic techniques can attenuate the tachycardia induced by pancuronium. Rocuronium, vecuronium, and cisatracurium have no major cardiovascular effects, but their intermediate duration of action may necessitate repeated administration of the relaxant. Pancuronium has fallen out of favor for use in muscle relaxation because of studies demonstrating residual paralysis is common even if given as a single dose during induction of anesthesia.

The need for muscle relaxation after intubation during cardiac surgery was challenged by a prospective study by Gueret et al. where 87 patients undergoing normothermic CPB were given a single dose of atracurium (0.5 mg per kg) or cisatracurium (0.15 mg per kg). They found that the patients did not move during surgery and did not have diaphragmatic contractions. Moreover, the surgeons did not observe any negative impact during the surgery. They concluded that if anesthetic depth is well maintained throughout surgery, there is no need for continuous neuromuscular blockade.

With the advent of off-pump CABG and minimally invasive coronary artery surgeries that have resulted in smaller incisions and shorter operating times, there has being increasing interest in “fast-track” cardiac anesthesia, defined by Murphy et al. as extubation 1 to 6 hours postoperatively. It is achieved by using decreased amount of opioids and use of short-acting NMBs to ensure normal neural transmission and adequate respiratory drive at the end of surgery. Concerns about increased incidence of residual neuromuscular blockade has led to a decrease in popularity in pancuronium.

Murphy et al. compared pancuronium (0.08 to 0.1 mg per kg) with rocuronium (0.6 to 0.8 mg per kg) and found that, with similar maintenance dosing of NMB to achieve one to two twitches in the train-of-four (TOF) by facial nerve twitch monitoring and no NMB dosing in the last half hour of surgery, rocuronium was associated with reductions in tracheal extubation times. Using TOF ratios >0.9 as complete neuromuscular recovery, 39 of the 40 patients in the rocuronium group achieved recovery compared to 6 of 39 patients in the pancuronium group. When preparing for extubation, significant neuromuscular blockade was present in the pancuronium group compared with the rocuronium group, and more patients in the pancuronium group (32 of 39) noted at least one symptom of muscle weakness when compared with the rocuronium group (7 of 40).

Gueret G, Rossignol B, Kiss G, et al. Is muscle relaxant necessary for cardiac surgery? *Anesth Analg*. 2004;99:1330-1333.

Hemmerling TM, Russo G, Bracco D. Neuromuscular blockade in cardiac surgery: an update for clinicians. *Ann Card Anaesth*. 2008;11(2):80-90.

Mittnacht AJC, Weiner M, London MJ, et al. Anesthesia for myocardial revascularization. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:522-569.

Murphy GS, Szokol JW, Marymont JH, et al. Recovery of neuromuscular function after cardiac surgery: pancuronium versus rocuronium. *Anesth Analg*. 2003;96:1301-1307.

C.I-18. If ST-segment depression is seen during surgery, how would you treat it? What is the relation between perioperative myocardial ischemia and postoperative MI?

An ST-segment depression is indicating ischemia and should be treated by:

- *Increasing oxygen supply*: correct hypotension (with IV phenylephrine), hypoxemia, anemia
- *Decrease oxygen demand*: correct hypertension, tachycardia, and increased PAOP or CVP by deepening anesthesia with a volatile agent or by using vasodilators (nicardipine or

nitroglycerin) or β-blockers (metoprolol, esmolol, or labetalol). All the major determinants of decreased oxygen demand have to be considered and corrected to their normal levels.

If there are no obvious changes in BP, HR, and pulmonary wedge pressure, nitroglycerin is indicated if coronary spasm is suspected. Nitroglycerin may be given by IV drip. IV nicardipine or diltiazem may also be given to relieve coronary spasm.

Slogoff and Keats reported that perioperative myocardial ischemia occurred in 37% of all patients undergoing CABG. They proved that perioperative MI was almost three times as frequent in patients with ischemia (6.9%) compared with patients without ischemia (2.5%). Intraoperative tachycardia was associated with a higher incidence of myocardial ischemia and infarction. However, Knight et al. demonstrated that 42% of CABG patients had preoperative episodes of myocardial ischemia, 87% of which were clinically silent. They further found that anesthesia and surgery did not worsen the preoperative ischemic pattern. Furthermore, Slogoff and Keats in another study postulated that approximately 90% of new myocardial ischemia observed during anesthesia was the manifestation of silent ischemia observed in the patient before the operation, and only 10% was related to anesthetic management. Therefore, the relationship between intraoperative ischemia and postoperative outcome is still unsolved.

It is important to note that ST-segment changes, suggestive of myocardial ischemia may be observed with alteration of the patients' position, particularly during retraction of the sternum for internal mammary harvesting. In addition to being attentive to the ECG, addressing presence of ischemia by echocardiography and by changes in PA catheter is advised.

Hill AB, Bowley CJ, Nahrwold ML, et al. Intranasal administration of nitroglycerin. *Anesthesiology*. 1981;54:346-348.

Knight AA, Hollenberg M, London MJ, et al. Perioperative myocardial ischemia: importance of the preoperative ischemia pattern. *Anesthesiology*. 1988;68:681-688.

Mangano DT. Perioperative cardiac morbidity. *Anesthesiology*. 1990;72:153-184.

Slogoff S, Keats AS. Does perioperative myocardial ischemia lead to postoperative myocardial infarction? *Anesthesiology*. 1985;62:107-114.

Slogoff S, Keats AS. Randomized trial of primary anesthetic agents on outcome of coronary artery bypass operations. *Anesthesiology*. 1989;70:179-188.

C.I-19. Would you use prophylactic nitroglycerin during CABG to prevent intraoperative myocardial ischemia or perioperative MI?

No. It has been reported that prophylactic administration of nitroglycerin, 0.5 or 1.0 μg/kg/min, during fentanyl anesthesia in patients undergoing CABG did not prevent myocardial ischemia or reduce the incidence of perioperative MI.

Royster RL, Butterworth J, Groban L, et al. Cardiovascular pharmacology. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:239-297.

C.I-20. How would you correct hypertension?

Blood pressure = blood flow × resistance

Hypertension is usually due to inadequate depth of anesthesia and/or activation of the sympathoadrenal pathways that occurs with stress/surgery. Rarely, it is due to fluid overloading. The treatment of hypertension includes the following:

- *Deepening the anesthetic level*. Inhalation agents such as isoflurane and sevoflurane are more effective than narcotics because of their vasodilator effect.
- Administering *vasodilators*, when inhalation agents are not used
- Nicardipine. Dose: 0.5 μg/kg/min, titrate to effect

- Labetalol. Dose: 5-mg increments, titrate to effect
- Nitroglycerin produces more venodilation than arteriolar dilation. Dose: 20 to 200 μg per minute IV drip titration or bolus in 20-μg increments. It is important to note that this

agent affects BP mainly via venodilation, which frequently will drop preload and may lower the cardiac output such that greater fluid intake may be required.

Also, see Chapter 11, section C.10.

C.I-21. How would you treat hypotension?

Hypotension is usually caused by acute hypovolemia, deep anesthesia, bradycardia, or ventricular failure. The treatment options are as follows:

- Increase fluid infusion when CVP or PAOP is low (but beware of hemodilution in patients with anemia) or TEE shows decreased ventricular size.
- Lighten the level of anesthesia or use a vasoconstrictor: phenylephrine, 0.1 mg IV increments, to correct vasodilation produced by anesthesia.
- For bradycardia, epicardial pacing may be used to increase the HR. Rarely, atropine or other chronotropic agent is used. These would include isoproterenol, ephedrine, dobutamine, epinephrine, and dopamine.
- Treat cardiac failure when PAOP is high and TEE shows global hypokinesis (poor diastolic and systolic function):
  - Avoid deep levels of anesthesia.
  - Restrict fluids.
  - Inotropes
    - Epinephrine: 2 to 8 μg per minute IV drip
    - Dobutamine or dopamine: 5 to 20 μg/kg/min IV drip
    - Milrinone 0.025 mg per kg then 0.2 to 0.5 μg/kg/min IV drip
    - Norepinephrine and/or vasopressin if peripheral vascular resistance is low
  - Insertion of an IABP

C.I-22. What are the indications for IV metoprolol, labetalol, or esmolol during surgery? How much would you give? What are the relative contraindications?

Indications

- ST-segment depression associated with tachycardia; no response to deepening the level of anesthesia
- Supraventricular tachycardia
- Recurrent ventricular arrhythmias

Contraindications

- Asthma, reactive chronic obstructive pulmonary disease

Esmolol is cardioselective and appears to have little effect on bronchial or vascular tone at doses that decrease HR in humans. Esmolol is a short-acting β-blocker with an elimination half-life of 9 minutes and a pharmacologic half-life of 10 to 20 minutes. It has been used successfully in low doses in patients with asthma. Esmolol is metabolized rapidly in the blood by an esterase located in the erythrocyte cytoplasm.

Dosage

- Metoprolol, 1- to 2-mg increments every 1 to 2 minutes, total dose 5 to 10 mg
- Esmolol, 10-mg increments up to 0.5 mg per kg followed by 50 to 300 μg/kg/min IV drip
- Labetalol, 5-mg increments, titrate to effect. Not indicated if BP is decreased.

Royster RL, Butterworth J, Groban L, et al. Cardiovascular pharmacology. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:239-297.

C.I-23. How would you correct increased PAOP?

It is important to consider all hemodynamics and not concentrate on one specific abnormal value. Increased PAOP during surgery is usually due to a light level of anesthesia or left ventricular dysfunction. Combining the readings of PAOP and BP will produce a differential diagnosis. Occasionally, an increased PAOP with hypotension and low cardiac output is caused by dynamic obstruction of the left ventricular outflow tract and also found in idiopathic hypertrophic subaortic stenosis. This can be diagnosed by TEE, which demonstrates systolic

anterior motion of mitral valve and left ventricular outflow obstruction, mitral regurgitation, and usually good left ventricular contractility.

Inadequate anesthesia: Increased PAOP with hypertension

- Deepen the level of anesthesia with inhalation agents such as isoflurane, sevoflurane, or an IV agent such as propofol which has vasodilator effects.
- Give a vasodilator. Nitroglycerin is a better venodilator than nitroprusside.

Congestive heart failure: Increased PAOP with hypotension and low cardiac

output

- Lighten the level of anesthesia.
- Use inotropes.
- Restrict fluids.
- Use arterial vasodilators to lower afterload in cases of very poor LV function and/or moderate to severe mitral insufficiency.
- Give diuretics. While an important agent for outpatient and for inpatient and/or postoperative management of heart failure, they have extremely little to *no* role intraoperatively.

Hypertrophic obstructive cardiomyopathy

- *β*-Blocker and volatile agents to decrease HR and contractility
- Fluid loading to keep LV full and decrease LV outflow tract obstruction
- Increase afterload to keep LV full

Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:416-451.

C.I-24. What should you do during sternotomy?

For first-time sternotomy, it is recommended that ventilation be held to protect the lungs from injury from the electric saw.

C.I-25. Would you monitor PAOP continuously? Why?

No. If the Swan-Ganz catheter balloon is inflated continuously, pulmonary infarction or injury distal to the occlusion may ensue. Usually, the gradient between PA diastolic pressure and PAOP is estimated after initial insertion and periodically intraoperatively; PA diastolic pressure is monitored continuously instead.

Skubas N, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1076-1111.

C.I-26. Discuss autologous transfusion and blood conservation for cardiac surgery.

Autologous transfusion is the collection and reinfusion of the patient's own blood or blood components. The realization that homologous blood is responsible for transmission of AIDS, hepatitis, transfusion reaction, and autosensitization has led to increased interest in autologous transfusion and blood conservation. Most often, the easiest, safest, and most cost-effective approach for blood conservation is intraoperative normovolemic hemodilution, pharmacologic treatment, and perioperative blood salvage, while options such as preoperative autologous blood donation, preoperative use of erythropoietin, and intraoperative plasmapheresis are rarely used nowadays.

Preoperative Autologous Blood Donation

Donations are appropriate for properly selected patients with stable CAD, stable valvular disease, and congenital heart disease. The risk of blood donation may be higher for patients with unstable angina or severe aortic stenosis; these patients are usually not considered good candidates for autologous blood donation. The patient should have a hemoglobin of greater than 11 g per dL to donate blood.

The optimal donation period begins 4 to 6 weeks before surgery, and the last donation is usually collected no later than 72 hours before surgery. Despite the potential benefits of the method, it is rarely used currently because of logistical reasons (multiple preoperative visits to the hospital, cost).

Preoperative Use of Erythropoietin

This is an established, efficacious, but relatively expensive therapy to reduce blood transfusions. To optimize the hemoglobin response, oral or IV iron supplementation is recommended.

The method is particularly indicated in anemic patients such as those with renal failure or patients of the Jehovah's Witness faith.

Intraoperative Normovolemic Hemodilution

This is the removal of blood through an arterial or venous catheter immediately after induction of anesthesia, before CPB, or the administration of heparin. Depending on the patient's size and hematocrit, 500 to 1,000 mL of blood is collected into blood bags containing Citrate Phosphate Dextrose Adenine (CPDA-1) anticoagulant and is kept at room temperature.

This blood is spared the rigors of CPB, including hemolysis, platelet destruction, and clotting factor degradation. The autologous blood is transfused after reversal of the heparin with protamine. It has been demonstrated that the effect of 1 unit of fresh whole blood on platelet aggregation after CPB is at least equal, if not superior, to the effect of 8 to 10 stored platelet units. However, if the patient's hematocrit is below 33% or the hemoglobin is below 11 g per dL, normovolemic hemodilution is not recommended because further decreasing the oxygen-carrying capacity may worsen myocardial ischemia. In addition, hemodilution during CPB will further decrease hematocrit to levels that require homologous blood transfusion. Normovolemic hemodilution should be performed cautiously in patients with critical left main coronary stenosis and aortic stenosis because sudden cardiac arrest has been observed during the procedure.

Pharmacologic Treatment

The prophylactic use of *ε*-aminocaproic acid (EACA) and tranexamic acid reduces blood transfusions in cardiac surgery. The synthetic antifibrinolytics, EACA and tranexamic acid, bind to plasminogen and plasmin, thereby

inhibiting binding of plasminogen at the lysine residues of fibrinogen. Effective antifibrinolysis requires a loading dose of 100 to 150 mg per kg for EACA or 10 mg per kg for tranexamic acid and a constant infusion for each at onetenth the loading dose each hour.

Perioperative Blood Salvage

This is the collection and reinfusion of blood lost during and immediately after surgery. The posttransfusion survival of perioperatively salvaged red blood cells has been shown to be comparable to that of allogeneic red blood cells. At the conclusion of CPB, all blood remaining in the oxygenator and bypass circuits should be salvaged and, if needed, infused. Blood salvaged intraoperatively may be transfused directly (unwashed) or processed (washed) before infusion. Commercially available equipment exists for each option. Blood collected by intraoperative salvage represents an excellent source of red blood cells support. However, salvaged blood is deficient in coagulation factors and platelets.

Postoperative blood salvage is another technique of autologous blood transfusion utilizing blood lost following surgery. Blood salvaged following cardiac surgery generally is collected from mediastinal and chest drains and transfused without washing. Because usually it is defibrinated, it does not require anticoagulation before transfusion. Although dilute, the blood is sterile and contains viable red blood cells.

Drummond JC, Petrovich CT. Hemotherapy and hemostasis. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:369-412.

Fergusson DA, Hébert PC, Mazer CD, et al. A comparison of aprotinin and lysine analogues in high-risk cardiac surgery. *N Engl J Med*. 2008;358:2319-2331.

Gravlee GP, Davis RF, Kurusz M, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2000:536-542.

Greilich PE, Jessen ME, Satyanarayana N, et al. The effect of epsilon-aminocaproic acid and aprotinin on fibrinolysis and blood loss in patients undergoing primary, isolated coronary artery bypass surgery: a randomized, double-blind, placebo-controlled, noninferiority trial. *Anesth Analg*. 2009;109:15-24.

Lilly KJ, O'Gara PJ, Treanor PR, et al. Cardiopulmonary bypass: it's not the size, it's how you use it! Review of a comprehensive blood-conservation strategy. *J Extra Corpor Technol*. 2006;36(3):263-268.

Shander A, Moskowitz D, Rijhwani TS. The safety and efficacy of “bloodless” cardiac surgery. *Semin Cardiothorac Vasc Anesth*. 2005;9(1):53-63.

Spahn DR, Casutt M. Eliminating blood transfusions: new aspects and perspectives. *Anesthesiology*. 2000;93:242-255.

Van der Linden P. Perioperative blood conservation strategies: an update for clinicians. *Can J Anaesth*. 2003;50(suppl 6):S1-S2.

C.II. During Cardiopulmonary Bypass

C.II-1. What anticoagulant would you give before cardiopulmonary bypass (CPB)? How much would you give? What is its mechanism?

Heparin has been used conventionally in doses of 300 (200 to 400) units per kg of body weight, assuming an initial concentration of at least 2 to 4 units per mL of whole blood. Empirically, after 2 hours of the initial dose, subsequent doses of 100 units per kg are given for each additional hour of bypass. Because there is marked individual variation, heparin doses are best monitored by the celite-ACT test.

Heparin acts indirectly by means of a plasma cofactor. The heparin cofactor, or antithrombin III (AT III), is an α_2-globulin and a protease inhibitor that neutralizes several activated clotting factors: XIIa, kallikrein, XIa, IXa, Xa, IIa, and XIIIa. AT III forms irreversible complexes with thrombin (IIa) and, as a result, both proteins are inactivated. Inhibition of thrombin and factor Xa accounts for most of the anticoagulant effect of heparin. Heparin increases the rates of the thrombin-antithrombin reaction at least 1,000-fold by serving as a catalytic template to which both the inhibitor and the protease bind. Heparin also binds to cofactor II, a glycoprotein of 65,000 Da that inactivates thrombin independently of AT III. This reaction occurs more slowly and requires higher heparin concentrates than does thrombin inhibition through the heparin-AT III complex.

Spiess BD, Horrow JC, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:949-991.

C.II-2. What is the half-life of heparin? How is it eliminated?

The biologic half-life of heparin varies with dosages and temperature. It has a remarkable individual variation. The average half-life is approximately 100 minutes in normothermic man for the initial doses of 300 units, increasing with higher doses and decreasing temperature. When 100, 400, or 800 units of heparin are given intravenously, the approximate half-life is 1, 2.5, and 5 hours, respectively. Heparin concentrations decline progressively at all temperatures, but the rate of decline is delayed in proportion to the hypothermia.

The primary mechanism for heparin elimination remains uncertain. Heparin appears to be cleared and degraded primarily by the reticuloendothelial system; a small amount of heparin also appears in the urine.

Spiess BD, Horrow JC, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:949-991.

C.II-3. How do you monitor heparin dosage? What is the activated coagulation time (ACT) test?

Heparin therapy can be assessed by the partial thromboplastin time, heparin assay, heparinprotamine titration, and the ACT test. The most convenient and practical method used to monitor heparin therapy in the operating room is the celite-ACT test. There is a very good correlation among the ACT, plasma heparin units, and thrombin time. After central venous injection of a heparin bolus, the onset of maximal ACT prolongation in the radial artery blood sample occurs within 1 minute. Previous work suggested that heparin action peaks 10 to 20 minutes after administration, but this finding probably represented an artifact from other factors prolonging the ACT such as hemodilution and hypothermia. Two milliliters of blood are put into a test tube containing celite to activate coagulation. Then, the tube is kept at 37°C (98.6°F) and clot formation is watched for ACT. The normal control value of ACT is 105 to 167 seconds. A baseline value is determined before the administration of heparin, and the test is repeated 3 to 5 minutes after heparin is given and at intervals of 30 to 60 minutes thereafter. With the dose of heparin in milligrams per kilogram on the vertical axis and ACT in seconds on the horizontal axis, a dose-response curve can be plotted. ACT values are maintained at least twice the control value and should never decrease less than 300 seconds during normothermia.

Precise determination of plasma heparin concentration can also be used. The patient's plasma is incubated with factor Xa in the presence of its inhibitor, Xai. Heparin accelerates

factor Xa inhibition, and residual factor X remaining after 2 minutes is measured and converted to a heparin concentration, expressed in units per milliliter. This method has been shown to decrease the amount of heparin used compared to heparin-ACT dose-response curves. The major disadvantage of this technique is the time delay before results are available.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:504-505.

Shore-Lesserson L. Coagulation monitoring. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:496-521.

C.II-4. What is total CPB? What is partial bypass?

Total bypass indicates that all the venous return from superior and inferior venae cavae, and the coronary sinus is drained to the oxygenator, and no blood is pumped by the RV to the lungs. The PA and systemic pressure tracings become nonpulsatile. Partial bypass means that some of the blood return is still pumped by both RV and LV. Some venous blood is drained to the oxygenator and pumped back to the arterial side. Femoral-femoral bypass is one example of partial CPB.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:674-675.

C.II-5. What is the purpose of venting the LV? How can it be done?

Although all the venous return is bypassed from the RV, 2% to 5% of cardiac output is draining to the LV. This represents the physiologic shunt from the bronchial, Thebesian, and pleural veins. Other sources of blood flow to the left heart during CPB include aortic regurgitation from aortic insufficiency and extracardiac left-to-right shunts such as patent ductus arteriosus and Blalock-Taussig, Waterston, and Potts shunts. The left ventricular sump drain prevents overdistention of the LV, which may cause postpump heart failure. A suction needle inserted proximal to the aortic cross-clamp may serve the same purpose.

Venting of the LV can be accomplished by inserting a catheter to the following sites:

- Aortic root such as cardioplegia cannula for CABG
- Junction of the right superior pulmonary vein and the left atrium and advancing through the left atrium and mitral valve into the LV
- Apex of the LV
- PA or the left atrium only

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:89-92.

C.II-6. How many types of oxygenators are there? What are the advantages of each type?

There are two basic types of oxygenators in terms of their interface with blood.

Direct gas interface

- Disk
- Vertical screen
- Bubble

Without gas interface

- Membrane—solid or microporous
- Fluid—fluid using fluorocarbon liquid

The disk and screen oxygenators are not disposable and have proven to be somewhat difficult to clean, prepare, and resterilize. The bubble oxygenator has the advantages of simplicity, disposability, and relatively low cost.

The disadvantages of gas interface oxygenators include the following:

- Protein denaturation
- Increased fragility of cells

- Susceptibility to hemolysis
- Denaturation of platelet membrane materials resulting in platelet aggregation, clumping
- Formation of air embolism
- Large priming volume
- Variable reservoir level resulting in potential shifts of blood volume between intracorporeal and extracorporeal circuit

Direct gas interface oxygenators are not used anymore. The membrane oxygenator has become more popular, economical, efficient, and less traumatic to blood. Its advantages include the following:

- Less trauma to blood components
- No defoaming
- Decreased complement activation
- Independent control of oxygen and CO_2 exchange
- Use of air-oxygen mixture without the risk of gaseous microemboli

However, the advantage of a membrane oxygenator for a short perfusion (<2 hours) is unclear, although lower plasma hemoglobin levels are present using membrane oxygenators.

The disadvantages of membrane oxygenators include the following:

- Expense
- Potential difficulty in eliminating all bubbles during priming
- Moderately large priming volume

The major differences in changes of clotting factors between the bubble and membrane oxygenators become apparent after 4 to 6 hours of ECC.

Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: a systematic review. *Anesth Analg*. 2015;120:749-769.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:47-50.

Skubas N, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1087. Wegner JA. Oxygenator anatomy and function. *J Cardiothorac Vasc Anesth*. 1997;11:275-281.

C.II-7. What kind of priming solution would you use? How much priming solution would you use? When would you prime with blood? Why?

The usual priming solution includes a balanced salt solution, albumin, and mannitol. The priming volumes vary with the size of the oxygenators used and the tubing volume; most oxygenators for adult patients have priming volumes of 500 to 1,000 mL. In general, blood is added to the oxygenator if the patient is markedly anemic (prepump hematocrit below 30%) or if the priming volume is large in relation to the patient's blood volume, such as in pediatric patients. In order to maintain oxygen-carrying capacity, the hematocrit is kept at levels above 18% to 20%. Mannitol has long been used as an osmotic diuretic in situations where hemolysis or diminished renal function is expected. Mannitol has been found to decrease the incidence of renal failure during hypotension by promoting osmotic diuresis and increasing renal blood flow by decreasing renal vascular resistance. Heparin, 3,000 to 10,000 units, is added to the prime depending on the size of the prime volume. This allows heparin to be distributed over the thrombogenic surfaces of the CPB circuit.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:417-419, 691.

C.II-8. What are the advantages and disadvantages of hemodilution?

Advantages of hemodilution

- An increase in microcirculation due to a reduction of blood viscosity
- Improved oxygen delivery to tissues

- Decreased metabolic acidosis

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- Reduced risk of hypertension
- Reduced blood demands
- Reduced incidence of hepatitis, AIDS, or reactions from blood transfusions
- Reduced postoperative blood loss
- Improved blood flow at lower perfusion pressure, especially during hypothermic perfusion

Disadvantages of hemodilution

- Decreased oxygen-carrying capacity
- Postoperative extracellular fluid overload
- Possible pulmonary edema
- Increased risk of postoperative renal dysfunction
- Hypotension from decreased viscosity and peripheral resistance
- Decreased concentration of calcium, magnesium, phosphate, and zinc

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:411-422.

Habib RH, Zacharias A, Schwann TA, et al. Role of hemodilutional anemia and transfusion during cardiopulmonary bypass in renal injury after coronary revascularization: implications on operative outcomes. *Crit Care Med*. 2005;33:1749-1756.

Karkouti K, Beattie WS, Wijeysundera DN, et al. Hemodilution during cardiopulmonary bypass is an independent risk factor for acute renal failure in adult cardiac surgery. *J Thorac Cardiovasc Surg*. 2005;129:391-400.

Murphy GS, Hessel EA II, Groom RC. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. *Anesth Analg*. 2009;108:1394-1417.

Vermeer H, Teerenstra S, de Sévaux RG, et al. The effect of hemodilution during normothermic cardiac surgery on renal physiology and function: a review. *Perfusion*. 2008;23:329-338.

C.II-9. What kinds of pumps are used in CPB? Are they pulsatile or not?

There are three types of pumps available for modern CPB machines: the double-headed nonocclusive roller pump, the centrifugal blood pump, and the ventricular-type pneumatic or hydraulic pump. Only the first two types are in common use.

The roller pump is the most commonly used pump. It is driven by an afterloadindependent motor. Once the pump speed is set, it will continue the forward displacement of the same blood volume (or even air volume) even if the resistance is increased by kinking or clamping the arterial line. This will result in the rupture of connections between sections of tubing. Some centers use pressure gauges on the arterial inflow line to avoid this type of disaster.

The centrifugal pump is a kinetic pump that operates on the constrained vortex principle. Blood is driven through the pump by centrifugal forces generated by a vortex in the pump. The advantages of centrifugal pumps are as follows:

- Less trauma to blood components than the roller pump
- Less risk of increasing arterial line pressure because blood flow decreases when line resistance is increased
- Inflow responsiveness—if a large quantity of air is introduced into the pump, cohesive forces will no longer exist between layers of blood and pumping will stop.
- Less risk of micro-air embolism because small, low-density air bubbles are trapped in the center of the vortex

Ventricular-type pumps, although potentially more powerful, are rather cumbersome and have not been well accepted. This type of pump is mainly used for pulsatile bypass.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:42-43, 284-288.

Hornick P, Taylor K. Pulsatile and nonpulsatile perfusion: the continuing controversy. *J Cardiothorac Vasc Anesth*. 1997;11:310-315.

Ji B, Undar A. An evaluation of the benefits of pulsatile versus nonpulsatile perfusion during cardiopulmonary bypass procedures in pediatric and adult cardiac patients. *ASAIO J*. 2006;52(4):357-361.

C.II-10. How do you monitor the patient during CPB?

Clinical monitoring

- MAP should be kept between 50 and 100 mm Hg to maintain tissue perfusion. In hypertensive patients and in older patients, a higher MAP is frequently utilized—there is very little support for this in the literature.
- PA pressure should be low or zero to prevent overdistention of the LV.
- CVP should be low or zero to make sure there is no obstruction to venous return from the head (when monitored from a site proximal to the RA) or there is adequate drainage of blood to the CPB circuit (when monitored from inside the

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RA).

- Pump-flow rate should be adequate for tissue perfusion and oxygenation.
- Urine output should be maintained above 1 mL/kg/hr by adequate perfusion.
- ECG
- Electroencephalogram is used in patients in whom cerebral circulation problems may occur.
- Bladder and esophageal temperatures are recorded (tympanic also may be used).
- Anesthesia should be maintained at the appropriate level.
- Pupillary size should remain normal and equal.
- Transcranial Doppler and/or TEE may be used to detect aortic and cerebral embolism.
- Cerebral oximeter to maintain adequate brain oxygen saturation (>40%)

Laboratory monitoring at least once every hour

- Arterial blood gases are kept at normal range.
- Venous PO_2 should be 40 to 45 mm Hg.
- Hematocrit maintained between 20% and 30%
- Electrolytes Na^+, K^+, ionized Ca^{2+}
- ACT measured each hour and maintained above 400 to 480 seconds
- Blood sugar probably should be kept below 250 mg per dL.

Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: a systematic review. *Anesth Analg*. 2015;120:749-769.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:556-565.

Grocott HP, Stafford-Smith M, Mora Mangano CT. Cardiopulmonary bypass management and organ protection. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:838-887.

Murkin JM, Adams SJ, Novick RJ, et al. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. *Anesth Analg*. 2007;104:51-58.

Skubas NJ, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1073-1107.

Yao FS, Tseng CC, Ho CY, et al. Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth*. 2004;18: 552-558.

C.II-11. How much BP would you keep during CPB? Why?

Controversy continues over what constitutes adequate pressures while the patient is on bypass. The MAP is usually maintained at approximately 50 to 100 mm Hg to ensure adequate tissue perfusion. BP depends on cardiac output (pump flow) and total peripheral resistance (TPR). Adequate cardiac output (pump flow) is more important for tissue perfusion than BP.

During hypothermic cardioplegia, higher systemic pressures (mean BP >70 mm Hg) are often avoided because of increased noncoronary collateral blood flow into the heart through the pericardium and pulmonary venous drainage. Such collateral flow of relatively warm blood tends to wash the colder cardioplegic solution out of the heart and decreases the hypothermic protection against myocardial ischemia.

The range of cerebrovascular autoregulation during hypothermia is controversial. Although pooled data from clinical studies indicate a lower autoregulatory threshold of 20

to 30 mm Hg in patients without cerebrovascular disease or preexisting hypertension, other studies suggest a pressure-dependent cerebral circulation when MAP is less than 50 mm Hg. Until prospective studies clearly define the autoregulatory threshold under various clinical conditions, BP of less than 50 mm Hg should be regarded as potential physiologic trespass, which may compromise cerebral circulation. In patients with cerebrovascular disease or hypertension, higher perfusion pressure is recommended. Gold et al. studied 248 patients randomized to either low MAP (50 to 70 mm Hg) or high MAP (80 to 100 mm Hg) during CPB and found a trend toward improvement in cardiac and neurologic outcome with higher MAP. However, MAP had no significant effect on neurologic outcome in those patients at low risk for cerebral embolization (normal to mild aortic atherosclerosis by TEE). Patients at high risk for adverse neurologic outcome (severe aortic atherosclerosis by TEE) had a significantly lower risk of worse neurologic outcome when randomized to higher MAP. More recently, widened pulse pressure was shown to be a better predictor of cerebral and renal ischemic outcomes over that of systolic or diastolic BP. Other recent data suggest that MAP during CPB is not a primary predictor of cognitive decline or stroke following cardiac surgery. However, there was an association among hypotension (<50 mm Hg) and age and decline in spatial and image memory. It is recommended to maintain high MAP during CPB in patients with increased risk of neurologic outcome such as history of cerebrovascular accident or transient ischemic attack, hypertension, carotid stenosis, advanced age, and severe aortic atherosclerosis detected by TEE.

With the recent introduction of noninvasive cerebral oximetry, the frontal cortex oxygen saturation can be monitored by

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near-infrared spectroscopy. The technique measures the oxygen saturation of the mixed arterial and venous blood in the brain cortex. Because the volume of blood is predominantly venous, it reflects the balance between oxygen supply and demand in the brain. Yao et al. showed good correlation between brain oxygen saturations and neurologic and cognitive outcomes. The MAP should be kept at levels enough to maintain adequate cerebral oxygen saturations (at least 70% of baseline values or >40% saturation). In a randomized controlled trial, Murkin et al. showed that in patients undergoing coronary artery bypass in whom cerebral regional oxygen saturation was monitored, profound cerebral desaturation was avoided. This led to significantly fewer incidences of major organ dysfunction and death.

Aronson S, Fontes ML. Hypertension: a new look at an old problem. *Curr Opin Anaesthesiol*. 2006;19:59-64.

Fontes ML. New insights in hypertension. In: *ASA Refresher Courses in Anesthesiology*. 2006;34:43-53.

Gold JP, Charlson ME, Williams-Russo P, et al. Improvement of outcomes after coronary artery bypass. A randomized trial comparing intraoperative high versus low mean arterial pressure. *J Thorac Cardiovasc Surg*. 1995;110:1302-1311.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:383-384.

Hartman GS, Yao FS, Bruefach M, et al. Cardiopulmonary bypass at high pressure reduces stroke incidence in patients with TEE diagnosed severe aortic atheromatous disease. *Anesthesiology*. 1995;83:A141.

Murkin JM, Adams SJ, Novick RJ, et al. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. *Anesth Analg*. 2007;104:51-58.

Murkin JM, Farrar JK, Tweed WA, et al. Cerebral autoregulation and flow/metabolism coupling during cardiopulmonary bypass: the influence of $PaCO_2$. *Anesth Analg*. 1987;66:825-832.

Murphy GS, Hessel EA II, Groom RC. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. *Anesth Analg*. 2009;108:1394-1417.

Newman MF, Kramer D, Croughwell ND, et al. Differential age effects of mean arterial pressure and rewarming on cognitive dysfunction after cardiac surgery. *Anesth Analg*. 1995;81:236-242.

Yao FS, Tseng CC, Ho CY, et al. Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth*. 2004;18(5):552-558

C.II-12. How would you treat hypotension during CPB?

Mean arterial pressure (MAP) = cardiac output (CO) × total peripheral resistance (TPR)

Hypotension may be caused by low cardiac output or low peripheral resistance. First, cardiac output should be corrected by increasing the pump-flow rate. Then, if the cardiac output is

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adequate, peripheral resistance can be raised by giving primarily α-adrenergic vasopressor, phenylephrine in increments of 0.1 mg to raise the MAP to 50 mm Hg. In cases of more profound vasoplegia, agents such as norepinephrine and vasopressin may be required. According to Poiseuille's law, low TPR usually is due to decreased viscosity or increased vascular diameter (vasodilation). During CPB using blood-free priming solutions, total viscosity is reduced by hemodilution, although plasma viscosity is increased by hypothermia. A short period of hypotension with a MAP of approximately 30 to 40 mm Hg usually is seen in the first 5 to 10 minutes of bypass. It is due to the following causes:

- Inadequate pump flow at the beginning of bypass
- Hypoxic vasodilation from initial perfusion with blood-free primes carrying no oxygen
- Vasodilation from vasoactive materials released because of the initial reaction of the serum proteins, blood cells, and platelets with the foreign surfaces of the heart-lung machine
- Decreased plasma levels of catecholamines by hemodilution

Balasaraswathi K, Glisson SN, El-Etr AA, et al. Effect of priming volume on serum catecholamine during cardiopulmonary bypass. *Can Anaesth Soc J*. 1980;27:135-139.

Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: a systematic review. *Anesth Analg*. 2015;120:749-769.

Grocott HP, Stafford-Smith M, Mora Mangano CT. Cardiopulmonary bypass management and organ protection. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:838-887.

C.II-13. How would you treat hypertension (a mean arterial pressure [MAP] of over 100 mm Hg)?

Hypertension during bypass is usually the result of inadequate depth of anesthesia, which causes increased catecholamine output and increased vascular resistance. Pump-flow rate should not be reduced to lower the pressure.

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Low pump flow may cause tissue hypoxia, although BP is high. The most effective treatment involves administering an inhalation agent such as through the vaporizer in the heart-lung machine. IV agents such as propofol, midazolam, and narcotics may be used, but they are frequently not as effective and have to be supplemented with vasodilator drugs. Previously, nitroprusside and nitroglycerin were commonly used, but more recently, the IV calcium channel blockers (nicardipine and clevidipine) are frequently used.

Aronson S, Dyke CM, Stierer KA, et al. The ECLIPSE trials: comparative studies of clevidipine to nitroglycerin, sodium nitroprusside, and nicardipine for acute hypertension treatment in cardiac surgery patients. *Anesth Analg*. 2008;107:1110-1121.

Singla N, Warltier DC, Gandhi SD, et al. Treatment of acute postoperative hypertension in cardiac surgery patients: an efficacy study of clevidipine assessing its postoperative antihypertensive effect in cardiac surgery-2 (ESCAPE-2), a randomized, double-blind, placebo-controlled trial. *Anesth Analg*. 2008;107(1):59-67.

C.II-14. How do you prepare an IV infusion of sodium nitroprusside, nicardipine, and nitroglycerin? What are the usual doses? Which do you prefer to use?

IV solutions may be prepared by adding to 250 mL of 5% dextrose in water 50 mg of nitroglycerin or sodium nitroprusside, or 25 mg of nicardipine, to make a concentration of 200 μg per mL (nitroglycerin or nitroprusside) or 100 μg per mL nicardipine. The usual doses are nitroglycerin or nitroprusside 0.5 to 10 μg/kg/min, or 0.05 μg/kg/min nicardipine, determined by careful titration (Table 5.2). Nitroglycerin or nicardipine infusion is preferred. Sodium nitroprusside dilates both arterial and venous smooth muscle. It is very effective in reducing both preload and afterload. At high doses and prolonged duration, it may cause cyanide and thiocyanate toxicity. Because nitroprusside dilates the intramyocardial arterioles, intracoronary steal may occur. The solution has to be covered with aluminum foil to prevent decomposition from exposure to light. Nitroglycerin primarily causes venodilation, resulting in reduction of preload and myocardial oxygen consumption. At larger doses and by the IV route, it has mild arteriolar dilation and reduces afterload. It has no known toxicity and does not produce intracoronary steal because it dilates epicardial arteries. It may redistribute blood flow to the subendocardium and increase collateral circulation through the myocardium. Nicardipine is

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a systemic and coronary arterial dilator. The afterload is decreased, while the preload is not affected. It may cause a slight increase in HR (reflex tachycardia).

TABLE 5.2 Cardiac Anesthesia Intravenous Medications[a]

DRUG	AMOUNT TO ADD	TOTAL VOLUME WITH D_5W	CONCENTRATION	DOSAGE RANGE
Amicar (EACA)	15 g	150 mL	1 mL = 100 mg 10 mL = 1 g	Load: 10 g over 1/2 hr Maintenance: 1 g/hr × 5 hr
Amiodarone	450 mg	250 mL	1 mL = 1.8 mg	Initial: 150 mg over 10 min Followed by: 1 mg/min × 6 hr (360 mg). Then: 0.5 mg/min × 18 hr
Dexmedetomidine			1 mL = 4 μg	Load: 1.0 μg/kg over 10 min Maintenance: 0.2-0.7 μg/kg/hr
Diltiazem	25 mg	100 mL	1 mL = 0.25 mg	Load: 0.1-0.15 mg/kg Maintenance: 0.5-0.25 μg/kg/min
Dobutamine	500 mg	250 mL	1 gt = 33.3 μg 1 mL = 2 mg	5-20 μg/kg/min
Dopamine	400 mg	250 mL (premixed)	1 gt = 26.6 μg 1 mL = 1.6 mg	Renal: 1-5 μg/kg/min β: 10 μg/kg/min α: 10-15 μg/kg/min
Epinephrine	2 mg	250 mL	8 gtt = 1 μg	2-8 μg/min
Esmolol	5 g	250 mL	1 gt = 333 μg 1 mL = 20 mg	50-300 μg/kg/min
Levophed	8 mg	250 mL	2 gtt = 1 μg	4-32 μg/min
Lidocaine	2 g	500 mL (premixed)	15 gtt = 1 mg 1 mL = 4 mg	1-4 mg/min

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Milrinone	20 mg	100 mL	3 gtt = 1 μg 1 mL = 200 μg	0.375-1 μg/kg/min
Nicardipine	25 mg	250 mL	1 gt = 1.66 μg	Load: 5 mg/hr Maintenance: Increase by 2.5 mg/hr every 15 min Maximum amount: 15 mg/hr
Nitroprusside	50 mg	250 mL (premixed)	1 gt = 3.33 μg	1-10 μg/kg/min
Nitroglycerin	50 mg	250 mL (premixed)	1 gt = 3.33 μg	10-80 μg/min
Phenylephrine	20 mg	250 mL	19 gtt = 25 μg	25-125 μg/min
Procainamide	2 g	500 mL (premixed)	15 gtt = 1 mg 1 mL = 4 mg	Load: 500-1,000 mg (20 mg/min) Dosage: 1-4 mg/min
Sodium bicarbonate	100 mEq	100 mL undiluted	1 mL = 1 mEq	1-3 mEq/kg/hr (titrate to pH)
Tranexamic acid			1 mL = 100 mg	Load: 10 mg/kg Maintenance: 1 mg/kg/hr
Vasopressin	100 units	100 mL	1 mL = 1 unit	Initial dose: 0.04 U/min, 2.4 U/hr Titrate: 0.005-0.01 U/min (0.3-0.6 mL/hr) every 10 min to max of 0.1 U/min or 6 U/hr

[a]There are 60 guttae per milliliter (gtt/mL), therefore, gtt/min = mL/hr.
EACA, ε-aminocaproic acid.

Johnson JO, Grecu L, Lawson NW. Autonomic nervous system: physiology and pharmacology. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:326-368.

C.II-15. How much pump flow would you maintain during CPB?

The pump blood flow is equivalent to cardiac output and to supply tissue oxygenation. The normal average cardiac output for adults is 70 mL/kg/min or 3.1 L/min/m^2. Because of higher metabolism, pediatric patients need higher flow rates for each unit of body weight. Usually, 70% of normal cardiac output is enough to maintain tissue oxygenation. When body surface is used, both pediatric and adult patients require about the same pump flow, 2.2 to 3.1 L/min/m^2. In summary, at normothermia and normal hemoglobin levels, the pump flow is as follows:

Adults 50 to 70 mL/kg/min or 2.2 to 3.1 L/min/m^2

Children 100 to 150 mL/kg/min or 2.2 to 3.1 L/min/m^2

However, some perfusion teams use low-flow (40 mL/kg/min), low-pressure (approximately 40 mm Hg) bypass quite successfully. This technique has the advantages of less bleeding through intracardiac collaterals, less trauma to blood cells and platelets, and lower fluid requirements, but it also has the potential for inadequate organ, especially cerebral, perfusion. Although there have been studies demonstrating good clinical results with low-flow and low-pressure techniques used in conjunction with hypothermia and hemodilution, the minimal safe flow rate during CPB has not been established.

The review article by Oakes and Mangano discussed many studies have shown that CBF remained relatively constant despite variations in flow rate (1.0 to 2.4 L/min/m^2). It mentioned some studies suggesting a low rate of neurologic dysfunction postoperatively from low flow rates, and animal studies suggest visceral organ dysfunction from low flow rates. However, because no large-scale randomized trials have been done, it concluded that optimal flow rate that resulting in good organ perfusion has yet to be determined.

Therefore, pump blood flow should be adjusted accordingly to match the oxygen supply with demand.

Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: a systematic review. *Anesth Analg*. 2015;120:749-769.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:555.

Grocott HP, Stafford-Smith M, Mora Mangano CT. Cardiopulmonary bypass management and organ protection. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:838-887.

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Kolkka R, Hilberman M. Neurologic dysfunction following cardiac operation with low-flow, low-pressure cardiopulmonary bypass. *J Thorac Cardiovasc Surg.* 1980;79:432-437.

Oakes DA, Mangano CT. Cardiopulmonary bypass in 2009: achieving and circulating best practices. *Anesth Analg*. 2009;108:1368-1370.

C.II-16. How would you adjust the pump flow during hypothermia?

Hypothermia decreases oxygen consumption. Therefore, the pump flow may be decreased proportionally if the blood oxygen content does not change. The oxygen consumption at different body temperatures is listed in the following text:

Temperature (°C)	37	32	30	28	25	20	10
O_2 consumption (%)	100	60	50	40	25-30	20	10

Because the O_2 consumption at 30°C (86°F) is half of that at 37°C (98.6°F), the required pump flow at 30°C (86°F) is 50% of the flow at 37°C (98.6°F) (50 to 70 mL/kg/min).

Therefore, a pump flow of 25 to 35 mL/kg/min is adequate for adults at 30°C (86°F) if there is no hemodilution. During profound hypothermia (10°C to 20°C [50°F to 68°F]), the patients usually can tolerate total circulatory arrest without pump support for approximately 60 to 90 minutes. The decrease in metabolism during hypothermia is not a linear process. From 37°C to 30°C (98.6°F to 86°F), the metabolism decreases approximately 7% by each degree centigrade. Below 30°C (86°F), the rate of metabolism decrease slows down. Usually, every 7°C to 8°C (44.4°F to 46.4°F) decrease in temperature reduces oxygen consumption by 50%. Clinically, it has been demonstrated that pump flows as low as 30 mL/kg/min or 1.2 L/min/m^2 will not compromise whole-body oxygen delivery when moderate systemic hypothermia is employed.

C.II-17. How would you adjust the pump flow during hemodilution?

Oxygen delivery = cardiac output × arterial oxygen content Arterial oxygen content = 1.34 × hemoglobin × O_2 saturation + (0.003 × PaO_2)

Hemodilution reduces hemoglobin concentration and hence decreases oxygen content. In order to deliver the same amount of oxygen, the pump flow has to be increased accordingly during hemodilution. For example, if the hematocrit is diluted from 40% to 20% during CPB, the pump flow has to be doubled (increased by a factor of 40 / 20 = 2). Clinically, both hypothermia and hemodilution are applied simultaneously so that the adjustment has to be done at the same time. For example, the pump flow for adults at a temperature of 30°C (86°F) and a hematocrit of 25% will be as follows:

50 to 70 mL/kg/min × 50% × 40/25 = 40 to 56 mL/kg/min

C.II-18. What are the advantages of hypothermia? Does hypothermia offer neuroprotection?

Hypothermia decreases oxygen consumption and helps to preserve the function of tissues during a hypoxic or ischemic insult. However, the balance between oxygen supply and demand can be impaired by reductions in tissue oxygen delivery due to increased blood viscosity, reduced microcirculatory flow, and a leftward shift of the oxygen-hemoglobin dissociation curve.

Hypothermia has been shown to confer significant protection in the setting of transient, but not permanent, ischemia. The mechanism is unclear. The reduction in cerebral metabolic rate is believed to be less important when compared with the effect of hypothermia on the release of excitatory neurotransmitters, catecholamines, or other mediators of cellular injury. It is for this reason that mild hypothermia (33°C to 35°C [91.4°F to 95°F]) provides significant neuroprotection.

The effect of hypothermia during CPB on postoperative cognitive or neurologic function remains controversial. Animal models show profound reduction in infarct size and release of excitatory amino acid with minimal levels of hypothermia. However, clinical studies comparing normothermic and moderately hypothermic CPB have yielded conflicting results and did not produce evidence of protection from cognitive decline. This may relate to differences in defining normothermia. Many groups allow temperature to drift downward during normothermic CPB, with temperature decreasing to below 34°C (93.2°F). McLean and Wong, in a recent study of this type, showed no difference in cognitive or neurologic outcome between warm and moderately hypothermic groups. In actuality, this is a study of mild versus moderate hypothermia confirming the experimental animal data that as little as 2°C to 3°C (35.6°F to 37.4°F) of hypothermia markedly reduces excitatory amino acid release and neurologic injury compared to normothermia. The single large study comparing true normothermia with hypothermia during CPB showed a significantly greater incidence of focal neurologic injury in the warm group, supporting the beneficial role of hypothermia in neuroprotection. In addition, recent data showed that minimum CPB temperatures greater than 35°C (95°F) increased the incidence of perioperative stroke approximately fourfold (4.5% vs. 1.2%).

In this context, the avoidance of cerebral hyperthermia deserves comment. Hyperthermia as little as a 2°C (35.6°F) increase in temperature significantly worsens neurologic outcomes. It has been demonstrated in a rat model, that following 10 minutes of ischemia during which temperature was increased from 35°C to 39°C (95°F to 102.2°F), the percentage of

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damaged neurons increased from 15% to 80%. This is clinically relevant because cerebral temperatures above 39°C (102.2°F) have been documented in patients during rewarming, a period when cerebral embolic risk is greatest. Therefore, hyperthermia should be carefully monitored and avoided. Grigore et al. found greater neuropsychological dysfunction in patients randomized to a faster rather than slower rewarming rate in the setting of CABG surgery. Of note, the patients rewarmed at a faster rate were also exposed to higher peak temperatures and a higher mean temperature of greater than 37°C than patients rewarmed slower with lower peak temperatures.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:383-388.

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McLean RF, Wong BI. Normothermic versus hypothermic cardiopulmonary bypass: central nervous system outcomes. *J Cardiothorac Vasc Anesth*. 1996;10:45-52.

Murphy GS, Hessel EA II, Groom RC. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. *Anesth Analg*. 2009;108:1394-1417.

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C.II-19. How does blood viscosity change during hypothermia and hemodilution?

Blood viscosity varies inversely with temperature; a 2% increase occurs for every 1°C (1.8°F) decrease in temperature. At a hematocrit of 40%, a decrease in temperature from 37°C to 27°C (98.6°F to 80.6°F) increases viscosity by approximately 25%. Hemodilution with balanced salt solution will decrease blood viscosity. Decreasing the hematocrit from 40% to 20% at 27°C (80.6°F) decreases viscosity by approximately 40%. It has been recommended that the hematocrit be adjusted to the same numerical value as the core body temperature in degree centigrade if blood viscosity is to be kept approximately constant. For example, normal viscosity at 37°C (98.6°F) with hematocrit of 40% approximates that seen at 25°C (77°F) with hematocrit of 25%.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:413.

C.II-20. What are the main causes of death associated with accidental hypothermia?

Ventricular fibrillation and asystole are the major rhythm disturbances leading to cardiac arrest during hypothermia. In humans externally cooled for cardiac surgery, ventricular fibrillation generally occurs at 23°C (73°F) and asystole at 20°C (68°F). However, asystole and ventricular fibrillation have been reported at 21°C to 28°C (69.8° to 82.4°F). Respiratory arrest usually accompanies cardiac arrest during accidental hypothermia.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:676-677.

Southwick FS, Dalglish PH Jr. Recovery after prolonged asystolic cardiac arrest in profound hypothermia. A case report and literature review. *JAMA*. 1980;243:1250-1253.

C.II-21. Would you give anesthesia during CPB? Why?

Anesthesia is maintained with intermittent administration of IV propofol, benzodiazepines, narcotic, and/or inhalation agents through the pump oxygenator to achieve unconsciousness and analgesia, to control BP, and to prevent shivering. IV agents are diluted by the priming solution during CPB. Meanwhile, hypothermia itself produces anesthesia and prolongs the action duration of IV agents by decreasing hepatic metabolism and urinary excretion.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:247.

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C.II-22. Would you give muscle relaxants during CPB? How is the action of muscle relaxant affected during CPB?

Yes. Muscle relaxants are given to prevent diaphragmatic movement that interferes with surgery and to prevent shivering during hypothermia. Shivering may increase oxygen consumption to as high as 486% of normal. The effect of a muscle relaxant is altered by both hypothermia and hemodilution. The plasma concentration of muscle relaxants is diluted by the priming solution. Therefore, more relaxant is required to maintain the same degree of relaxation. Hypothermia was originally reported to decrease the effect of nondepolarizing relaxants because decreased cholinesterase enzyme activity during hypothermia resulted in more acetylcholine accumulation to compete with the nondepolarizing relaxant. Contrary to the earlier reports, it is now established that atracurium, vecuronium, or pancuronium is needed to maintain muscle relaxation during hypothermia because hypothermia reduces renal and biliary excretions. Hypothermia does prolong the onset of paralysis. Moreover, hypothermic CPB per se facilitates neuromuscular transmission at the electrochemical level yet compromises mechanical contractility. The duration of action of rocuronium is prolonged by hypothermic CPB.

Modifications of partial neuromuscular blockade by hypothermic bypass are the result of muscle relaxation enhancing or interfering with the impact of hypothermia on normal neuromuscular transmission. The best way to monitor muscle relaxation is by using a peripheral nerve stimulator.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:227-247.

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Hemmerling TM, Russo G, Bracco D. Neuromuscular blockade in cardiac surgery: an update for clinicians. *Ann Card Anaesth*. 2008;11(2):80-90.

C.II-23. How do you know the patient is well perfused during CPB?

If the perfusion pressure is maintained between 50 mm Hg and 100 mm Hg, and the pumpflow rate is adequately maintained according to the degree of hypothermia and hemodilution, there should be adequate urine output, greater than 1 mL/kg/hr, no metabolic acidosis, and normal mixed venous oxygen tension of 40 to 45 mm Hg. However, cerebral perfusion is not routinely monitored, and the autoregulation range of BP may be higher than the normal range in the elder and high-risk patients. Cerebral oximetry should be used for patients with increased risk for neurologic and cognitive outcomes. It is recommended to keep cerebral oxygen saturation over 40%.

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Yao FS, Tseng CC, Ho CY, et al. Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth*. 2004;18:552-558.

C.II-24. How much gas flow would you use for the oxygenator? What kind of gas would you use? Why?

Normal alveolar ventilation is 4 L per minute and pulmonary circulation is 5 L per minute. The [V with dot above]/[Q with dot above] ratio is 0.8. The oxygenator is not as efficient as human lungs. Usually 2 L of gas are used for each liter of pump-flow rate and then the gas-flow rate is adjusted according to blood $PaCO_2$ and PaO_2. The gas flow may be decreased if the $PaCO_2$ is low and the PaO_2 is too high. The ratio may be increased if the $PaCO_2$ is over 40 mm Hg or the PaO_2 is under 100 mm Hg. Meanwhile, air-oxygen mixtures allow better control of oxygen tension during CPB. Because α-stat regulation is used for acid-base management, it is not necessary to add CO_2 to the ventilating gas during hypothermia to elevate $PaCO_2$ and decrease the pH.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:157-164.

C.II-25. What are the disadvantages of hypocapnia during CPB?

- Cerebral blood flow decreases approximately 2% to 4% for each mm Hg decrease in $PaCO_2$ when $PaCO_2$ is in the range of 20 mm Hg to 60 mm Hg due to cerebral vasoconstriction. Cerebral O_2 saturation decreases approximately

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1% for each mm Hg decrease in $PaCO_2$.

- Respiratory alkalosis shifts the oxygen dissociation curve to the left, which increases the O_2 affinity to hemoglobin and decreases the release of O_2 to the tissues.
- Hypokalemia occurs because alkalosis shifts the potassium intracellularly.
- Alkalosis decreases ionized calcium.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:157-164.

Smith AL, Wollman H. Cerebral blood flow and metabolism: effects of anesthetic drugs and techniques. *Anesthesiology*. 1972;36:378-400.

Yao FSF, Tseng CC, Yu J, et al. Relationship between $ETCO_2$ and cerebral oxygen saturation. *Anesthesiology*. 2000;93(3A):A320.

C.II-26. The arterial blood gases and electrolytes during CPB are as follows: pH, 7.36; $PaCO_2$, 42 mm Hg; PaO_2, 449 mm Hg; CO_2 content, 24 mEq per L; sodium (Na), 128 mEq per L; potassium (K), 5.8 mEq per L; and hematocrit (Hct), 20%. The patient's temperature is 27°C (80.6°F). At what temperature are blood gases measured? How would you correct the blood gases according to patient's body temperature? Would you treat the arterial blood gases at 37°C (98.6°F) or at patient's body temperature?

Blood gases are measured at a constant temperature of 37°C (98.6°F). They may be corrected according to body temperature. Each degree centigrade below 37°C (98.6°F) increases blood pH by 0.015. If pH is 7.40 at 37°C (98.6°F) in vitro, in vivo pH will be 7.55 at 27°C (80.6°F) body temperature (7.40 + 0.015 × [37 - 27] = 7.55). The pH increases at lower temperatures because of increased Pka and decreased CO_2 tension from increased CO_2 blood solubility during hypothermia. In vivo PaO_2 is decreased because of increased oxygen solubility during hypothermia. Nowadays, blood gases are measured at 37°C (98.6°F) and interpreted at 37°C (98.6°F) without correcting them to body temperature. The normal values of blood gases at 37°C (98.6°F) are as follows: pH, 7.40 ± 0.05; $PaCO_2$, 40 ± 5; and PaO_2, 95 ± 5. During hypothermia, the normal values of blood gases are not the same as those at 37°C (98.6°F). The same blood specimen has different PO_2 values when measured at different temperatures. Yet, the oxygen content remains unchanged. It is easier to calculate the oxygen content at 37°C (98.6°F) than at other temperatures where oxygen dissociation curves are shifted.

Optimal management of pH and $PaCO_2$ for patients undergoing hypothermic CPB remains controversial. The two strategies for interpreting blood gases are the pH-stat (temperature-corrected)

method and the *α*-stat (temperature-uncorrected) method. The pH-stat strategy aims at keeping constant arterial pH at 7.40 and $PaCO_2$ at 40 mm Hg at any given temperature. A $PaCO_2$ of 60 mm Hg analyzed at 37°C (98.6°F) would be equivalent to a $PaCO_2$ of 40 mm Hg if "corrected" for a body temperature of 27°C (80.6°F). The *α*-stat strategy aims at keeping a constant ratio of $[OH^-]$:$[H^+]$ at approximately 16:1. This is based on the premise that the pH of blood is regulated to keep the state of dissociation of imidazole moiety (i.e., the alpha of imidazole) constant. Histidine, which contains the imidazole moiety, is an integral part of the active site of many enzyme systems. The function of enzyme systems has been shown to be optimal when the ratio of $[OH^-]$:$[H^+]$ is approximately 16:1. This ratio represents different pH values at different temperatures.

The differences between pH-stat and *α*-stat strategies are listed in Table 5.3. With the pH-stat strategy, the blood gas values are corrected to the patient's temperature; the patient is treated as if he were a hibernating animal. With the *α*-stat strategy, the blood gas values are not corrected regardless of the patient's actual temperature; the patient is treated as if he were a poikilotherm. Studies indicate that myocardial function is better preserved when the *α*-stat strategy is employed. Moreover, maintenance of cerebral blood flow autoregulation appears to remain intact with *α*-stat management, whereas flow becomes pressure dependent with pH-stat management. *α*-Stat blood gas management preserves cerebral blood flow-metabolism coupling such that hypothermic-induced decreases in metabolic rate are accompanied by proportionate decreases in cerebral blood flow. Therefore, most medical centers use *α*-stat management of blood gases during hypothermic CPB. However, Bashein et al. found no difference in neuropsychological outcome between patients randomized to *α*-stat and those randomized to pH-stat management.

However, more recent studies have shown less decline in cognitive performance when *α*-stat management is used, especially in cases with prolonged CPB times. These data may support an embolic threshold above which recognizable neurologic injury occurs.

During deep hypothermic circulatory arrest, both animal and clinical studies have shown that pH-stat is associated with better neurologic outcome probably because of increased cerebral blood flow, which provides better brain cooling and greater cellular oxygen availability. In summary, most recent outcome studies support the utilization of *α*-stat for adult CPB and pH-stat for children under deep hypothermic circulatory arrest.

Bashein G, Townes BD, Nessly ML, et al. A randomized study of carbon dioxide management during hypothermic cardiopulmonary bypass. *Anesthesiology*. 1990;72:7-15.

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Philadelphia, PA: Lippincott Williams & Wilkins; 2008:157-164.

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Murkin JM, Farrar JK, Tweed WA, et al. Cerebral autoregulation and flow/metabolism coupling during cardiopulmonary bypass: the influence of $PaCO_2$. *Anesth Analg*. 1987;66:825-832.

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Shann KG, Likosky DS, Murkin JM, et al. An evidence-based review of the practice of cardiopulmonary bypass in adults: a focus on neurologic injury, glycemic control, hemodilution, and the inflammatory response. *J Thorac Cardiovasc Surg*. 2006;132:283-290.

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TABLE 5.3 Different Hypothermic Acid-Base Regulatory Strategies

STRATEGY	AIM	TOTAL CO_2 CONTENT	pH AND $PaCO_2$ MAINTENANCE	INTRACELLULAR STATE	α-IMIDAZOLE AND BUFFERING	ENZYME STRUCTURE AND FUNCTION	CEREBRAL BLOOD FLOW AND COUPLING	EFFECT ON ISCHEMIC TISSUE
pH-stat	Constant pH	Increases	Normal corrected values	Acidotic (excess H^+)	Excess (+) charge	Altered and activity decreased	Flow close to normothermic	? Lessens hypothermic protection
					Buffering decreased		? Flow and metabolism uncoupled	
α-Stat	Constant OH^-/H^+	Constant	Normal uncorrected values	Neutral ($H^- = OH^-$)	Constant net charge	Normal and activity maximal	Flow decreases (appropriate)	? Allows full hypothermic protection
					Buffering constant		? Flow and metabolism coupled	

?, questionable.
From Tinker JH, ed. *Cardiopulmonary Bypass: Current Concepts and Controversies*. Philadelphia, PA: JB Lippincott; 1989:16, with permission.

C.II-27. If the blood level of the venous reservoir is low, what would you replace it with? Blood or balanced salt solution?

The hematocrit should be maintained around 18% to 20% during hemodilution. If the hematocrit decreases below 18%, blood is added to the CPB circuit. If the hematocrit is above 20%, a balanced salt solution is added to the oxygenator. However, hematocrit values in the range of 15% to 18% appear to be well tolerated clinically. When cerebral oxygen saturation (rSO_2) is less than 40%, packed red blood cells are used to improve oxygen-carrying capacity. When rSO_2 is

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over 40%, it means the patient has acceptable cerebral oxygenation, although hematocrit is below 18%.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:417-418.

Likosky DS, FitzGerald DC, Groom RC, et al. Effect of the perioperative blood transfusion and blood conservation in cardiac surgery clinical practice guidelines of the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists upon clinical practices. *Anesth Analg*. 2010;111:316-323.

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Yao FSF, Tseng CC, Woo D, et al. Maintaining cerebral oxygen saturation during cardiac surgery decreased neurological complications. *Anesthesiology*. 2001;95:A152.

C.II-28. How do you estimate the fluid balance during CPB?

During CPB, all IV lines are shut off. The intake includes cardioplegic solution, fluid or blood added to the oxygenator during CPB, and the decreased blood level in the oxygenator. The output includes urine and the increased blood level in the oxygenator.

C.II-29. How would you preserve the myocardium during CPB?

The most popular and effective method of protecting the myocardium is to reduce myocardial oxygen demand by hypothermia and cardioplegia. Hypothermia is induced by a combination of systemic blood cooling by heat exchangers in the oxygenator; local application of cold saline solution or iced slush to the external surface and chambers of the heart (if the heart is open); and infusion of cold cardioplegic solution through the aortic root, venous grafts, retrograde coronary sinus, or coronary ostium to the coronary arterial tree. The myocardial temperature may be decreased to 10°C to 15°C (50°F to 59°F).

In addition to inducing hypothermia and cardioplegia, one may take the following measures before aortic cross-clamping:

- Avoid tachycardia or increased contractility by discontinuing pacing at rapid rate and discontinuing inotropes if they were utilized.
- Initiate rapid arrest (asystole).
- Utilize proper venting methods and ensure adequate venous drainage to the pump to avoid ventricular distention, which decreases subendocardial blood supply.
- Prevent and treat ventricular fibrillation, which increases oxygen demand in normothermic myocardium.
- Maintain adequate coronary perfusion pressure of at least 50 mm Hg and greater than 70 mm Hg in the presence of severe coronary disease or left ventricular hypertrophy.

Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: a systematic review. *Anesth Analg*. 2015;120:749-769.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:172-184.

C.II-30. What is the cardioplegic solution? How much would you use?

Cardioplegic solution contains mainly high concentrations of potassium (10 to 30 mEq per L) or magnesium (160 mEq per L) to relax the heart. Cardioplegia reduces myocardial oxygen consumption and provides optimal conditions for surgery. Bicarbonate or tris(hydroxymethyl)-aminomethane (THAM) is usually added to raise the pH to levels between 7.40 and 7.80 to increase the intracellular shift of potassium and to decrease the metabolic acidosis from ischemia. Steroids, calcium, and procaine may be added to stabilize lysosomal and cell membranes. Glucose and insulin are added to provide energy and improve the intracellular shift of potassium. Nitroglycerin is added to dilate coronary vessels, resulting in better perfusion to the myocardium, including ischemic areas.

When blood cardioplegia is used, four parts of bypass blood are mixed with one part of cardioplegic solution. Blood cardioplegia seems to have several advantages over crystalloid cardioplegia. The heart is arrested while being oxygenated, so that adenosine triphosphate (ATP) is not depleted before asystole. Repeated infusions provide a source of oxygen and glucose for continued metabolism and ATP repletion. Although little oxygen is released from hemoglobin during hypothermia, enough is probably dissolved in the plasma to sustain metabolism when reinfusion is performed every 30 minutes. Buffering capacity is improved because of the presence of the histidine buffering system present in red blood cells. Myocardial edema is reduced because of the osmolarity of blood. The risk of calcium paradox following ischemia is reduced and functional recovery is improved because of the physiologic calcium concentration provided by blood. The presence of red blood cell enzyme catalase may scavenge free radicals produced by ischemia. Capillary perfusion is improved and more homogeneous because of the presence of red blood cells. However, results of clinical studies in which blood cardioplegia was compared with crystalloid cardioplegia either detected no significant difference or showed that blood cardioplegia improved contractility late in the postoperative course. Multiple-dose cardioplegia is required for satisfactory results, whereas single-dose blood cardioplegia results in poor ventricular function.

Intermittent, continuous, or single infusions of cardioplegic solution have been used. Usually 300 to 600 mL of cold cardioplegic solution is needed to paralyze the myocardium and cool the myocardium to 10°C to 20°C (50°F to 68°F).

In the case of severe obstructive coronary lesions, antegrade infusion into the aortic root may cause maldistribution of the cardioplegia. Therefore, retrograde infusion through the coronary sinus into the coronary veins may be additionally employed to ensure homogeneous distribution of cardioplegia.

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In the late 1980s and early 1990s, warm cardioplegia with near-systemic normothermia was popular for better myocardial protection. In a prospective randomized study by Franke et al., there was no difference in mortality, MI, IABP use, or postoperative inotropic requirements between patients receiving cold cardioplegia and those receiving warm cardioplegia. Patients receiving warm cardioplegia were less likely to require defibrillation following crossclamp release and have less postoperative ventricular dysrhythmias and a lower reoperation rate for bleeding. However, one study identified a threefold increase in strokes in the "warm" patients.

Franke UF, Korsch S, Wittwer T, et al. Intermittent antegrade warm myocardial protection compared to intermittent cold blood cardioplegia in elective coronary surgery—do we have to change? *Eur J Cardiothorac Surg*. 2003;23:341-346.

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McLean RF, Wong BI. Normothermic versus hypothermic cardiopulmonary bypass: central nervous system outcomes. *J Cardiothorac Vasc Anesth*. 1996;10:45-52.

C.II-31. For how long a period can the aorta be cross-clamped?

When cardioprotective strategies including intermittent hypothermic blood cardioplegia, initiation of rapid arrest, and left ventricular venting are employed, the limits of "safe" ischemic time during aortic cross-clamping can be increased from as little as 15 to 45 minutes to as

much as 240 minutes in animal models with normal ventricular function. However, many patients have preoperative ventricular dysfunction and the protection from hypothermic cardioplegia may not be optimal because of coronary artery obstruction. Clinically, the aorta may be safely cross-clamped for 60 to 120 minutes without perfusion. The shorter the crossclamping time, the better the myocardial function will be.

Nissinen et al. evaluated the impact of prolonged CBP and aortic cross-clamp times (XCT) in 3,280 patients undergoing adult cardiac surgery, with myocardial protection maintained by continuous anterograde and retrograde cardioplegia. They found that XCT greater than 150 minutes and bypass times greater than 240 minutes were both associated with higher 30-day mortality (1.8% vs. 12.2% for increased XCT and 1.9% vs. 31.5% for CPB). Both increased XCT and CBP times also correlated significantly to increased transfusion of blood products, hospital length of stay, time to extubation, and postoperative morbidity such as stroke.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:217.

Nissinen J, Biancari F, Wistbacka JO, et al. Safe time limits of aortic cross-clamping and cardiopulmonary bypass in adult cardiac surgery. *Perfusion*. 2009;24(5):297-305.

Salis S, Mazzanti VV, Merli G, et al. Cardiopulmonary bypass duration is an independent predictor of morbidity and mortality after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2008;22(6):814-822.

C.II-32. Why would urine become pink in some cases of CPB? What is the renal threshold for plasma hemoglobin?

Pink urine is a sign of massive hemolysis. Hemolysis is mainly associated with the frothing, violent turbulence, acceleration, and shear forces of negative pressures generated by the suction apparatus and is associated to a lesser degree with the action of the pumps or with the gas-blood interface effects in the oxygenator. The renal threshold for hemoglobin is 100 to 150 mg per 100 mL. It is advisable to maintain a high output of alkaline urine to prevent possible tubular damage from acid hematin crystals, which are converted from hemoglobin.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:42, 59, 99.

C.II-33. At what temperature can the patient be weaned from CPB?

An esophageal or nasopharyngeal temperature of 37°C (98.6°F) and a rectal or bladder temperature at least 35°C (95°F) must be reached before the patient can come off the pump. After discontinuation of the pump, surface warming should be continued in pediatric patients to prevent hypothermia owing to redistribution of heat in the body. However, in adults, the use of warming blankets and warmed humidified airway gases has not been found beneficial in preventing the expected temperature "afterdrop." Usually, esophageal or nasopharyngeal temperature will decrease and rectal or bladder temperature will increase during heat redistribution.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:614-615.

C.II-34. Why does it take longer to rewarm than to cool the patient by the pump oxygenator?

It usually takes 5 to 10 minutes to cool the patient from 37°C to 25°C (98.6°F to 77°F) of average body temperature. It takes 20 to 40 minutes to rewarm the patient from 28°C to 35°C (82.4°F to 95°F). The speed of heat exchange by the bloodstream depends on the temperature gradient between venous blood and water in the heat exchanger, the pump blood-flow rate, and the water-flow rate of the heat exchanger. The initial venous blood temperature is 37°C (98.6°F) and

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the water temperature of the heat exchanger is 0°C to 4°C (32°F to 39.2°F) during cooling, creating a temperature gradient of 34°C to 37°C (93.2°F to 98.6°F). During rewarming, the water temperature is limited to 42°C (107.6°F) or less to prevent denaturation and destruction of blood proteins. The temperature gradient is limited to 10°C (18°F) or less to prevent gas embolism from a decrease of gas solubility in the blood associated with a sharp

increase in temperature. The heat exchanger water flow does not differ much during cooling and rewarming. However, the pump blood flow is usually maintained to a very high level during the initial cooling because of low BP in the beginning of cooling. During rewarming, the pump blood flow is frequently maintained at a low level because the BP is usually high and the body temperature is still low. Rewarming may be accelerated by administering inhalation anesthetics, or employing vasodilators, to decrease vascular resistance and thereby increase pump flow to maintain the same BP. Because the increased vascular resistance is usually due to inadequate anesthesia during rewarming, inhalation anesthetics are preferred over vasodilators in patients with good ventricular function. In cases of poor ventricular function, inhalation agents are avoided because of the potential cardiac depression after CPB.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:57-58.

C.II-35. How would you defibrillate the heart internally during CPB?

The heart is defibrillated internally by a direct current (DC) defibrillator, with 5 to 10 wattseconds (joules). If the heart remains in ventricular fibrillation, blood gases, electrolytes, and temperature are rechecked and lidocaine, 1 to 2 mg per kg, is administered before repeated DC defibrillation attempts. MAP is usually increased to 80 mm Hg. Occasionally, esmolol, metoprolol, and amiodarone are added to treat intractable ventricular fibrillation or tachycardia.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:992-1009.

C.II-36. Why is calcium chloride usually administered right before the patient comes off the pump?

With hemodilution, the ionized calcium frequently falls to approximately 1.5 to 1.8 mEq per L (normal 2.2 to 2.6 mEq per L, 1.1 to 1.3 mmol per L, or 4.5 to 5.6 mg per dL). Calcium chloride, 0.5 to 1.0 g, frequently is given to increase myocardial contractility and reverse potassium cardioplegia. Calcium increases the inotropic state of the myocardium and induces an increase in systemic vascular resistance that outlasts the inotropic effects. However, some believe that calcium administration is contraindicated at this time because of the compromised calcium hemostasis that accompanies the insult of aortic cross-clamping. Administration of calcium may exacerbate ischemic and reperfusion injury by causing accumulation of intracellular calcium. β-Blockers, on the other hand, increase intracellular calcium but also promote its reuptake into the sarcoplasmic reticulum and may be more appropriate in this setting. Therefore, use of calcium salts at the conclusion of bypass should be guided by determination of ionized calcium levels. Calcium salts should probably not be given to patients with good ventricular function in the absence of hypocalcemia or hyperkalemia because of the potential detrimental effects of iatrogenic hypercalcemia; whether this is true in patients with ventricular dysfunction is unknown.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:299-301, 615-616, 628.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:992-1009.

C.II-37. If the HR is 40 beats per minute, what should you do?

A temporary AV block is often found at the end of bypass because of potassium cardioplegia and ischemic insult during aortic cross-clamping. Although atropine may be theoretically administered to treat sinus or nodal bradycardia, more frequently, a temporary epicardial pacemaker is usually employed. Atrial pacing is preferred because of improved cardiac output when the atrial kick is preserved. Ventricular pacing is necessary if there is complete AV block. AV sequential pacing is indicated when ventricular pacing does not provide adequate cardiac output.

Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:992-1009.

C.II-38. How does the blood sugar level change during CPB? Why? What is optimal glucose control intraoperatively? Does hyperglycemia increase neurologic complications during CPB?

Blood sugar levels are elevated during the perioperative period in patients undergoing cardiac surgery with the use of CPB. Hyperglycemia is most profound during hypothermic CPB, with approximately 100% of patients (diabetic and nondiabetic) achieving plasma glucose levels greater than 200 mg per dL. There are several reasons for this: First, the practice of making patients nothing by mouth (NPO) overnight induces a state of starvation, marked by peripheral resistance to insulin at the level of muscle and fatty tissues, therefore allowing glucose uptake by the brain; second, sympathoadrenal activation, in response to surgical stress, also tends to induce a diabetogenic state; third, active cooling the body during bypass causes a profound reduction in insulin production, induces peripheral insulin resistance, and is associated with renal tubular impairment in glucose regulation; and lastly, use of dextrosecontaining cardioplegia is a major contributor to intraoperative hyperglycemia. Of interest, postoperative hyperglycemia continues despite insulin administration and has been shown to remain above normal up to several weeks postoperatively. At the cellular level, the alterations in insulin receptor/resistance are very similar to that of type 2 diabetes. It is controversial whether

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hyperglycemia increases neurologic complications during CPB. Under conditions of limited cerebral oxygen delivery, anaerobic glucose oxidation becomes the primary method of ATP production, resulting in intracellular lactic acidosis. Hyperglycemia, by providing more glucose for anaerobic oxidation, increases the degree of intracellular acidosis, which, in numerous animal studies, correlates with the severity of subsequent injury.

Given the tendency of hyperglycemia during cardiac surgery, there have been several large-scale studies evaluating the question of how much of glycemic control is optimal during CPB. The first by Ouattara et al., an observational study of 200 consecutive diabetic patients undergoing cardiac surgery, demonstrated that poor intraoperative control of blood glucose concentrations was associated with an increased incidence of in-hospital morbidity, including neurologic, cardiovascular, infectious, respiratory, and renal. Based on these findings, “tight” glucose control had been recommended for all patients undergoing CPB. More recently, tight intraoperative glycemic control for all patients has come under scrutiny due to equivocal results in nondiabetic patients, finding that tight glucose intraoperatively either did not make a difference or had increased morbidity and mortality.

Butterworth et al. studied the effects of tight glucose control in 381 patients without diabetes undergoing isolated CABG surgery with one group receiving an insulin infusion for glucose levels above 100 mg per dL and the other group receiving no insulin. Although glucose levels were lower in the patients who received insulin infusions, there was no difference between the incidences of neurologic complications, mortality, need for inotropic support, or length of hospital stay between the groups.

Gandhi et al. studied the effects of strict glucose control in 400 CABG patients (20% diabetic) randomized to a continuous insulin group (glucose levels maintained between 80 and 100 mg per dL) and a conventional group (glucose <200 mg per dL) using boluses of insulin. They found no difference in number of deaths, sternal wound infections, prolonged ventilation, cardiac arrhythmias, strokes, and renal failure within 30 days of surgery, or hospital length of stay between the two groups. There was a tendency for more deaths and strokes in the intensive insulin group.

As a result of these studies, the Society of Thoracic Surgeons (STS) revised guidelines in 2009 state that glycemic control is best achieved with insulin drip (Level A) and diabetic patients should receive insulin infusions intraoperatively (Level B). However, insulin infusions are not necessary intraoperatively for patients without diabetes for glucose levels <180. These patients can be treated initially IV insulin bolus. However, in those patients with persistently elevated serum glucose levels (>180 mg per dL) after CPB, an insulin infusion should be instituted (Level B).

Butterworth J, Wagenknecht LE, Legault C, et al. Attempted control of hyperglycemia during cardiopulmonary bypass fails to improve neurologic or neurobehavioral outcomes in patients without diabetes mellitus undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg*. 2005;130:1319.

Carvalho G, Moore A, Qizilbash B, et al. Maintenance of normoglycemia during cardiac surgery. *Anesth Analg*. 2004;99:319-324.

Fontes ML, Koval KJ, Desvarieux T, et al. Epidemiology of hyperglycemia in non-diabetic patients undergoing hypothermic cardiopulmonary bypass. *Anesthesiology*. 2006;105:A749.

Fontes ML, Skubas N, Girardi L, et al. Glucosuria during cardiopulmonary bypass: does hypothermia provide protection or a blow to the kidneys? *Anesth Analg*. 2007;104:SCA81.

Gandhi GY, Nuttall GA, Abel MD, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery: a randomized trial. *Ann Intern Med*. 2007;146:233-243.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:363-364, 388.

Grocott HP, Stafford-Smith M. Organ protection during cardiopulmonary bypass. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2006:992-993.

Lanier WL. Glucose management during cardiopulmonary bypass: cardiovascular and neurologic implications. *Anesth Analg*. 1991;72:423-427.

Lazar HL, Chipkin SR, Fitzgerald CA, et al. Tight glycemic control in diabetic coronary artery bypass graft patients improves perioperative outcomes and decreases recurrent ischemic events. *Circulation*. 2004;109:1497-1502.

Lazar HL, McDonnell M, Chipkin SR, et al. The Society of Thoracic Surgeons practice guideline series: blood glucose management during adult cardiac surgery. *Ann Thorac Surg*. 2009;87:663-669.

Murkin JM. Pro: tight intraoperative glucose control improves outcome in cardiovascular surgery. *J Cardiothorac Vasc Anesth*. 2000;14:475-478.

Ouattara A, Lecomte P, Le Manach Y, et al. Poor intraoperative blood glucose control is associated with a worsened hospital outcome after cardiac surgery in diabetic patients. *Anesthesiology*. 2005;103:687-694.

Shann KG, Likosky DS, Murkin JM, et al. An evidence-based review of the practice of cardiopulmonary bypass in adults: a focus on neurologic injury, glycemic control, hemodilution, and the inflammatory response. *J Thorac Cardiovasc Surg*. 2006;132:283-290.

van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med*. 2001;345:1359-1367.

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C.II-39. What are the effects of CPB on platelet and coagulation factors?

Platelet dysfunction and thrombocytopenia are found on and after CPB. Platelet dysfunction is the most common cause of a bleeding problem following CPB after heparin is reversed and surgical bleeding is controlled. Transient defects in platelet plug formation and aggregation are seen in all patients put on CPB. Generally, platelet function returns to near-normal status 2 to 4 hours following CPB. The defects are exacerbated and prolonged by drugs such as aspirin and platelet glycoprotein GPIIb/IIIa inhibitors (clopidogrel, tirofiban), which inhibit platelet function.

Platelet counts fall more with the bubble-type oxygenator than with the membrane-type oxygenator but rarely below the levels clinically required for hemostasis. Thrombocytopenia is mainly caused by hemodilution, aggregation, adhesion, and the adenosine diphosphate-release reaction induced by the foreign surfaces and the blood-gas interface. Heparin may potentiate platelet aggregation and adhesions.

The level of coagulation factors decreases at the beginning of bypass because of hemodilution; surface absorption by the plastic, glass, and metal; and protein denaturation induced by the blood-gas interface. At the same time, the synthesis of clotting factors by the liver increases so that the concentration of clotting factors returns to normal within a period of hours. Membrane oxygenators cause few changes in clotting factors.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:325-326, 427-428, 450-453.

C.II-40. How would you prepare for termination of CPB?

Before termination of CPB, cardiac and pulmonary function must be optimized. To ensure that all important steps are not inadvertently omitted, the patient and all monitors should be carefully checked. The mnemonic LAMPS for Laboratory data, Anesthesia machine, Monitors, Patient (Pump), and Support is one useful approach.

Laboratory data

- Arterial pH, PCO_2, PO_2 within normal limits
- Hematocrit—20% to 25%

- K^+—4.0 to 5.5 mEq per L
- Ionized calcium 1.1 to 1.2 mmol per L
- Pump mixed venous O_2 saturation greater than 70%

Anesthesia machine

- Adequate anesthesia
- Anesthesia machine functional

Monitors

- ECG—stable rate and rhythm (use pacing if necessary)
- Systemic BP restored to normothermic levels
- PA catheter functional
- Transducers rezeroed and calibrated
- TEE out of freeze mode
- Nasopharyngeal/PA catheter temperature 36°C to 37°C (96.8°F to 98.6°F)
- Bladder/rectal temperature greater than 35°C (95°F)

Patient/Pump

- The heart—contractility, size, rhythm, and air removed
- The lungs—atelectasis reexpanded, fluid in thoracic cavities drained, ventilation reinstituted

Support

- Inotropes/vasopressors/vasodilators
- IABP if needed

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:614-619.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:992-1009.

Skubas NJ, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1073-1107.

C.II-41. How would you decide the need for inotropic support?

The need for inotropic support after CPB is usually assessed by the following (Fig. 5.9):

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- Preoperative ventricular function (ejection fraction)
- Effectiveness of intraoperative myocardial protection
- Adequacy of surgical repair
- Duration of aortic cross-clamping and CPB
- Patient's age

If LV ejection fraction is predicted to be 25% to 35%, milrinone infusion may be added. Norepinephrine infusion is usually needed during milrinone therapy. Generally, IABP is also employed when LV ejection fraction is predicted to be below 25%. The choice of vasoactive and cardioactive agents used is frequently center- and/or physician-specific and, in most cases, initiated as prophylaxis. Recent data suggest that this practice should be avoided because inotropic and vasopressors can have negative effects, which can result in both morbid and fatal events.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:619-629.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:992-1009.

C.III. After Cardiopulmonary Bypass

C.III-1. How would you reverse heparin? How much protamine would you use? What are the other drugs used to neutralize heparin?

It has been recommended that 1 mg of protamine sulfate is needed to reverse each 100 units of remaining heparin calculated by ACT dose-response curve or protamine

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titration test. Protamine, 1 mg is given to reverse each 100 units or 1 mg of heparin initially administered. Only the initial dose of heparin is counted. The subsequently added dose of heparin, to keep the ACT level above 480 seconds, is not considered because of its metabolism and elimination. The ACT test is repeated 10 minutes after the administration of protamine. ACT usually returns to its control level. If the ACT is still prolonged, additional protamine is given according to the ACT dose-response curve. However, the ACT is affected by dilution and by hypothermia; dose-response curves utilizing data obtained during hypothermia may be misleading. In addition, severe thrombocytopenia

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also prolongs the ACT because clot formation using the ACT depends on platelet phospholipid surface. Furthermore, because heparin rebound is possible, it may be optimal to administer protamine at two times following CPB: once after bypass and again 1 or 2 hours later to counteract heparin rebound. Of note, recent work by Bolliger and colleagues suggests that increase in bleeding may occur paradoxically from “extra” protamine administration.

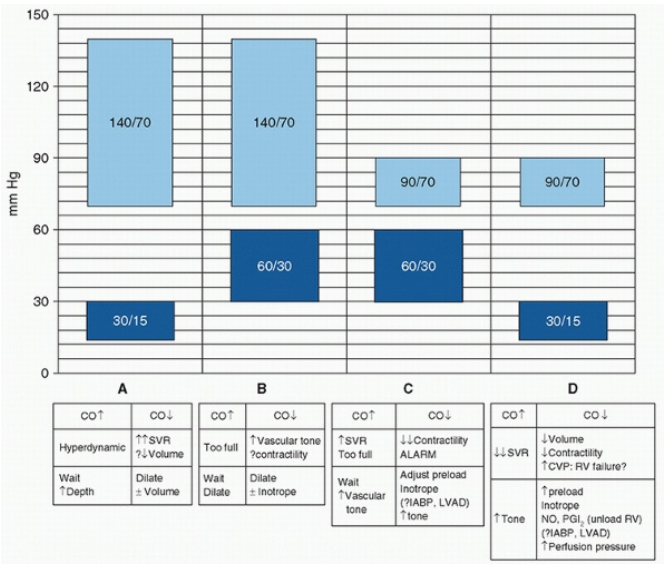


FIGURE 5.9 Hemodynamic management during weaning from cardiopulmonary bypass. The hemodynamic evaluation is performed by combining information from the systemic *(light shade boxes)* and pulmonary *(dark shade boxes)* arterial pressures. **A.** A combination of elevated systemic arterial and low pulmonary arterial pressure suggests either a hyperdynamic cardiac function (if cardiac output is high) or a vasoconstrictive state (if the peripheral vascular resistance is high). **B.** If systemic hypertension is accompanied by pulmonary hypertension, then either the volume status is elevated (if cardiac output is high), or there is generalized vasoconstriction (if cardiac output is decreased). **C.** In case of systemic hypotension and pulmonary hypertension, the cardiac output may be high (systemic vasodilation) or low (depressed contractility, requiring immediate intervention). **D.** When both systemic and pulmonary pressures are decreased, there is either vasodilation (if the cardiac output is high) or hypovolemia or depressed contractility or right-sided failure is suspected (if cardiac output is decreased). The relative treatment for each hemodynamic derangement is shown in the table. CO, cardiac output; CVP, central venous pressure; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; NO, nitric oxide; PGI_2, prostacyclin; RV, right ventricle; SVR, systemic vascular resistance; ↑, increase; ↑↑, marked increase; ?, questionable.

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Other drugs that have been used to neutralize heparin include platelet factor 4 (PF4), heparinase, protamine variants, Polybrene, and toluidine blue. Human or recombinant PF4 has been used in animals and humans to reverse heparin and does not cause systemic arterial hypotension, or pulmonary hypertension, or changes in white blood cell count, platelet count, or complement levels. Heparinase neutralizes heparin by enzymatic cleavage of α-glycoside linkages at AT III binding site. Heparinase is an effective antagonist of heparin and has minimal effects on platelets, whereas protamine markedly inhibits platelet responsiveness. It appears to be a potential alternative to protamine.

Lastly, reversal for low molecular weight heparin compounds does not exist, but recently, a recombinant antithrombin variant was shown to be a potent antidote to fondaparinux and other heparin derivatives.

Bolliger D, Szlam F, Azran M, et al. The anticoagulant effect of protamine sulfate is attenuated in the presence of platelets or elevated factor VIII concentrations. *Anesth Analg*. 2010;111(3):601-608.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:473-478.

Nielsen VG, Malayaman SN. Protamine sulfate: crouching clot or hidden hemorrhage? *Anesth Analg*. 2010;111(3):593-594.

Spiess BD, Horrow JC, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:958-966.

C.III-2. What is the action mechanism of protamine?

Heparin is a strong organic acid (polyanion). Protamine is a strong organic base (polycation). They combine ionically to form a stable salt and lose their own anticoagulant activity. Protamine contains two active sites, one that neutralizes heparin and another that exerts a mild anticoagulant effect independent of heparin.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:471.

Spiess BD, Horrow JC, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:959.

C.III-3. What are the complications of too much protamine?

Protamine itself is an anticoagulant. Protamine administered intravenously in the absence of heparin interacts with platelets and with many clotting proteins. Protamine induces transient thrombocytopenia in humans. Platelet aggregation is impaired by the protamine-heparin complex, but protamine alone has no deleterious effects. Protamine may bind to thrombin and inhibit thrombin's ability to convert fibrinogen to fibrin.

Bolliger D, Szlam F, Azran M, et al. The anticoagulant effect of protamine sulfate is attenuated in the presence of platelets or elevated factor VIII concentrations. *Anesth Analg*. 2010;111(3):601-608.

Gravlee GP, Davis RF, Kurusz M, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2000:473.

Nielsen VG, Malayaman SN. Protamine sulfate: crouching clot or hidden hemorrhage? *Anesth Analg*. 2010;111(3):593-594.

Spiess BD, Horrow JC, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:949-991.

C.III-4. Why did the patient develop hypotension after protamine was administered? How do you treat and prevent this condition?

Three different types of circulatory reactions to protamine reversal of heparin have been proposed by Horrow:

Type I: Systemic Hypotension from Rapid Injection: A Predictable Pharmacologic Reaction Type II: Anaphylactic or Anaphylactoid Reaction

- Antibody-medicated
- Immediate anaphylactoid response without antibody involvement
- Delayed anaphylactoid response (noncardiac pulmonary edema)

Type III: Catastrophic Pulmonary Vasoconstriction with Systemic Hypotension

However, etiologically, there are only two types of reaction: (1) pharmacologic side-effect reactions and (2) idiosyncratic reactions. Therefore, an alternative classification was proposed by Lowenstein as follows:

- Pharmacologic histamine release

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- True anaphylaxis (immunoglobulin E-mediated)
- Anaphylactoid reactions
  - Pulmonary vasoconstriction
  - Noncardiogenic pulmonary edema

Mild to moderate systemic hypotension from pharmacologic side effects is almost always the reaction seen when protamine is given rapidly or is given to patients who are relatively hypovolemic and vasoconstricted. Because it can be elicited in most patients, it is classified as a pharmacologic side effect, not an idiosyncratic reaction. This side effect is possibly mediated by histamine and is characterized by venodilation, reduced cardiac filling pressures, and decreased vascular resistance. Mild cardiac depression by protamine is suggested but probably does not occur. This type of hypotension can be corrected by rapid volume administration from the CPB pump while the arterial cannula is in place and by administration of phenylephrine in 0.1-mg increments. There have been many attempts to modify the hypotensive response (e.g., intra-aortic or left atrial administration, protamine pretreatment), with little evidence of predictable success. Only slower rates of IV infusion over 5 to 10 minutes and simultaneous maintenance of an adequate blood volume have been shown to decrease the incidence of hypotension.

Anaphylactic or anaphylactoid reaction is uncommon and rarely seen in infants and children. The reaction varies from mild skin flushing and urticaria to severe vascular collapse. Systemic hypotension is usually accompanied by low pulmonary arterial pressure and low right-sided and left-sided filling pressures. This type of hypotension may be treated and prevented with rapid volume infusion and administration of vasoconstrictors. The use of antihistamines and steroids is commonly employed by many cardiovascular anesthesiologists with few, if any, existing data supporting this practice. There are several unanswered questions such as: When should these agents be given? What dose to give? Which agent? and so forth. Diabetic patients taking neutral protamine Hagedorn (NPH) insulin may develop antibodies to protamine and would appear to be at increased risk. However, clinical reactions do not predictably occur in these patients. Suspected cross-sensitivity in cases of fish allergy or autosensitization in men after vasectomy does not seem to put most patients at increased risk.

Catastrophic pulmonary hypertension occurs in approximately 0.2% to 4.0% of patients. There are several-fold increases in PA pressure leading to right ventricular failure, elevated CVP, low flow across the pulmonary circuit, and low left atrial pressure. Elevated plasma levels of C5a anaphylatoxins and thromboxane are responsible for pulmonary vasoconstriction and accompanied bronchoconstriction. Treatment with isoproterenol, milrinone, or amrinone is reasonable; epinephrine in 0.1-mg increments has been successfully used. If severe hypotension persists, the patient should be heparinized again and return to bypass to maintain circulation. A recent study has shown that left ventricular infusion of protamine provides no protection from pulmonary hypertension and that

histamine and platelet-activating factors are not involved in acute pulmonary vasoconstriction. Therefore, antihistamines and steroids may not be effective in preventing this reaction. However, it has been shown that the rate of IV protamine infusion in sheep is an important factor in the generation of sufficient mediators required to initiate a characteristic physiologic response, including pulmonary vasoconstriction and thromboxane B_2 generation. Slowing the rate of protamine infusion results in a proportional attenuation of the response (Figs. 5.10 and 5.11).

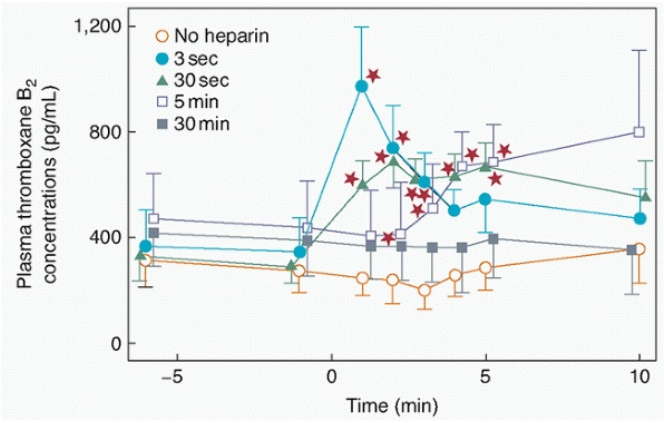


FIGURE 5.10 Plasma thromboxane B_2 concentrations before and after administration of protamine infused over 3 seconds, 30 seconds, 300 seconds, and 30 minutes. Heparin is injected at 5 minutes; protamine infusion is started at 0 minute. Data points represent mean ± *SE* values; n = 6 in each group (*P < .05 from unheparinized group). (From Morel DR, Costabella PM, Pittet JF. Adverse cardiopulmonary effects and increased plasma thromboxane concentrations following the neutralization of heparin with protamine in awake sheep are infusion rate-dependent. *Anesthesiology*. 1990;73:415-424, with permission.)

In conclusion, the treatment of hypotension after protamine administration depends on pulmonary arterial pressure. Hypotension with low pulmonary arterial pressure may be corrected with rapid volume infusion and vasoconstrictors, and hypotension with high pulmonary arterial pressure should be treated with inotropes that have a vasodilating effect. The only effective prevention is a slow infusion of diluted protamine solution.

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:480-488.

Horrow JC. Protamine allergy. *J Cardiothorac Anesth*. 1988;2:225-242.

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Lowenstein E. Lessons from studying an infrequent event: adverse hemodynamic response associated with protamine reversal of heparin anticoagulation. *J Cardiothorac Anesth*. 1989;3(1):99-1071.

Spiess BD, Horrow JC, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:949-991.

C.III-5. What are the indications for intra-aortic balloon pump (IABP)?

IABP is primarily used for pump failure and myocardial ischemia that are not responsive to maximal pharmacologic support. The indications include the following:

Ischemic heart disease

- Cardiogenic shock
- Acute MI complicated by
  - Mechanical defects: ventricular or septal rupture, acute mitral insufficiency, or ventricular aneurysm

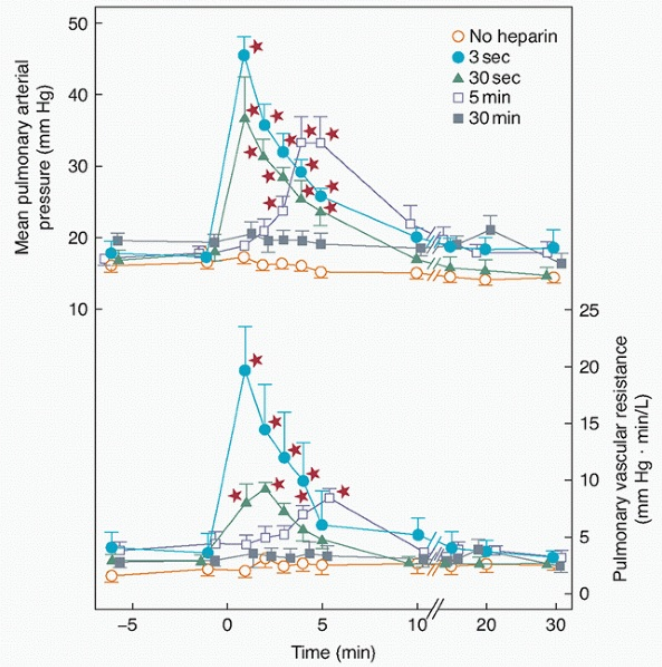


FIGURE 5.11 Pulmonary hemodynamics before and after administration of protamine infused over 3 seconds, 30 seconds, 300 seconds, and 30 minutes. Heparin is injected at 5 minutes; protamine infusion is started at 0 minute. Data points represent mean ± *SE* values; n = 6 in each group ($P < .05$ from unheparinized group). (From Morel DR, Costabella PM, Pittet JF. Adverse cardiopulmonary effects and increased plasma thromboxane concentrations following the neutralization of heparin with protamine in awake sheep are infusion ratedependent. *Anesthesiology*. 1990;73:415-424, with permission.)

  - Continued ischemic pain and extension of infarction
  - Refractory ventricular arrhythmias
- During cardiac catheterization
- Undergoing noncardiac surgery
- Failed PCI and awaiting CABG
- Acute mitral insufficiency with CHF

Cardiac surgery

- Before CPB and postoperatively
- After CPB: low output syndrome

Pulsatile CPB: rare

Pediatric congenital heart disease: rare

Neurosurgery: temporarily increases total cerebral blood flow in specific circumstances

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:135-136.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Savino JS,

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eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:992-1009.

Skubas N, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:1073.

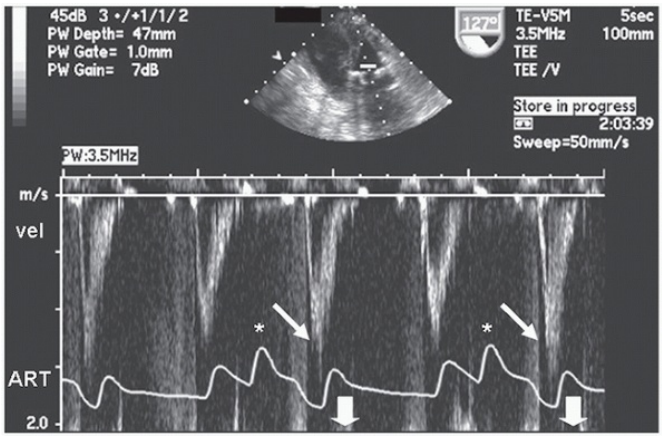


FIGURE 5.12 The function of the intra-aortic balloon pump (IABP). In this patient with an IABP in place, the velocity (vel) of the blood flow, as it exits the left ventricle (LV), is recorded. The arterial waveform is shown in the following text. The IABP is set on a 1:2 ratio; that is, it inflates every other beat, in diastole *(asterisks)*. The velocity (and the amount) of blood exiting the LV is increased *(diagonal arrows)* after the diastolic inflation of the IABP because the LV is ejecting against lower systemic resistance. This is the reason that the systolic arterial pressure following IABP inflation is lower *(down arrows)*.

C.III-6. What are the principles of IABP?

IABP counterpulsation is designed to increase the myocardial oxygen supply during diastole and to decrease myocardial oxygen demand during systole (Fig. 5.12). The balloon is inflated during diastole to increase the diastolic aortic pressure, resulting in increased coronary blood flow. The balloon should be inflated immediately following the closure of the aortic valve at the dicrotic notch of arterial tracing. The balloon is deflated just before the next systole to decrease the intra-aortic pressure and afterload, resulting in decreased myocardial oxygen consumption. The cardiac output is increased because of increased coronary perfusion (diastolic augmentation) and decreased resistance (systolic unloading).

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:135-136.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:992-1009.

Skubas N, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:1073.

C.III-7. What are the complications of IABP?

- Ischemia of the leg
- Dissection of the aorta
- Thrombus formation and embolization
- Renal artery occlusion
- Splenic, mesenteric, and spinal cord infarction
- Internal mammary occlusion
- Thrombocytopenia

- Infection
- Gas embolization
- Inability to place the IABP
- Retroperitoneal bleeding
- Arterial-venous fistula

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:435-442.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Savino JS,

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eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:992-1009.

Skubas N, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:1073.

C.III-8. Can PAOP represent left ventricular end-diastolic volume (LVEDV) after CABG?

It has been demonstrated that in nonsurgical patients, there was a significant correlation between changes in PAOP and LVEDV. However, in patients during the first few hours after CABG, there was a poor correlation between changes in PAOP and LVEDV. The poor correlation was not explained by changes in systemic or pulmonary vascular resistance. The altered ventricular pressure-volume relation may reflect acute changes in ventricular compliance. Although measurement of PAOP remains valuable in clinical management to avoid pulmonary edema, it cannot reliably be used as an index of left ventricular preload while attempting to optimize stroke volume. TEE can accurately assess LVEDV and cardiac contractility.

Harsen RM, Viquerat CE, Matthay MA, et al. Poor correlation between pulmonary arterial wedge pressure and left ventricular end-diastolic volume after coronary artery bypass graft surgery. *Anesthesiology*. 1986;64:764-770.

Reich DL, Mittnacht A, London M, et al. Monitoring of the heart and vascular system. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:416-451.

D. Postoperative Management

D.1. What are the postoperative complications?

Cardiovascular: CHF, arrhythmias, low output syndrome, myocardial ischemia or infarction due to surgical manipulation, prolonged CPB and aortic cross-clamp (coronary ischemia), use of cardioplegic solution, and occlusion or kinking of grafts

Pulmonary: acute lung injury or adult respiratory distress syndrome due to the following:

- Decreased blood flow to the lung during total CPB
- Collapsed alveoli during CPB, resulting in decreased surfactant and decreased distensibility
- Fluid overloading
- Hyperoxia during CPB
- Left ventricular failure
- Microemboli
- Reperfusion injury
- Inflammatory response
- Infections
- Transfusion-related lung dysfunction

Renal

- Polyuria from hemodilution and diuretics
- Oliguria from hypoperfusion
- Acute kidney injury
  - Hypoperfusion
  - Ischemia
  - Inflammatory response
  - Nephrotoxins (preoperative contrast dyes, antibiotics)
- Acute tubular necrosis
- Acute or chronic renal insufficiency

Hemorrhage

- Too much or too little protamine to reverse heparin
- Thrombocytopenia and decreased coagulation factors
- Qualitative and quantitative platelet defect
- Disseminated intravascular coagulopathy
- Fibrinolysis with low levels of fibrinogen
- Poor surgical hemostasis

Embolism: due to air, destroyed or aggregated formed blood elements, fat, endogenous and exogenous debris

Neurologic: stroke and neurocognitive dysfunction marked by functional changes in behavior, personality, or other brain functions; cerebral embolism; and seizures

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Hyperglycemia: hypothermia, dextrose-containing cardioplegia, increased catecholamine levels, and diabetogenic state associated with surgery and CPB

Hypopotassemia: due to hemodilution, alkalosis, and diuretics

Gravlee GP, Davis RF, Stammers AH, et al, eds. *Cardiopulmonary Bypass: Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:382, 403, 506, 628-629.

Levy JH, Tanaka KA, Bailey JM, et al. Postoperative cardiovascular management. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:98-131.

D.2. Would you reverse the muscle relaxants? Why?

Yes and no. If early extubation (fast-track) is planned, short- or intermediate-acting muscle relaxants should be used after CPB, and the neuromuscular function should be monitored. At the end of the procedure, reversal agent can be given to ensure that the patient does not experience paralysis while awake. It may be advisable to continue a short-acting sedative/hypnotic agent such as propofol or midazolam during transport to the intensive care unit (ICU) and for the immediate period required to establish criteria for extubation. In patients who are hemodynamically unstable, with profound hypoxemia (acute respiratory distress syndrome) and/or “open” chest, paralysis should be continued postoperatively until the clinical state has improved. However, it is important to recognize that prolonged paralysis can lead to marked skeletal myopathy.

D.3. When will you wean the patient from the respirator?

Ventilator management, weaning strategy, and extubation time vary significantly among centers practicing cardiac surgery. Historically, patients were weaned from the respirator the following morning after surgery. More recently, if the operative course is smooth and if the patient is hemodynamically stable, weaning and extubation can be performed early (usually 2 to 6 hours after surgery).

Early tracheal extubation (fast-track) after CABG surgery may have cost benefits and improvement in resource use when compared with late tracheal extubation. In one report, early tracheal extubation 1 to 6 hours after surgery reduced total cost per CABG surgery by 25% without increasing the rate or costs of complications in patients younger than 75 years.

Cheng DC, Karski J, Peniston C, et al. Early tracheal extubation after coronary artery bypass graft surgery reduces costs and improves resource use. A prospective, randomized, controlled trial. *Anesthesiology*. 1996;85:1300-1310.

Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:1046-1060.

D.4. What criteria would you use in deciding when to wean the patient from the respirator?

- Consciousness—awake and alert
- Stable vital signs
- Acceptable arterial blood gases—pH, 7.35 to 7.45; PaO_2, over 80 mm Hg with FIO_2, 0.4; $PaCO_2$, 35 to 45 mm Hg

- Acceptable respiratory mechanics
- Vital capacity greater than 10 to 15 mL per kg
- Maximal inspiratory force—greater than 20 to 25 cm H_2O
- Hemostasis—less than 100 mL per hour of chest tube drainage
- Stable metabolic state—normal temperature and electrolytes

The patient should tolerate being on continuous positive airway pressure of 5 cm H_2O and pressure support of 5 cm H_2O with 40% oxygen. If the patient tolerates the continuous positive airway pressure well for 30 minutes and arterial blood gases are acceptable, the patient may be extubated.

Higgins TL, Yared JP. Postoperative respiratory care. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:1046-1060.

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Chapter 6
Mechanical Circulatory Support

Adam Lichtman

Nikolaos J. Skubas

A 58-year-old man is scheduled to undergo an upper gastrointestinal (GI) endoscopy under monitored anesthesia care (MAC). The patient underwent aortic and mitral valve replacement 4 weeks earlier, and the procedure was complicated by cardiogenic shock, for which he had an intra-aortic balloon pump (IABP). The patient's cardiac function did not recover, and a left ventricular assist device (LVAD) was inserted 6 days later.

A. Medical Disease and Differential Diagnosis

1. What is an IABP?
2. How is an IABP placed and positioned?
3. Describe the timing of the IABP inflation and deflation.
4. How does the IABP help improve hemodynamics?
5. List the indications for IABP placement.
6. What are the contraindications and potential complications of IABP placement?
7. What are the pitfalls of IABP timing?
8. When and how is a patient weaned off IABP support?
9. What is mechanical circulatory support?
10. What is a ventricular assist device (VAD)?
11. List the types of VAD.
12. How does VAD work?
13. When is circulatory support needed?
14. What are the physiologic considerations in patients requiring a VAD?
15. Describe the reasons for suboptimal VAD support.

B. Preoperative Evaluation and Preparation

1. What is the focus of the preoperative assessment of an LVAD patient?

C. Intraoperative Management

1. Detail the anesthetic management for a patient undergoing LVAD placement.
2. How is a VAD patient monitored during an anesthetic?
3. Prescribe an anesthetic for a VAD patient.
4. What is extracorporeal membrane oxygenation (ECMO)? What are the different types of ECMO?
5. How are patients monitored and managed while on ECMO?
6. What are the complications of ECMO?

D. Postoperative Management

1. How is weaning from ECMO accomplished?

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A. Medical Disease and Differential Diagnosis

A.1. What is an IABP?

An IABP is a device used to improve the function of a failing heart. It is an 8.5 to 9.5 French dual-lumen catheter with a 40- to 60-mL helium-filled balloon attached at its tip. The IABP provides counterpulsation, whereby the systolic afterload to cardiac ejection is reduced and the perfusion of the coronaries and proximal aortic arteries is augmented.

Kapur NK, Esposito M. Hemodynamic support with percutaneous devices in patients with heart failure. *Heart Fail Clin*. 2015;11:215-230.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24:335-341.

A.2. How is an IABP placed and positioned?

The IABP is placed either percutaneously or under surgical exposure into a peripheral large artery (primarily femoral) and directed retrograde into the thoracic aorta. The size of the balloon used is dictated by the height of the patient (50 mL balloon being most common). The optimal position is with the balloon tip positioned just distal to the origin of left subclavian artery and the proximal end of the balloon before the orifice of the renal arteries. The positioning of an IABP is done either blindly, with subsequent verification of the depth of position with fluoroscopy or x-ray, or under the guidance of transesophageal echocardiography (TEE) in the anesthetized patient. The incorrect placement may cause obstruction of the head or visceral vessels. This may result in possible cerebral or visceral organ ischemia and an ineffective counterpulsation. During IABP support, the patient is anticoagulated.

Klopman MA, Chen EP, Sniecinski RM. Positioning an intraaortic balloon pump using intraoperative transesophageal echocardiogram guidance. *Anesth Analg*. 2011;113:40-43.

A.3. Describe the timing of the IABP inflation and deflation.

The balloon is connected to a control console that is regulating the inflation and deflation of the balloon at the tip of the IABP. The IABP balloon is inflated in diastole and deflated in systole. The triggers for balloon inflation are (1) the electrocardiogram (ECG) T wave; (2) the dicrotic notch on the arterial waveform, which is recorded from the tip of the IABP; and (3) an internal, predetermined ratio. The balloon deflation is timed to occur prior to the ECG Q wave or the upstroke of the arterial line waveform.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24:335-341.

A.4. How does the IABP help improve hemodynamics?

The balloon is timed to inflate in diastole causing an augmented diastolic pressure with resultant increase in blood flow to the coronary arteries, great vessels, and visceral organs. The balloon deflates in systole (just prior to the opening of the aortic valve) causing a “void” or “potential” space in the aorta that reduces left ventricular afterload, which in turn facilitates ventricular systolic ejection and an increase in stroke volume. The decreased systolic afterload reduces the left ventricular wall tension, decreases the myocardial oxygen demand, and ameliorates the effects of coronary ischemia. The IABP counterpulsation is at variable intervals, regulated by the operator, from 1:1 ratio to 1:3 ratio (each beat, to every third beat, respectively). In a properly functioning IABP, the operator looks for (1) the counterpulsation to create a diastolic pressure wave, which is usually higher than the preceding systolic wave, that is, the “assisted” diastolic aortic pressure, with a diastolic pressure value lower than the unassisted diastolic pressure; and (2) for the following systolic pressure wave that is lower than the unassisted systolic pressure.

Unverzagt S, Machemer MT, Solms A, et al. Intra-aortic balloon pump counterpulsation (IABP) for myocardial infarction complicated by cardiogenic shock. *Cochrane Database Syst Rev*. 2011;(7):CD007398.

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White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24:335-341.

A.5. List the indications for IABP placement.

- Cardiogenic shock
- Postcardiac surgery
- High-risk percutaneous coronary interventions (PCIs)
- Severe coronary artery disease (i.e., high-grade left main coronary artery disease)
- Post-myocardial infarction with or without acute mitral regurgitation or ventricular septal defect

In the majority of the cases, the patient is already on maximal vasoactive support without significant improvement in symptoms and/or signs of cardiac failure.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24:335-341.

A.6. What are the contraindications and potential complications of IABP placement?

The contraindications to IABP placement include the following:

- Significant aortic insufficiency (the IABP-induced increased diastolic pressure will worsen the severity of the aortic valvular incompetence and increase the left ventricular diastolic pressure)
- Major aortic pathology (aneurysm, dissection, severe atherosclerotic plaque), which may cause complications during the retrograde advancement of the IABP device retrograde inside the aortic lumen
- Sepsis, with the risk of colonization of the IABP catheter
- Uncontrolled coagulopathy

The most common complication of IABP placement is injury at the vascular entry site, especially in the face of severe peripheral vascular disease. Other complications include ischemia to the ipsilateral limb and bleeding at the insertion site.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24:335-341.

A.7. What are the pitfalls of IABP timing?

Correct diastolic inflation and systolic deflation are critical to optimize the benefits of IABP counterpulsation. Early diastolic inflation of the IABP balloon (inflation is initiated during late systole) will result in increased left ventricular afterload and increased myocardial oxygen consumption. Late diastolic inflation will result in suboptimal coronary perfusion and diastolic augmentation. Early deflation of the IABP will cause suboptimal diastolic augmentation, and the assisted aortic end-diastolic pressure may be equal to or less than the unassisted aortic end-diastolic pressure. In late deflation, the assisted aortic end-diastolic pressure may be equal to the unassisted aortic end-diastolic pressure, resulting in a prolonged isovolumetric contraction phase and increased left ventricular afterload and increased myocardial oxygen consumption.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24:335-341.

A.8. When and how is a patient weaned off IABP support?

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Weaning from IABP support is initiated once the patient's requirement for inotropic support is reduced. The IABP weaning is done in the presence of vasoactive support, so should cardiac output or overall hemodynamics worsen, inotropic support may be increased. Weaning is gradually undertaken over the course or 6 to 12 hours. During this time, the ratio of augmented to nonaugmented beats is decreased gradually from 1:1 to 1:2 to 1:3. At any time, if there are any hemodynamic derangements, the weaning process is halted and the vasoactive medications are adjusted to achieve a stable cardiac output (or mixed venous oxygen saturation). Following a successful weaning period, the IABP device is removed. Weaning from an

IABP may be also performed by sequentially reducing the volume of the balloon inflation during diastole.

Chumnanvej S, Wood MJ, MacGillivray TE, et al. Perioperative echocardiographic examination for ventricular assist device implantation. *Anesth Analg*. 2007;105:583-601.

A.9. What is mechanical circulatory support?

Mechanical circulatory support is a broad term that encompasses the use of devices that provide support (“assist”) or replace the function of the failing heart, lungs, or both. The cardiac support systems (“ventricular assist devices” or VAD) can be used as a short-term “bridge” until recovery occurs or as permanent cardiac replacement (“destination” therapy) in the case of end-stage cardiomyopathies. The mechanical circulatory support devices include IABPs, VAD (for a single or both ventricles “biventricular”), extracorporeal oxygenators, and total artificial hearts.

Ferrari M, Kruzliak P, Spiliopoulos K. An insight into short- and long-term mechanical circulatory support systems. *Clin Res Cardiol*. 2015;104:95-111.

A.10. What is a ventricular assist device (VAD)?

A VAD is a mechanical pump that supports one or both ventricles of a failing heart. The cardiac chamber that is supported is used to classify them: An LVAD provides support for a failing left ventricle, a right VAD (RVAD) supports a failing right ventricle, and a biventricular VAD (BiVAD) provides support of both ventricles. The VADs provide pulsatile or continuous flow. Early VADs used pulsatile flow primarily in an effort to mimic the native circulatory pattern. Unfortunately, they were prone to mechanical failure and infection. The newer VADs rely on the principle of continuous (or axial), nonpulsatile flow. This allows for simpler and smaller VADs with less moving parts.

Ferrari M, Kruzliak P, Spiliopoulos K. An insight into short- and long-term mechanical circulatory support systems. *Clin Res Cardiol*. 2015;104:95-111.

Werdan K, Gielen S, Ebelt H, et al. Mechanical circulatory support in cardiogenic shock. *Eur Heart J*. 2014;35:156-167.

A.11. List the types of VAD.

VADs may be fully implantable, with only the electrical or venting components exiting the skin, or may be paracorporeal, with cannulas that direct blood from the patient to an external device. Externally driven VADs are most likely seen following cardiac surgery and as a temporary bridge to recovery or definitive therapy.

Ferrari M, Kruzliak P, Spiliopoulos K. An insight into short- and long-term mechanical circulatory support systems. *Clin Res Cardiol*. 2015;104:95-111.

A.12. How does VAD work?

In the case of left ventricular support, blood is drained from either the left atrium or left ventricular apex and routed to the VAD and returned to the systemic circulation via a cannula in the ascending aorta. In the case of right ventricular (RV) support, blood is drained from the right atrium or right ventricle and is directed to the VAD, from which it is returned to the pulmonary circulation via a cannula in the main pulmonary artery.

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Ferrari M, Kruzliak P, Spiliopoulos K. An insight into short- and long-term mechanical circulatory support systems. *Clin Res Cardiol*. 2015;104:95-111.

A.13. When is circulatory support needed?

Circulatory support is indicated for temporary, long-term, and destination therapy. Temporary support is indicated in patients undergoing high-risk interventions, such as PCIs in patients with severely impaired left ventricular function or other complicated percutaneous or surgical interventions. Additional indications for circulatory support include the prevention of the sequels of cardiogenic shock (i.e., multisystem organ failure) following myocardial

infarction or cardiac surgery. Due to the severe shortage of donor hearts, long-term circulatory support is used as a "bridge" to cardiac transplantation and in the case of patients not eligible for cardiac transplantation, as terminal ("destination") therapy. A circulatory device may also be temporarily used as a "bridge to therapy" in a patient who requires additional time to allow determining the course of appropriate therapy. The goal when using circulatory support in patients that require hemodynamic support is to avoid the "bridge to nowhere" scenario, when circulatory support is initiated with no clear therapeutic end point.

Ferrari M, Kruzliak P, Spiliopoulos K. An insight into short- and long-term mechanical circulatory support systems. *Clin Res Cardiol*. 2015;104:95-111.

A.14. What are the physiologic considerations in patients requiring a VAD?

The most common ventricle that is supported with a VAD is the left ventricle. In the case of left ventricular failure, a VAD may be indicated. The LVAD will replace some or all of the left ventricular function in supplying systemic perfusion. This will leave the right ventricle unassisted and susceptible to failure from increased preload (the effect of LVAD). At the same time, pulmonary hypertension from any cause will increase RV afterload and RV ischemia will further decrease RV performance. In a similar fashion, an RVAD may increase the preload of the left ventricle and precipitate left ventricular failure. However, the most common scenario is for a patient to be supported with an LVAD or a BiVAD.

Nicolosi AC, Pagel PS. Perioperative considerations in the patient with a left ventricular assist device. *Anesthesiology*. 2003;98:565-570.

A.15. Describe the reasons for suboptimal VAD support.

The performance of a VAD (its systemic output) may decrease from hypovolemia and increased left-sided afterload. Relative or absolute hypovolemia reduces VAD output in the same way hypovolemia would reduce stroke volume in a normal heart. Increased afterload increases the resistance to pump outflow.

Nicolosi AC, Pagel PS. Perioperative considerations in the patient with a left ventricular assist device. *Anesthesiology*. 2003;98:565-570.

B. Preoperative Evaluation and Preparation

B.1. What is the focus of the preoperative assessment of an LVAD patient?

The increasing population of patients supported with a VAD is more and more frequently encountered for noncardiac surgical procedures. These procedures include common, minimally invasive procedures, such as upper and lower GI procedures for bleeding due to arteriovenous malformation, or larger and more extensive surgical procedures.

The preoperative evaluation should include a standard evaluation, taking note of the type of VAD (single ventricle vs. biventricular support), indication for device placement, and quantification of RV function. VAD patients require extensive support services, and there is frequently 24-hour coverage by a specialized nurse or physician assistant, specifically assigned to the hospital VAD program. These specialists often accompany the VAD patients to the operating room and

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are very facile in the intricacies of individual VADs. In addition, the device manufacturers, which have 24-hour support services, are also a source of useful clinical information.

Nicolosi AC, Pagel PS. Perioperative considerations in the patient with a left ventricular assist device. *Anesthesiology*. 2003;98:565-570.

C. Intraoperative Management

C.1. Detail the anesthetic management for a patient undergoing LVAD placement.

The management of patients requiring LVAD placement can be divided into the preoperative, intraoperative, and postbypass periods.

Preoperatively, a patient requiring an LVAD will, by definition, have severely reduced ventricular function. He may require mechanical ventilation, multiple inotropes, vasopressors, or an IABP. Due to chronic heart failure and its treatment, such a patient may have profoundly abnormal electrolytes, liver, renal, and coagulation function tests. Preoperative imaging studies showing the presence of pulmonary hypertension, impaired RV function, and tricuspid regurgitation are particularly important because these findings indicate the possible need for RV support or even placement of RVAD as well.

An arterial line is placed prior to the induction of anesthesia. For anesthetic induction, myocardial depression or rapid changes in systemic vascular resistance should be avoided, no matter what the induction agent may be. Given the slow circulation time, the preemptive administration of vasopressors is prudent to offset the unwanted side effects of induction agents. To avoid possible acute RV dysfunction due to hypoxia and hypercarbia, ventilation and intubation should be accomplished as expeditiously as possible. Early administration of muscle relaxants and controlled lung ventilation with low inspiratory airway pressure is suggested to avoid increases in intrathoracic pressure that may have deleterious effect on the right heart. Once the patient is successfully induced, any implantable cardioverter-defibrillator must be deactivated and any pacing mode changed to allow the use of intraoperative electrocautery. Large-bore peripheral and central intravenous access and a pulmonary artery catheter are placed. Large-bore venous access is especially important in the case of patients that have had prior cardiac surgery because the risk of adhesions and major hemorrhage is a major concern.

Intraoperatively, the anesthetic goals are to avoid deterioration of the existing cardiac function, to avoid hypovolemia and anemia, and to optimize the cardiovascular status while the LVAD is implanted under cardiopulmonary bypass (CPB). Because the primary concern in a patient undergoing an LVAD is RV failure, real-time monitoring of central venous pressure (and its association with pulmonary pressures) is mandatory. TEE is invaluable in patients undergoing LVAD placement, and a complete echocardiographic assessment should be performed on every patient. The focus of the transesophageal echocardiographic examination is (1) the presence of atrial septal defects, which may predispose to right-to-left shunting post-VAD and hypoxemia because the left ventricular pressures are decreased; (2) aortic regurgitation, which will cause a “recycling” of the blood from the aorta back to the left ventricle; (3) tricuspid regurgitation, which may cause or exacerbate RV failure; (4) mitral stenosis, which may decrease filling of the left ventricle and therefore the “preload” to the LVAD; (5) intracardiac thrombus; and (6) preexisting RV dysfunction.

Following the LVAD implantation, the focus is on maintaining euvolemia, treating coagulation abnormalities, and supporting the RV function as needed. A variety of vasoactive medications and inotropes are infused, and frequently inhaled nitric oxide (NO) or prostacyclin is administered to ameliorate any pulmonary hypertension. The VAD patients require long-term anticoagulation.

Nicolosi AC, Pagel PS. Perioperative considerations in the patient with a left ventricular assist device. *Anesthesiology*. 2003;98:565-570.

C.2. How is a VAD patient monitored during an anesthetic?

Standard American Society of Anesthesiologists (ASA) monitoring is used at a minimum. Due to the continuous flow of the newer VADs, noninvasive blood pressure cuffs and pulse oximeters may not reliably function in all patients. Nevertheless, the mean blood pressure should be monitored with noninvasive or direct measurement. When an arterial line placement is necessary, ultrasound may prove useful to locate the vessel because the systemic pulse is weak or

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nonpalpable. The use of central venous pressure monitors or pulmonary artery catheters must be individualized based on the procedure and the patient's underlying RV function. In patients with impaired RV function or for procedures involving large fluid shifts, intraoperative TEE is recommended if available.

In the event of periprocedure cardiac arrest, standard advanced cardiac life support (ACLS) should be employed with the exception of external chest compressions. Chest compressions are contraindicated because they may disrupt or dislodge VAD cannulas.

Nicolosi AC, Pagel PS. Perioperative considerations in the patient with a left ventricular assist device. *Anesthesiology*. 2003;98:565-570.

C.3. Prescribe an anesthetic for a VAD patient.

No specific type of anesthetic is recommended for patients with mechanical circulatory support. The presence of chronic anticoagulation and the acute decrease in systemic vascular resistance following neuraxial anesthesia makes spinal or epidural anesthesia undesirable. Patients with fully implantable VADs should be considered as having a “full stomach” and be treated accordingly. Regardless of the anesthetic technique chosen, physiologic derangements that increase pulmonary and systemic vascular resistance must be avoided because they impact negatively the RV function or the VAD performance. Hypoxemia, acidosis, and hypercarbia all contribute to RV failure and must be avoided at all costs. Adequate preload must be maintained to promote adequate VAD flows. Rapid changes in venous capacitance due to vasodilating medications (propofol) and patient positioning (i.e., reverse Trendelenburg) are poorly tolerated because decreased venous return will reduce LVAD flow. Intravascular volume must be administered carefully to avoid a rapid increase in central venous pressure and possible RV failure.

Nicolosi AC, Pagel PS. Perioperative considerations in the patient with a left ventricular assist device. *Anesthesiology*. 2003;98:565-570.

C.4. What is extracorporeal membrane oxygenation (ECMO)? What are the different types of ECMO?

ECMO is the mechanical support of the heart, lungs, or both using a modified heart-lung bypass machine. Although originally used for short-term therapy (days), the development of improved oxygenators and circuits have allowed patients to be supported on ECMO for weeks, as was the case of patients with respiratory failure due to novel influenza type A (H1N1). There are two basic types of ECMO: venoarterial (VA-ECMO) and venovenous (VV-ECMO). The terms illustrate the location of the cannulas. In each case, a modified CPB circuit is used that is composed of (1) the cannulas and tubing to drain and return the blood, (2) oxygenator/heat exchanger, and (3) pump.

VV-ECMO is used for primarily respiratory failure but may also be used during surgical procedures on the lungs or airway. In VV-ECMO, an oxygenator is placed in-series between an *outflow* cannula (usually internal jugular vein) and a venous *inflow* cannula (usually femoral vein). There is no pump, and the patient's native cardiac output supplies the driving pressure that creates flow across the oxygenator, where gas exchange occurs. Once deoxygenated venous blood has passed through the oxygenator, it is returned to the patient where it mixes with systemic venous blood and is returned via the pulmonary circulation to the left side of the heart and to systemic circulation. As such, there is no cardiac support provided by VV-ECMO. This allows patients on VV-ECMO the opportunity to ambulate or perform physical therapy as well as making the VV-ECMO circuit simpler. TEE is especially useful in directing placement of caval cannulas and diagnosing cannula malposition, obstructed flow, and left ventricular dilatation.

VA-ECMO is akin to conventional CPB, in which blood is drained via a cannula placed in the vena cava, routed to a blood pump and an oxygenator/heat exchanger, and returned via the aorta or a large artery. As a result, both cardiac and pulmonary support is achieved. The indications for VA-ECMO include (1) reversible postcardiotomy shock/failure to wean from CPB, (2) bridge to transplantation, and (3) recently as an adjunct to advanced life support for cardiac arrest (i.e., extracorporeal cardiopulmonary bypass [ECPB]).

Lafç G, Budak AB, Yener AÜ, et al. Use of extracorporeal membrane oxygenation in adults. *Heart Lung Circ*. 2014;23:10-23.

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Shekar K, Mullany DV, Thomson B, et al. Extracorporeal life support devices and strategies for management of acute cardiorespiratory failure in adult patients: a comprehensive review. *Crit Care*. 2014;18:219.

C.5. How are patients monitored and managed while on ECMO?

Due to the thrombotic nature of the circuit and oxygenator, all patients on ECMO require anticoagulation. Heparin is administered with a goal activated clotting time of 1.5 to 2.0 times normal. On VA-ECMO, the circuit flow is titrated to mean arterial pressure and the oxygen

saturation of blood in the drainage cannula (SDO_2). On VV-ECMO, flow is titrated to SpO_2 and SDO_2. Because VV-ECMO is primarily used in respiratory failure, once adequate oxygen saturation is achieved, mechanical ventilation is reduced and the lungs are “rested.” This is achieved by the use of protective lung ventilation strategies, that is, low respiratory rate, limited peak inflation pressures, and the use of positive end-expiratory pressure.

Lafç G, Budak AB, Yener AÜ, et al. Use of extracorporeal membrane oxygenation in adults. *Heart Lung Circ*. 2014;23:10-23.

C.6. What are the complications of ECMO?

Complications of ECMO can be either patient- or circuit-related. Blood clots are the most feared circuit-related complications and may develop at any part in the ECMO circuit, including the pump, oxygenator, or tubing. Rising plasma-free hemoglobin or D-dimers are laboratory signs of clot formation as is an increasing pressure gradient across the oxygenator and a fall in post-oxygenator PO_2.

Patient-related complications include cannula site and coagulopathic bleeding, hemodynamic instability, sepsis, and intracerebral hemorrhage. In VA-ECMO, hypotension, as evidenced by low mean arterial pressure in the presence of adequate ECMO flow, indicates reduced vascular tone. This can be treated with vasopressors such as norepinephrine or vasopressin. In a patient supported by VA-ECMO, low pump output and “line chatter” (visible oscillations of the circuit tubing) are signs of hypovolemia. Because VV-ECMO has no effect on cardiac function, hypotension in a patient supported by VV-ECMO may be caused by hypovolemia, reduced vascular tone, or myocardial dysfunction. In each case, the treatment must be tailored to the specific cause or causes. This includes the administration of volume and the use of inotropes/vasopressors.

Lafç G, Budak AB, Yener AÜ, et al. Use of extracorporeal membrane oxygenation in adults. *Heart Lung Circ*. 2014;23:10-23.

D. Postoperative Management

D.1. How is weaning from ECMO accomplished?

Weaning from VA-ECMO follows the typical sequence of actions as when weaning from CPB. Inotropic support is begun several hours before the planned weaning. Using TEE and a pulmonary artery catheter to guide therapy, ECMO circuit flows are slowly reduced over the course of several hours. With a combination of inotropes for contractility, vasopressors for tone, and volume for preload, the patient is weaned to minimal circuit flows. If the patient remains stable, the circuit is clamped and the cannulas are removed. The presence of pulsatility on the arterial waveform at full ECMO flows indicates myocardial recovery and is a promising sign for a successful wean. If there is declining hemodynamics or evidence of poor tissue perfusion (decreasing mixed venous saturation/low cardiac output), then the ECMO flows are increased and the weaning is abandoned.

Weaning from VV-ECMO requires the return adequate lung function and may take weeks or longer to occur. Signs that a patient can be weaned include improvements in chest radiograph, improved lung compliance, as well as an increasing SaO_2 for a given circuit flow.

Pappalardo F, Pieri M, Arnaez Corada B, et al. Timing and strategy for weaning from venoarterial ECMO are complex issues. *J Cardiothorac Vasc Anesth*. 2015;29:906-911.

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Platts DG, Sedgwick JF, Burstow DJ, et al. The role of echocardiography in the management of patients supported by extracorporeal membrane oxygenation. *J Am Soc Echocardiogr*. 2012;25:131-141.

Rihal CS, Naidu SS, Givertz MM, et al. 2015 SCAI/ACC/HFSA/STS clinical expert consensus statement on the use of percutaneous mechanical circulatory support devices in cardiovascular care (endorsed by the American Heart Association, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention). *J Card Fail*. 2015;21:499-518.

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Chapter 7
Valvular Heart Disease

Natalia S. Ivascu
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Nikolaos J. Skubas

A 78-year-old man was admitted with increasing shortness of breath. He had chest pain in the past but was able to continue with normal activities. He had passed out twice in the past year. On physical examination, a loud systolic murmur could be heard at the left sternal border radiating to the neck. His vital signs were blood pressure 150/90 mm Hg and heart rate 88 beats per minute and irregular. The electrocardiogram showed sinus rhythm with atrial premature contractions and left ventricular hypertrophy (LVH) with strain. A transthoracic echocardiogram (TTE) showed a hypertrophied left ventricle (LV), and Doppler examination demonstrated severe aortic stenosis (AS) with a pressure gradient of 64 mm Hg, mild aortic insufficiency (AI), and moderate mitral regurgitation (MR). He was scheduled for aortic valve (AV) replacement and possible mitral valve (MV) repair or replacement.

A. Medical Disease and Differential Diagnosis

1. What are the major etiologies of AS, AI, mitral stenosis (MS), and MR?
2. What are the major changes in the loading conditions of the LV that result from the four different lesions? Why do they occur? What changes result from them?
3. What are pressure-volume (P-V) loops? What do the different inflection points represent?
4. What are representative P-V loops for the four valvular lesions?
5. Draw the pressure/time curves for the LV, left atrium, pulmonary artery, and aorta for a normal patient and for patients with each of the four valvular lesions.
6. What are the basic principles of echocardiography? What are M-mode, B-mode, and Doppler color modalities? How do TTE and transesophageal echocardiography (TEE) differ?
7. What are the three TEE vantage points for the comprehensive imaging of the LV? How are pressure gradients measured by echocardiography? How do the pressure gradients derived from Doppler echocardiography differ from those obtained in the catheterization laboratory by direct pressure measurement?
8. What is the role for three-dimensional (3D) echocardiography in the operating room?
9. What are the echocardiographic and cardiac catheterization criteria for the four valvular lesions?

B. Preoperative Evaluation and Preparation

1. What are the presenting signs and symptoms of the four valvular lesions listed previously?
2. What is the New York Heart Association classification of heart failure?
3. Discuss the role of premedication for patients with the four different valvular lesions.
4. How would you premedicate the patient with severe AS and MR?

C. Intraoperative Management

1. Outline the hemodynamic management goals for each of the four valvular lesions. What are the anesthetic goals with respect to heart rate and rhythm, preload, afterload, and contractility?
2. What are the hemodynamic goals for this patient with the combination of severe AS and MR?
3. How would you monitor this patient with severe AS and MR?

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4. Should the patient have a pulmonary artery catheter placed before induction?
5. Is a pulmonary artery catheter with pacing capabilities indicated?
6. What anesthetic technique would you employ? Why?
7. What muscle relaxant would you use for this patient?
8. What are the usual TEE findings in a patient with AS or MR? How do you grade the severity of AS by TEE? How do you quantify the severity of MR? What is the impact of AS on the severity of MR?
9. What special considerations particular to cardiopulmonary bypass (CPB) operations do you have for each of the four lesions? Focus on these concerns with respect to the induction and prebypass, bypass, and postbypass periods.
10. The patient cannot be weaned from CPB following an AV replacement and MV replacement. What are the possible causes?
11. How would you diagnose right-sided heart failure and pulmonary hypertension? How would you treat it?
12. How does an intra-aortic balloon pump (IABP) work to benefit the failing heart?
13. What role does the IABP have in this setting?
14. What role does TEE play in the placement, timing, and demonstration of efficacy of an IABP?
15. How would you properly time the IABP cycle?
16. What are the contraindications to the use of an IABP?
17. What is the role for ventricular assist devices?

D. Postoperative Management

1. In the intensive care unit (ICU) 4 hours later, the patient became hypotensive with a low cardiac output. How could you distinguish between cardiac tamponade and pump failure? How would the TEE images differ?
2. Would you extubate this patient early in the ICU? Why?
3. What are the advantages and disadvantages of early extubation?

E. Alternative Treatments

1. What are the percutaneous options for MV repair?
2. How is percutaneous MV repair performed?
3. What are the percutaneous options for AV repair and replacement?
4. How is percutaneous AV replacement performed?
5. What anesthetic techniques and monitors are used?
6. What is minimally invasive cardiac valve surgery?

A. Medical Disease and Differential Diagnosis

A.1. What are the major etiologies of AS, AI, mitral stenosis (MS), and MR?

AS occurs as a congenital lesion but more commonly as an acquired disease. Stenosis may develop on a previously normal AV following rheumatic fever or from progressive calcification. Congenitally bicuspid AV are also prone to calcification with eventual stenosis. Calcification of the AV leaflets can result in incomplete closure of the valve with associated insufficiency.

AI is usually an acquired disease. The most common causes include bacterial endocarditis and rheumatic heart disease. Annular dilation with resultant AI may result from diseases such as cystic medial necrosis and collagen disorders or following aortic dissection.

MS is almost always caused by rheumatic fever, although only half of patients will have a history of an acute febrile illness. The inflammatory process of rheumatic fever results in thickening of the leaflets and fusion of the commissures. Other rare causes include congenital stenosis and other systemic diseases, such as systemic lupus erythematosus and carcinoid.

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Pathophysiology similar to that seen with valvular MS can occur with obstructing left atrial tumors and cor triatriatum. MS commonly occurs in conjunction with other valvular heart disease; only 25% of patients present with isolated MS, and approximately 40% have combined MS and MR.

MR can result from defects in the leaflets, the annular ring or the supporting chords or papillary muscles, or any combination of these. Primary leaflet dysfunction occurs with rheumatic fever but can also follow bacterial endocarditis, connective tissue disorders, and congenital malformations. Annular dilation can follow left ventricular dysfunction and dilation. MV prolapse and rupture of papillary muscles result in incomplete leaflet closure or coaptation with resultant MR. Left ventricular ischemia can affect papillary muscle contraction and is the cause of functional MR.

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Helms AS, Bach DS. Heart valve disease. *Prim Care*. 2013;40(1):91-108.

Iung B, Vahanian A. Epidemiology of acquired valvular heart disease. *Can J Cardiol*. 2014;30(9):962-970.

Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129(23):2440-2492.

A.2. What are the major changes in the loading conditions of the LV that result from the four different lesions? Why do they occur? What changes result from them?

AS represents a chronic systolic pressure load on the LV. This increases the wall tension (stress) in accordance with Laplace's law:

$$\text{Wall tension} = \frac{(\text{Pressure} \times \text{Radius})}{(2 \times \text{Wall thickness})}$$

The LV undergoes parallel duplication of muscle fibers in an attempt to compensate, and this results in increased wall thickness or concentric hypertrophy and some decrease in radius, thereby normalizing wall stress. If the MV remains competent, little change occurs in the other cardiac chambers.

AI causes left ventricular diastolic volume overload due to the additional volume flowing retrograde into the LV across the incompetent AV during diastole. This results in eccentric hypertrophy and left ventricular dilation (increased muscle mass and chamber radius). However, AI decreases the aortic diastolic pressure, which is the pressure that must be exceeded by the contracting LV to open the AV and result in LV systolic ejection. Therefore, LV work is performed against a lower outflow impedance (aortic diastolic pressure). Stroke volume and ejection fraction may be preserved until late in the disease process. As with AS, the presence of a competent MV confines the changes to the LV. However, the LV dilation that follows chronic AI may result in mitral annular dilation or alteration in the papillary muscle orientations with resultant MR. Left atrial enlargement secondary to MR, or left atrial pressure overload as LV end-diastolic pressure (LVEDP) rise in the course of AI can occur.

MS results in a chronically underfilled LV because of progressive obstruction to left atrial emptying. This chronic underloading condition can result in diminished contractile function (a “disuse atrophy” of sort). In addition, if the cause of the MS is rheumatic, myofibril damage may also occur. Contrary to the LV pressure and volume *under*loading, the left atrium is both pressure and volume *over*loaded in order to maintain flow across the progressively narrowing mitral orifice. According to Gorlin's equation for pressure gradient:

$$\text{Pressure gradient (mm Hg)} = \left\{ \frac{\text{Valve flow rate (mL/s)}}{[\text{K} \times \text{valve area (cm}^2\text{)}]} \right\}^2$$

It would predict that the pressure gradient increases by the square of any increase in flow rate or decrease in valve area. The elevated left atrial pressure leads to hypertrophy and eventually dilation that predisposes to premature atrial contractions and subsequent atrial fibrillation. The loss of atrial contraction will further diminish the flow across the stenotic

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MV. At the same time, the elevated left atrial pressure hinders pulmonary venous flow with consequent pulmonary vascular engorgement. This will lead to intimal hypertrophy that induces irreversible elevations in pulmonary vascular resistance. As a consequence of pulmonary hypertension, the right ventricular (RV) systolic pressure increases and RV dilates, and these may lead to RV failure and tricuspid regurgitation.

MR results in volume overload of the LV. In MR, the LV ejects into both systemic circulation (across the AV; high afterload and low compliance) and retrograde to the left atrium (low afterload and high compliance) across the incompetent MV. This “back and forth” of the regurgitant volume results in LV volume overload. However, this work is performed at a low pressure; therefore, LV wall tension is minimally increased initially. As with AI, the volume overload results in marked LV dilation and eccentric hypertrophy. At the same time, the left atrium is also volume overloaded and undergoes dilation. When the volume overload occurs slowly, the pulmonary pressures increases minimally, despite large regurgitant volumes. In contrast, acute MR, for example, following an acute myocardial infarction with papillary muscle rupture, presents a sudden volume overload to the left atrium. Without the time to dilate, the left atrial pressure rapidly rises, limiting pulmonary drainage with resultant pulmonary engorgement and acute increase in pulmonary pressures.

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A.3. What are pressure-volume (P-V) loops? What do the different inflection points represent?

The P-V loop analysis (Fig. 7.1) depicts the relation between LV volume and pressure during a single cardiac cycle. Opening and closing of the MV and AV are represented by the inflection points A, B, C, and D, respectively (Fig. 7.1). Moving from points A through D, AB depicts left ventricular filling, BC depicts isovolumetric contraction, CD shows left ventricular ejection, and DA shows isovolumetric relaxation. Point A coincides with opening of the MV and represents LV end-systolic volume and early diastolic pressure. Point B is closure of the MV and the relationship of end-diastolic pressure (LVEDP) and volume (LVEDV). Point C represents the opening of the AV and coincides with systemic, aortic diastolic pressure. Finally, point D is the closure of the AV and represents LV end-systolic pressure (LVESP) and volume (LVESV), coinciding with the dicrotic notch in the aortic pressure tracing (Fig. 7.1). LV compliance is the relation between pressure and volume and is defined by the slope of the filling phase (segment AB). Preload is the P-V relation before the onset of contraction (LVEDP). Contractility may be illustrated by the slope of a line termed the *end-systolic pressure-volume relation* (ESPVR). The ESPVR slope is created by connecting multiple points (D) from multiple P-V loops generated by changing the filling volume to the LV (Fig. 7.2). Increased contractility results in a steeper line, whereas diminished contractility results in a flatter line. The P-V loop analysis permits illustration of stroke volume and ejection fraction. Stroke volume is defined as difference in volume from the end of filling to the end of ejection (EDV-ESV), whereas the ejection fraction is the ratio of stroke volume to total volume in the heart at peak filling (SV/EDV). Therefore, the P-V loop analysis permits illustration of the volume-pressure relations and their changes with each of the four valvular lesions.

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Carabello BA. Volume overload. *Heart Fail Clin*. 2012;8(1):33-42.

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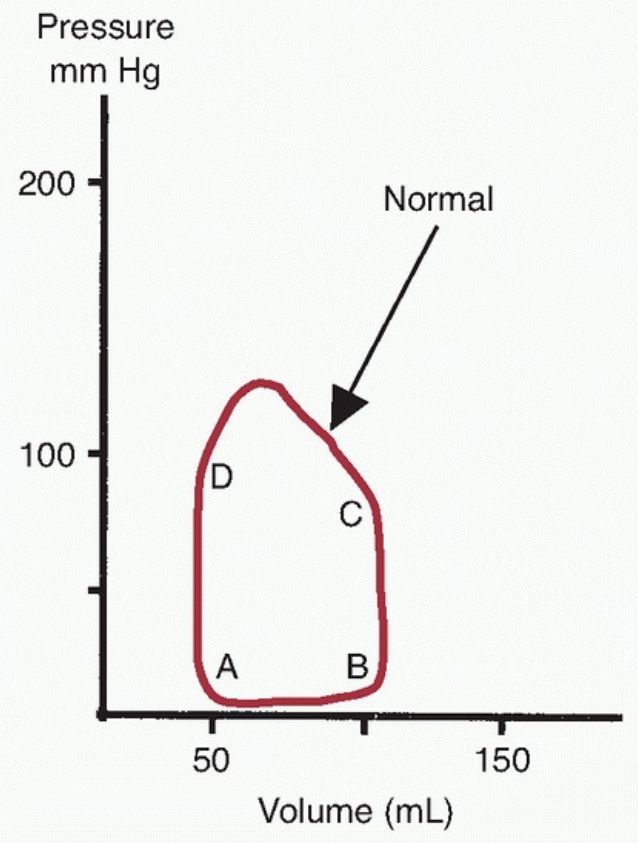


FIGURE 7.1 Normal pressure-volume loop and valve positions. A, mitral valve (MV) opening; AB, left ventricular filling; B, MV closure; BC, isovolumetric contraction; C, aortic valve (AV) opening; CD, ejection; D, AV closure; DA, isovolumetric relaxation.

A.4. What are representative P-V loops for the four valvular lesions?

The hallmarks of AS, illustrated by the P-V loop analysis, are an increased LV systolic pressure and an upward and counterclockwise rotation in the end-diastolic P-V relation (AB) indicative of decreased chamber compliance (Fig. 7.3). Stroke volume and ejection fraction are well preserved, but the ejection phase of the loop occurs at much higher pressures.

This is permitted by an increase in contractility (counterclockwise rotation of the ESPVR line).

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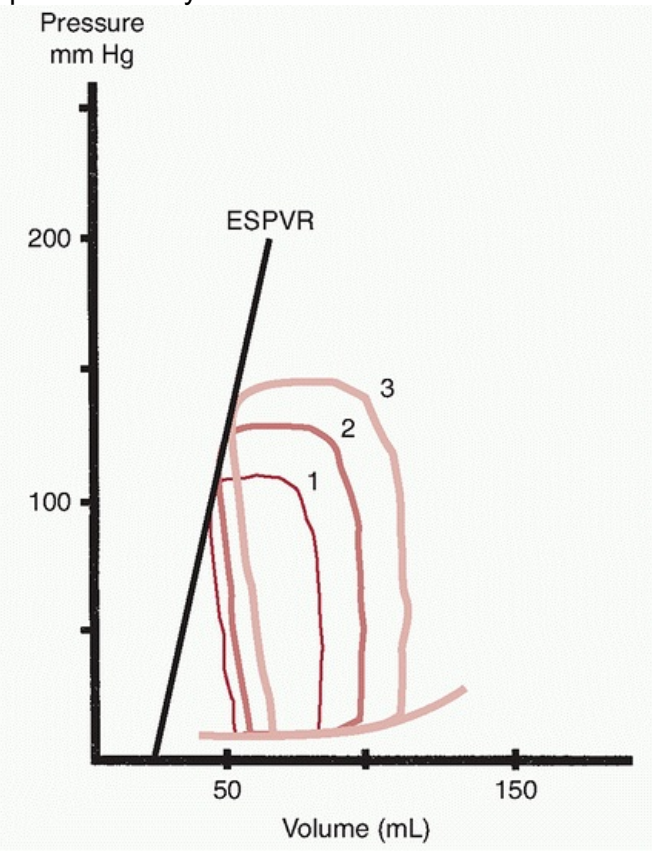


FIGURE 7.2 Contractility. ESPVR, end-systolic pressure-volume relations.

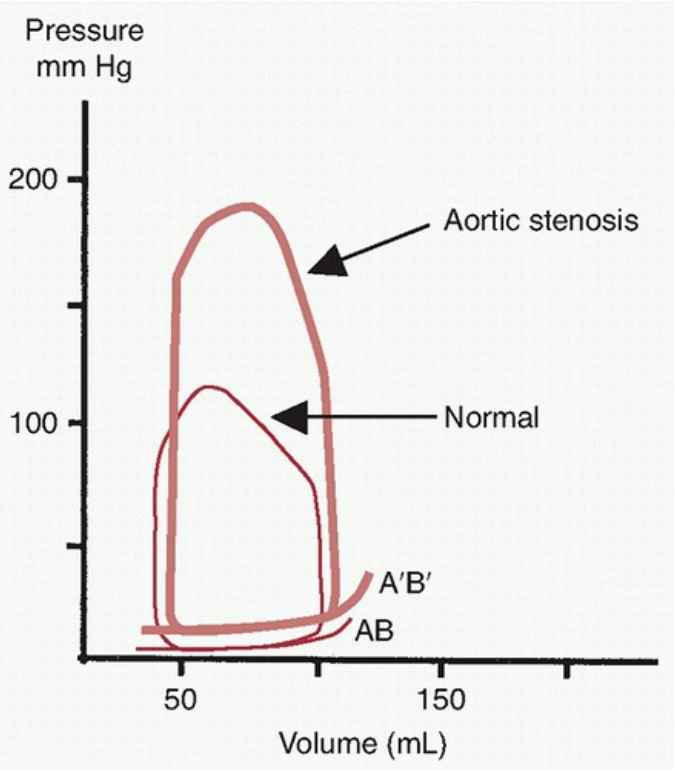


FIGURE 7.3 Pressure-volume loop of aortic stenosis.

The schematic P-V loop for chronic AI depicts an enlarged LV. The minimal change in LVEDP despite the large volume overload is seen by the shift in the diastolic P-V curve to the right (A″B″) (Fig. 7.4). Low systemic diastolic pressures

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result in a brief isovolumetric phase (B″C″) and early complete ejection. The isovolumetric relaxation phase is absent because the incompetent valve permits regurgitant filling of the LV from the aorta during diastole even before opening of the MV. In contrast, when acute AI occurs, the LV compliance is unchanged. Rapid increases in LVEDP from volume overload along the unshifted LV diastolic P-V curve (A′B′) rapidly lead to increased left atrial pressure and pulmonary congestion.

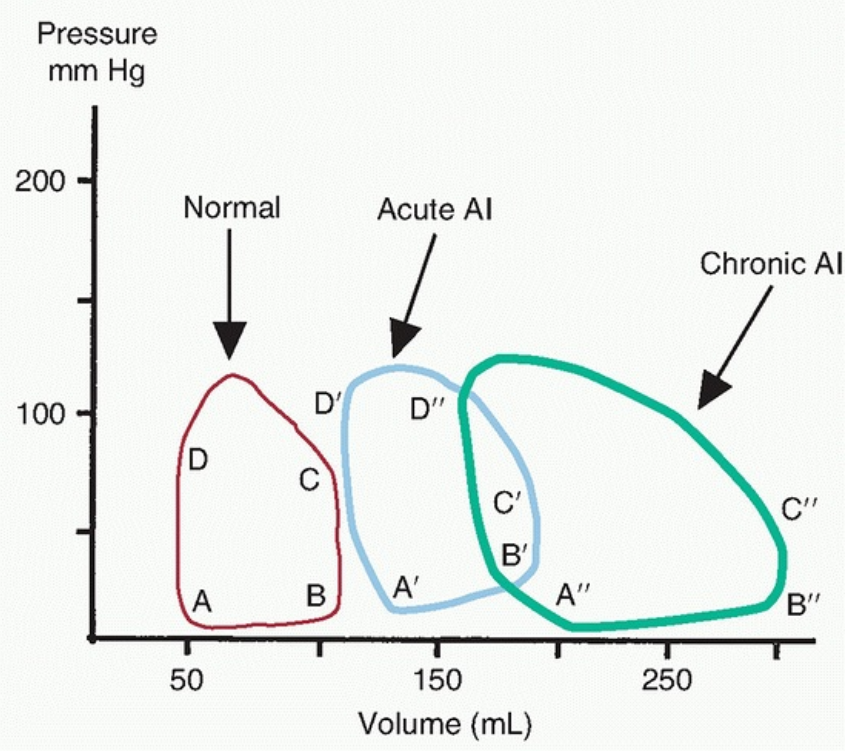
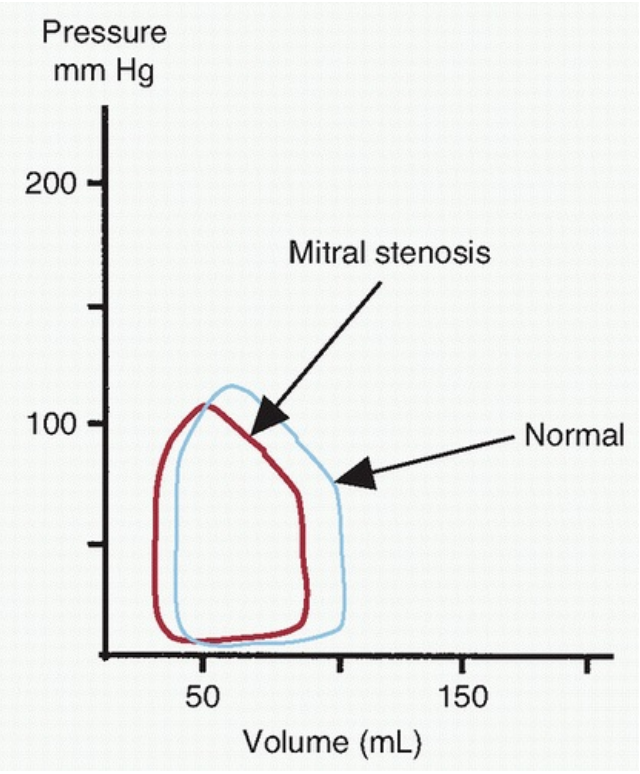


FIGURE 7.4 Pressure-volume loops of acute and chronic aortic insufficiency (AI).



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FIGURE 7.5 Pressure-volume loops of mitral stenosis.

The P-V loop of MS illustrates hypovolemia, the cause of which cannot be determined from the loop alone (Fig. 7.5). Because the predominant impact of MS occurs proximal to the LV, the P-V analysis format is less useful.

In MR, the diastolic P-V relation (line AB) is shifted to the right, as it is in chronic AI, consistent with a marked increase in compliance (Fig. 7.6). The isovolumetric phase (BC) is nearly absent because the left atrium generally serves as a low-pressure/high-compliance route for ejection through an incompetent MV. Decreases in contractility are depicted by a decrease in the slope of the end-systolic-PV line (line through D).

Carabello BA, Zile MR, Tanaka R, et al. Left ventricular hypertrophy due to volume overload versus pressure overload. *Am J Physiol*. 1992;263(4 pt 2):H1137-H1144.

Nishimura RA, Carabello BA. Hemodynamics in the cardiac catheterization laboratory of the 21st century. *Circulation*. 2012;125(17):2138-2150.

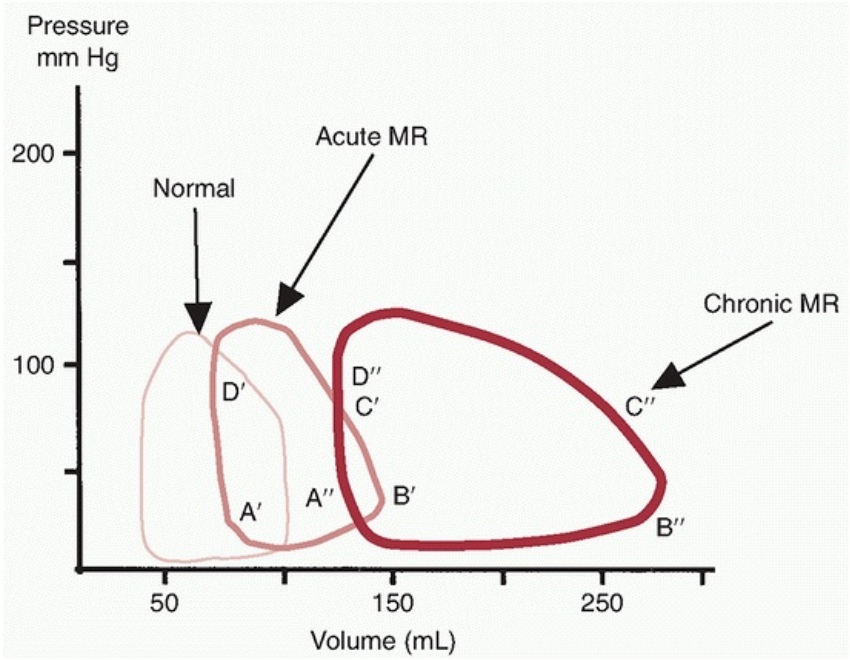


FIGURE 7.6 Pressure-volume loop of acute and chronic mitral regurgitation (MR).

A.5. Draw the pressure/time curves for the LV, left atrium, pulmonary artery, and aorta for a normal patient and for patients with each of the four valvular lesions.

Normal curves are shown in Figure 7.7. The points A, B, C, and D correspond to the same points in the P-V loops.

Aortic Stenosis

The additional systolic pressure work of AS can be seen in the LV pressure tracing (Fig. 7.8). Elevations in LVEDP (point B) can be seen to diminish the perfusion gradient for coronary flow to the LV. The augmentation in LV filling late in diastole secondary to atrial contraction (left atrial "kick" from sinus rhythm) is highlighted in the inset. Rising LV diastolic pressures secondary to decreased compliance necessitate elevations in left atrial pressures to permit complete LV volume loading. Atrial systole provides this elevation in left atrial pressure synchronous with elevations in LVEDP while keeping left atrial pressures relatively low during the remaining cardiac cycle facilitating pulmonary venous drainage.

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Aortic Insufficiency

The rapid upstroke and rapid decline of arterial pressure indicate absence of AV closure and low end-diastolic aortic pressure (Fig. 7.9). Elevations in LVEDV and LVEDP are typical of AI. The early increase in LVEDP can result in LV pressures exceeding those of the left atrium during diastole, with resultant premature closure of the MV.

Mitral Stenosis

Elevations in pressure are seen in both the left atrial and pulmonary artery tracing with MS (Fig. 7.10). The large gradient between left atrial and LV pressures is highlighted in the inset. Chronic elevation in pulmonary volume induces changes in the luminary vascular bed and leads to pulmonary hypertension.

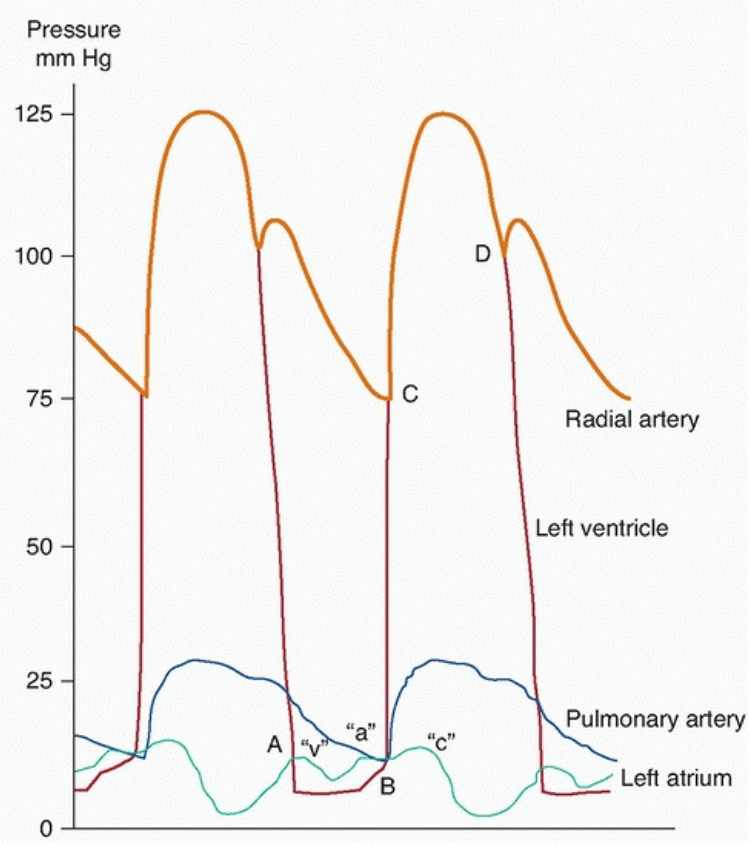


FIGURE 7.7 Pressure curves for the left ventricle, left atrium, pulmonary artery, and aorta in a healthy individual.

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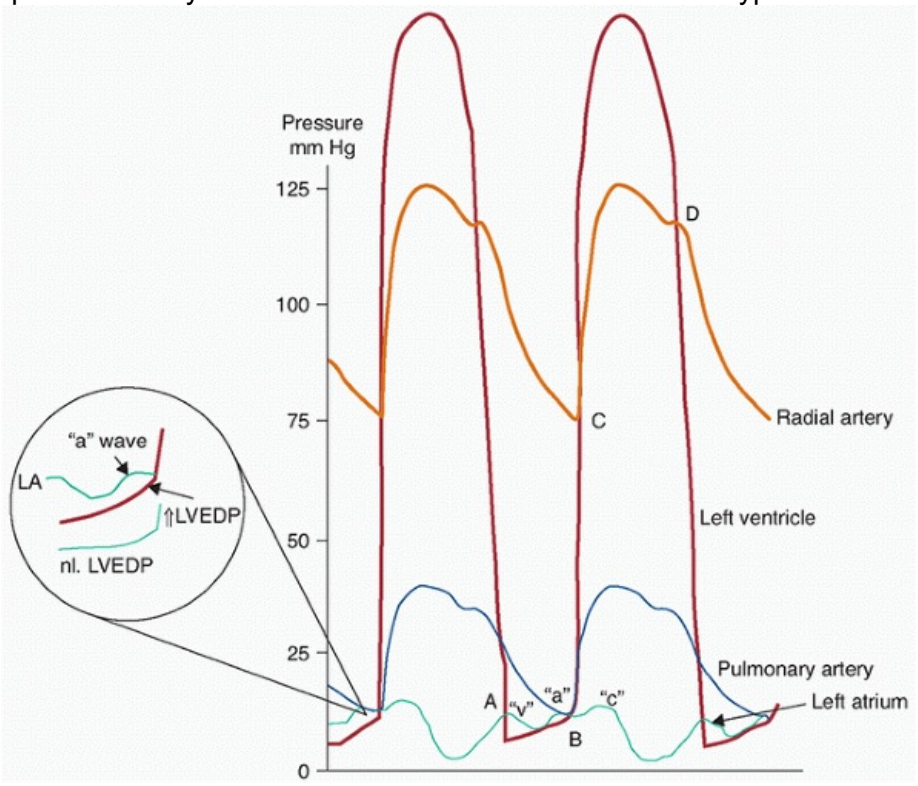


FIGURE 7.8 Pressure curves for the left ventricle, left atrium (LA), pulmonary artery, and aorta in patients with aortic stenosis. LVEDP, left ventricular end-diastolic pressure.

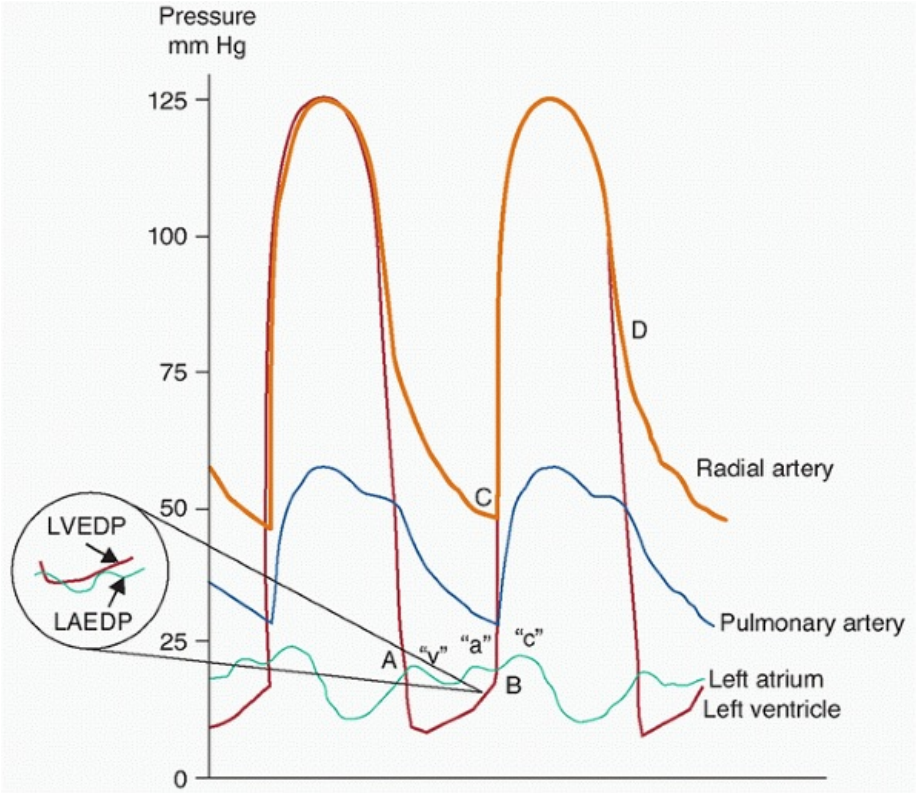


FIGURE 7.9 Pressure curves for the left ventricle, left atrium, pulmonary artery, and aorta in patients with aortic regurgitation. LAEDP, left atrium enddiastolic pressure; LVEDP, left ventricular end-diastolic pressure.

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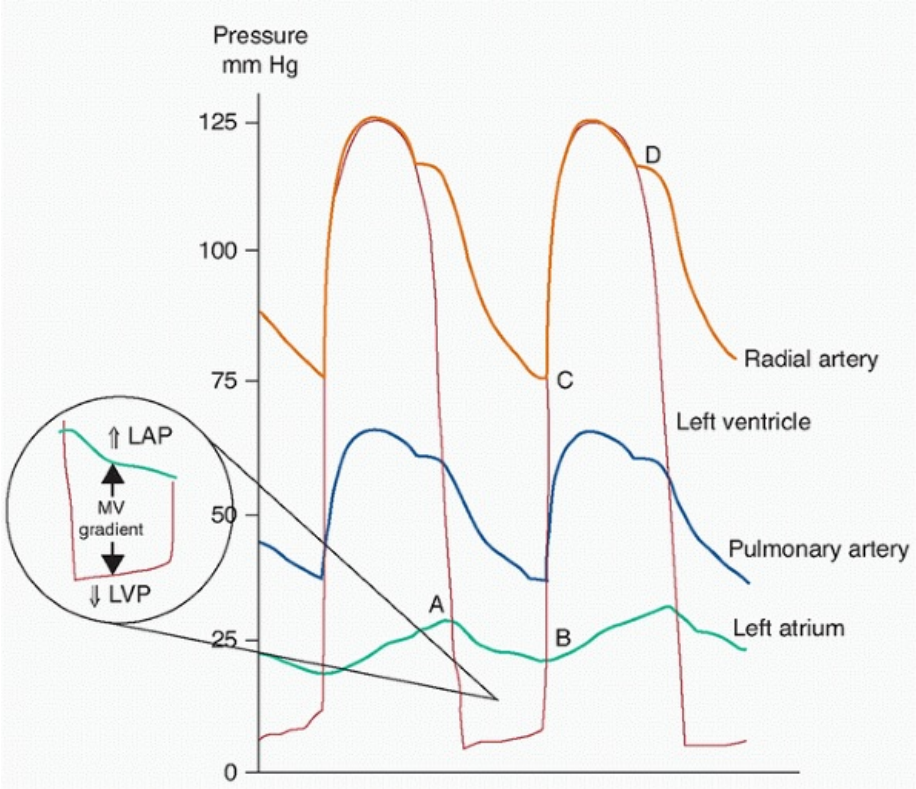


FIGURE 7.10 Pressure curves for the left ventricle, left atrium, pulmonary artery, and aorta in patients with mitral stenosis. LAP, left atrial pressure; LVP, left ventricular pressure; MV, mitral valve.

Mitral Regurgitation

The hallmark of MR is the marked elevations of left atrial pressure during systole and the occurrence of a giant “cv” wave and elevated pulmonary artery pressures (Fig. 7.11).

Carabello BA, Zile MR, Tanaka R, et al. Left ventricular hypertrophy due to volume overload versus pressure overload. *Am J Physiol*. 1992;263(4 pt 2):H1137-H1144.

A.6. What are the basic principles of echocardiography? What are M-mode, B-mode, and Doppler color modalities? How do TTE and transesophageal echocardiography (TEE) differ?

Echocardiography is the use of sound waves to image structures and blood flow within the heart and great vessels. To image tissue, sound waves are emitted from a transducer at known speeds and constant intervals. The sound packets bounce off structures in their path, and the reflected sound waves are received by the transducer during its “listening” mode. The time it takes for the reflected waves to return to the crystal is measured, and because the velocity of sound in tissues is relatively constant (1,540 m per second), solving for distance can be easily accomplished:

Distance = ½ (velocity × time)

(½ because the distance is traversed twice, once to the object and again on returning).

In this manner, the spatial orientation of cardiac structures can be determined. The strength of the returning signal can be quantified as an amplitude, therefore “A” or amplitude mode (Fig. 7.12B). The echocardiographic system codes this amplitude on a black and white scale, thereby converting the amplitude to brightness or B-mode scanning (Fig. 7.12C).

Figure 7.12D shows this “ice-pick” view through the LV of the heart. Each change in tissue density results in some sound waves being reflected and hence an interface. In this example, bold lines are seen at the epicardial, the endocardial-chamber, the chamber-endocardial, and the epicardial borders. If these amplitude bars are displayed in real time, a motion or M-mode display results (Fig. 7.12E). These images were difficult to reliably obtain and interpret because the views represent a linear slice without surrounding structural images for referencing. If the probe is moved in a sweeping

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mode, back and forth repetitively, multiple M-mode images can be obtained in a given instant and a two-dimensional (2D) image formed. This rapid back and forth sweep of the ultrasound beam is performed electronically in a phased array transducer. The images derived in this manner appear as a cineradiographic display of myocardial movement. Echocardiography can provide information about the size, shape, location, and movement of myocardial structures.

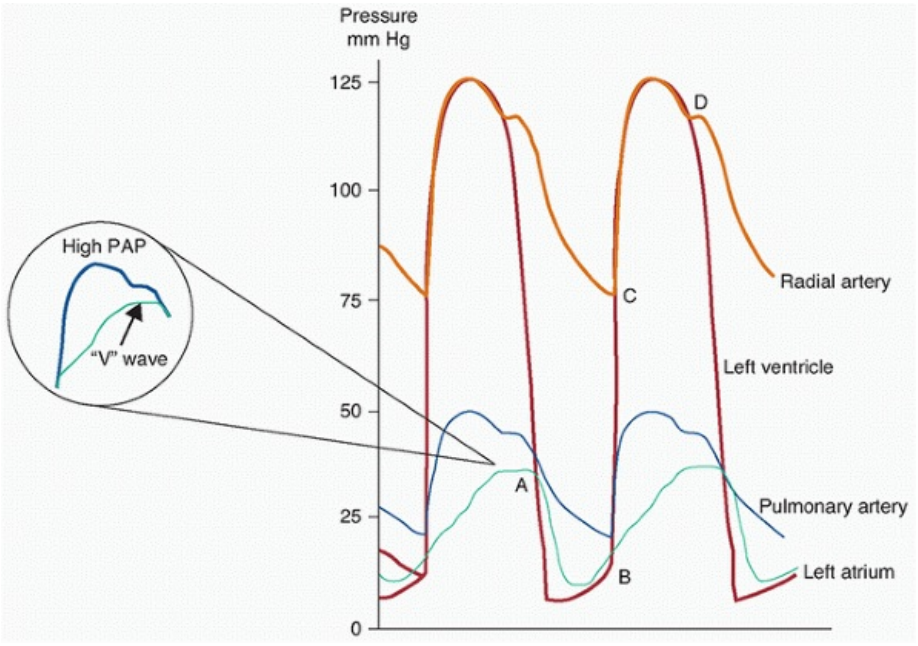


FIGURE 7.11 Pressure curves for the left ventricle, left atrium, pulmonary artery, and aorta in patients with mitral regurgitation. PAP, pulmonary artery pressure.

In addition to determining how long it takes for a given sound wave to return and thereby deriving the distance from the transducer, contact of the sound wave packet with the reflecting object (tissue, blood cells, air) will alter the wavelength of the sound packet according to the Doppler principle. When the object coming in contact with the sound wave is moving toward the source of the ultrasound, the reflected ultrasound wavelengths are compressed (shorter). The opposite occurs when the contacted object is moving away from the sound source. These shifts in frequency (ΔF) are proportional to the velocity of the contacted structure, and thereby, the velocity and direction of the encountered object (usually of blood flow) can be calculated. With Doppler ultrasound, only the component of blood flow parallel to the Doppler beam will be analyzed, since the Doppler equation: velocity = $c (\Delta F) / 2 F_T (\cos \theta)$, contains the cosine of the angle of incidence between the ultrasound beam and the moving object (F_T is the transmitted frequency). Because the cosine of 90 degrees is zero, blood flow that is perpendicular to the ultrasound beam will not cause any Doppler shift and, therefore, cannot be measured. For this reason, it is important to

choose an ultrasound "window" in which the expected blood flow direction is most parallel to the ultrasound. This velocity information can be displayed on a color map (Doppler color flow) or on a time/velocity scale (spectral Doppler display). Doppler-derived blood flow velocity information can determine laminar and turbulent flow patterns, regurgitant or stenotic lesions, and congenital anomalies and can permit quantification of pressure gradients.

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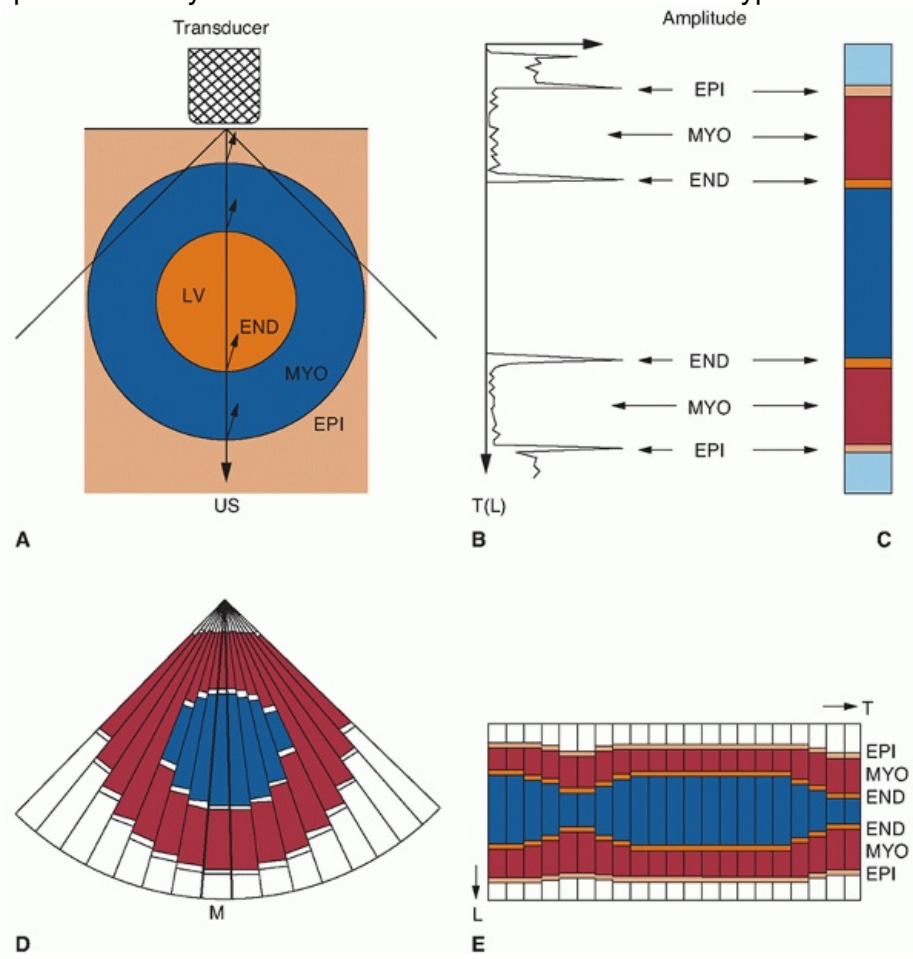


FIGURE 7.12 The process of producing the B-mode and M-mode images. **A.** A pulse of ultrasound is emitted into the object, and the backscattered echo is received by the same transducer. **B.** The received acoustic signal is converted to the electric signal (A-mode). **C.** The amplitude is modulated into brightness (B-mode). **D.** As subsequent pulses of ultrasound are emitted with the sequentially changing angles and the obtained one-dimensional (1D) B-mode images are compounded according to the direction of each ultrasound emission, the first frame of the sector-shaped image is formed. **E.** When the ultrasound is repeatedly transmitted in one direction, a series of 1D B-mode images is obtained. As these are arranged against time, an M-mode image is obtained. END, endocardium; EPI, epicardium; L, length; LV, left ventricle; M, motion; MYO, myocardium; T, time; US, ultrasound. (From Oka Y, Goldiner PL, eds. *Transesophageal Echocardiography*. Philadelphia, PA: JB Lippincott; 1992:12, with permission.)

Pressure gradients (ΔP) can be estimated from the measured blood flow velocity using the modified Bernoulli equation ($\Delta P = 4 \times \text{velocity}^2$). Simply, the greater the velocity of blood flow, the higher is the ΔP. TTE uses imaging points or "acoustic windows" obtained with the transducer handheld on the chest wall. TTE is simple and noninvasive. Most standard echocardiograms are obtained from this position. During cardiac surgery, the chest wall is in the sterile field and therefore unavailable. The esophagus lies immediately adjacent to the heart outside of the operative field and affords an excellent imaging vantage point. In 1976, Yasu Oka from the Albert Einstein College of Medicine developed a practical method of intraoperative imaging. She mounted an ultrasound crystal on the end of a gastroscope and, thereby, obtained images of the heart during surgery. This has been refined considerably since. TEE has become the standard of care for heart surgery at many institutions. The close proximity of the probe to the heart affords excellent resolution. The probe is not in the operative field, so surgery is unhindered and sterility is not an issue. Although mildly invasive, the risk for esophageal injury in the anesthetized state is very low.

Intraoperative TEE is beneficial for quantification of cardiac contractility, for determination of the severity of regurgitant and stenotic valvular disease, for detection of intracardiac shunts and the occurrence of dissections, and as a guide for catheter placement.

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Oka Y, Goldiner PL, eds. *Transesophageal Echocardiography*. Philadelphia, PA: JB Lippincott; 1992:9-27.

Savage RM, Aronson S, Shernan SK, eds. *Comprehensive Textbook of Intraoperative Transesophageal Echocardiography*. 2nd ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2011:3-41.

A.7. What are the three TEE vantage points for the comprehensive imaging of the LV? How are pressure gradients measured by echocardiography? How do the pressure gradients derived from Doppler echocardiography differ from those obtained in the catheterization laboratory by direct pressure measurement?

The heart has two main axes: the longitudinal axis running from the base to the apex and the short axis perpendicular to that. Multiple scan planes are required to completely image a 3D structure, such as the heart. The LV is divided into 17 segments: 6 at the basal level, 6 at the midpapillary level, 4 at the apical level, and 1 apical cap (Fig. 7.13). By moving the TEE probe in the esophagus and rotation of the crystal within the transducer tip, the LV can be imaged from three acoustic windows. These are the midesophageal four-chamber, the transgastric short axis, and the transgastric two-chamber view. Normal ventricular motion requires that each wall segment thickens and moves toward the LV cavity at systole. Segmental wall function is usually quantified as normal, hypokinesis, akinesis, and dyskinesis.

In addition to function, TEE permits the determination of wall thickness and chamber size—important parameters in understanding the pathophysiology of valvular heart disease.

As mentioned previously, pressure gradients are derived through analysis of the Doppler profiles of blood flow. A commonly determined echocardiography gradient is that which is present from the LV to the aorta in the setting of AS. To obtain the change in blood flow velocity across the AV with TEE, the probe is advanced far into the stomach and sharply anteflexed and left deflected to obtain the window from the apex of the heart (deep transgastric long axis) and align the ultrasound beam most parallel to the path of blood flow. From this window, the continuous-wave Doppler cursor is directed across the LV outflow tract and AV. An example of such a spectral Doppler display is seen in Figure 7.14. The large increase in blood flow velocity in this display occurs at the narrowest point along its path, which, in this case, is the stenosed orifice of the AV. Using the modified Bernoulli equation mentioned previously, a gradient is calculated (100 mm Hg in the example). This represents the maximum instantaneous systolic pressure difference between the LV and the aorta. AS is also quantified at the time of catheterization

by measuring the pressures from within the LV, and the aorta as a rapid response pressure transducer catheter is withdrawn from the LV back to the aorta across the stenotic valve. The standard reported pressure gradient is the difference between the maximum LV and aorta pressures. Figure 7.15 illustrates that these peaks are not simultaneous events. Therefore, Doppler-derived AS gradients are usually higher than those derived at the time of left heart catheterization.

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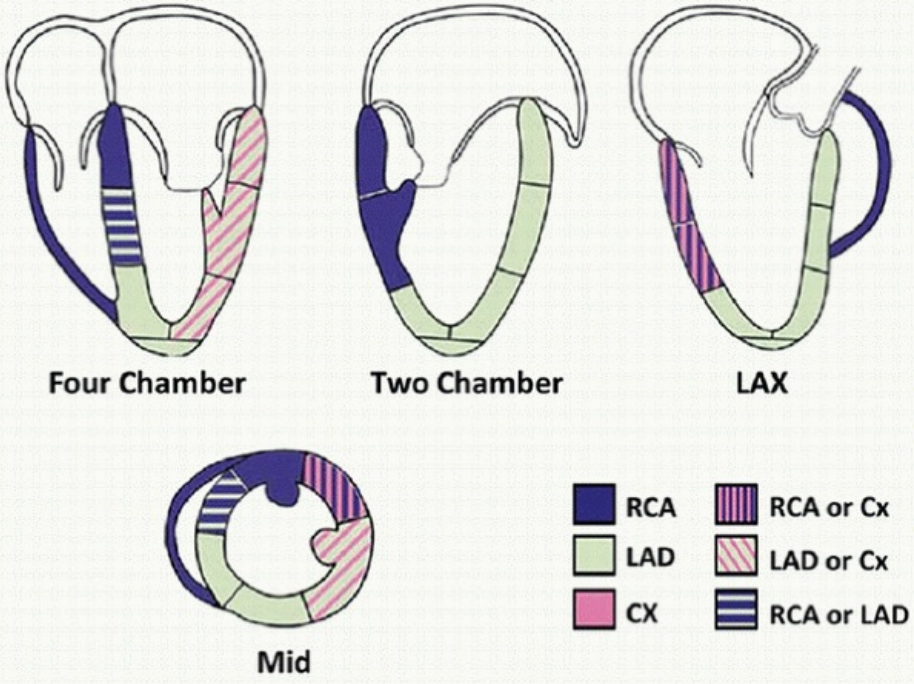


FIGURE 7.13 Wall segments of the left ventricle. (From Reeves ST, Finley AC, Skubas NJ, et al. Basic perioperative transesophageal echocardiography examination: a consensus statement of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. *J Am Soc Echocardiogr*. 2013;26(5):443-456.)

Hahn RT, Abraham T, Adams MS, et al. Guidelines for performing a comprehensive transesophageal echocardiographic examination: recommendations from the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. *J Am Soc Echocardiogr*. 2013;26(9):921-964.

Reeves ST, Finley AC, Skubas NJ, et al. Basic perioperative transesophageal echocardiography examination: a consensus statement of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. *J Am Soc Echocardiogr*. 2013;26(5):443-456.

Savage RM, Aronson S, Shernan SK, eds. *Comprehensive Textbook of Intraoperative Transesophageal Echocardiography*. 2nd ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2011:406-425.

A.8. What is the role for three-dimensional (3D) echocardiography in the operating room?

Modern TEE technology has progressed from 2D multiplane images to real-time 3D displays of the heart. The 3D probes are etched in such a way as to allow for a pyramidal scanning sector (volume). There are different 3D imaging modalities used to assess cardiac anatomy (real-time, zoom, and full-volume, usually gated to ECG signal). The 3D images can be further modified by cropping in any plane to investigate details in morphology. Studies have shown that intraoperative assessment of the MV with 3D TEE examinations have decreased interobserver variability and provided better correlation with surgical findings.

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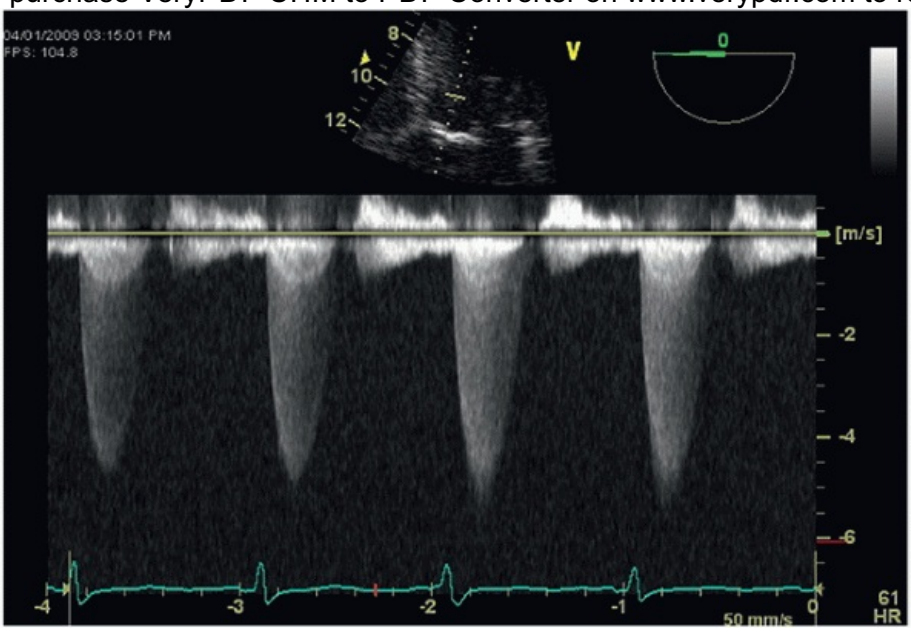


FIGURE 7.14 Continuous-wave Doppler across the aortic valve in the deep transgastric apical view from a patient with severe aortic stenosis.

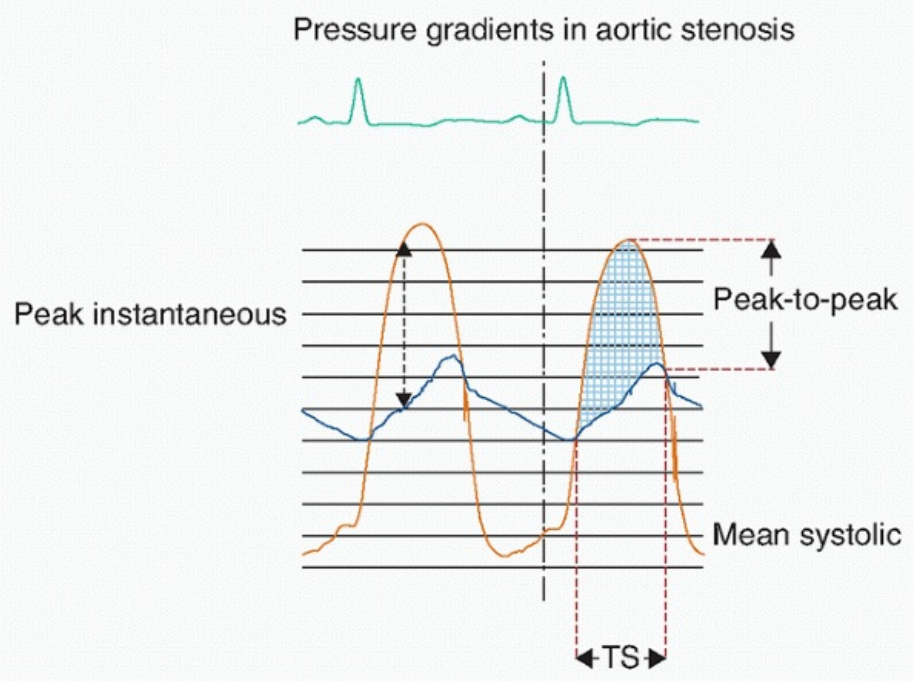


FIGURE 7.15 Pressure gradients in severe aortic stenosis are measured during systole as the difference between aortic and left ventricular pressures displayed using a scale of 0 to 20 mm Hg. The peak instantaneous gradient is the maximum gradient noted; the peak-to-peak gradient is the difference between peak left ventricular and aortic pressures. The mean systolic gradient is the average of all systolic pressure gradients noted during systolic ejection (TS). (Adapted from Nanda NC, ed. *Doppler Echocardiography*. Philadelphia, PA: Lea & Febiger; 1993:130.)

LV assessments including volume and wall motion can easily be done in the operating room. After identification of the LV walls and apex from two orthogonal 2D views, a 3D model of the heart is created using endocardial border tracking. Stroke volume and ejection fraction can be automatically calculated. However, 3D echocardiography can only be combined with color, not spectral, Doppler ultrasound, and is prone to all limitations related to 2D echocardiography.

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Jungwirth B, Mackensen GB. Real-time 3-dimensional echocardiography in the operating room. *Semin Cardiothorac Vasc Anesth*. 2008;12:248-264.

Vegas A, Meineri M. Core review: three-dimensional transesophageal echocardiography is a major advance for intraoperative clinical management of patients undergoing cardiac surgery: a core review. *Anesth Analg*. 2010;110:1548-1573.

A.9. What are the echocardiographic and cardiac catheterization criteria for the four valvular lesions?

The TEE severity scales of the various valvular lesions are summarized in Table 7.1.

Aortic Stenosis

Echocardiographic criteria for AS include 2D imaging demonstrating limited AV cusp motion, small orifice, and LV concentric hypertrophy (Fig. 7.16, Video 7.1). Doppler examination will reveal a turbulent, high-velocity jet across the AV, and color flow Doppler will demonstrate a turbulent, mosaic-appearing color map. The gradient across the AV measured at cardiac catheterization is different from that measured by echocardiography as mentioned previously. Quantification of the Doppler-derived AS pressure gradient relies on the modified Bernoulli equation.

Pressure gradient (mm Hg) = 4 (transaortic valve velocity, m/s)^2

TABLE 7.1 Transesophageal Echocardiography Severity Scales of Valvular Lesions

		SEVERITY SCALE		
MEASUREMENT	**NORMAL**	**MILD**	**MODERATE**	**SEVERE**
MS				
MVA (cm^2)	4.0-6.0	>1.5	1.0-1.5	<1.0
Mean pressure gradient (mm Hg)	<2.0	<5.0	5.0-10.0	>10.0
AS				
AVA (cm^2)	2.5-3.5	>1.5	1.0-1.5	<1.0
Mean pressure gradient (mm Hg)	<5	<20	20-40	>40
MR				
Jet area/LA area	0	<20%	20%-40%	>40%
Jet area (cm^2)	0	<4.0	4.0-10.0	>10.0
Pulmonary vein Doppler	S wave ≫ D	S > D	S < D	Systolic flow

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	wave			reversal
AI				
Jet width/LVOT width	0	<25%	25%-60%	>60%

AI, aortic insufficiency; AS, aortic stenosis; AVA, aortic valve area; LA, left atrial; LVOT, left ventricular outflow tract; MR, mitral regurgitation; MS, mitral stenosis; MVA, mitral valve area; PM, papillary muscle.

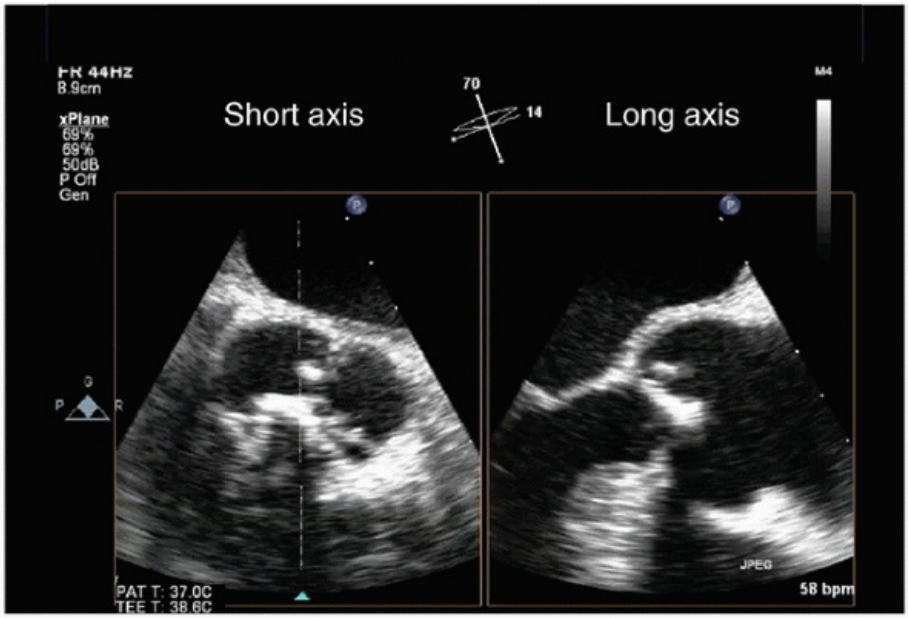


FIGURE 7.16 Transesophageal echocardiographic findings of moderate aortic stenosis (midesophageal aortic valve short-axis view **[left]** and long-axis view **[right]**). The aortic valve cusps are calcified and demonstrate limited systolic excursion.

Because flow is an important determinant of pressure gradients, both the catheterization and Doppler-derived values must be interpreted along with cardiac output. Calculations permit the determination of a valve area. Severe AS is present when the mean pressure gradient exceeds 40 mm Hg or the valve area is less than 1.0 cm^2.

Aortic Insufficiency

Catheterization criteria for AI rely on the qualitative estimation of the regurgitation volume and an estimation of LV size and ejection fraction. Similar quantification can be made from Doppler color echocardiography-derived data. A commonly used echocardiographic criteria compares the width of the regurgitant jet at the level of the AV to the width of the LV outflow tract. A ratio of greater than 0.6 corresponds with severe AI (Fig. 7.17, Video 7.2). Another sign of severe AI can be observed in the spectral Doppler display of blood velocity in the descending thoracic aorta. The TEE probe is advanced to the level of the descending thoracic aorta and rotated to 90 degrees to obtain a long axis view. Under normal conditions, flow remains forward (to distal beds) during diastole. In severe AI, regurgitation of blood back into the ventricle decreases proximal pressure in the aorta, and thus, the spectral display of blood velocities will demonstrate a reversal of blood flow during diastole back toward the aortic root.

Mitral Stenosis

The severity of MS can be obtained by the direct measurement of a diastolic gradient between the left atrium and ventricle at the time of cardiac catheterization. This requires a transatrial puncture, a procedure largely replaced by echocardiographic techniques. Echocardiographic diagnosis is based on gradient estimation by Doppler and by measuring the rate of decay in

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the pressure with the time spent in diastole (pressure halftime). The MV area (cm^2) can be derived from an empirical formula wherein the MV area equals 220 divided by this pressure halftime. Severe MS is present when the mean diastolic gradient exceeds 10 mm Hg, corresponding to a valve area of less than 1.0 cm^2 (Fig. 7.18, Video 7.3).

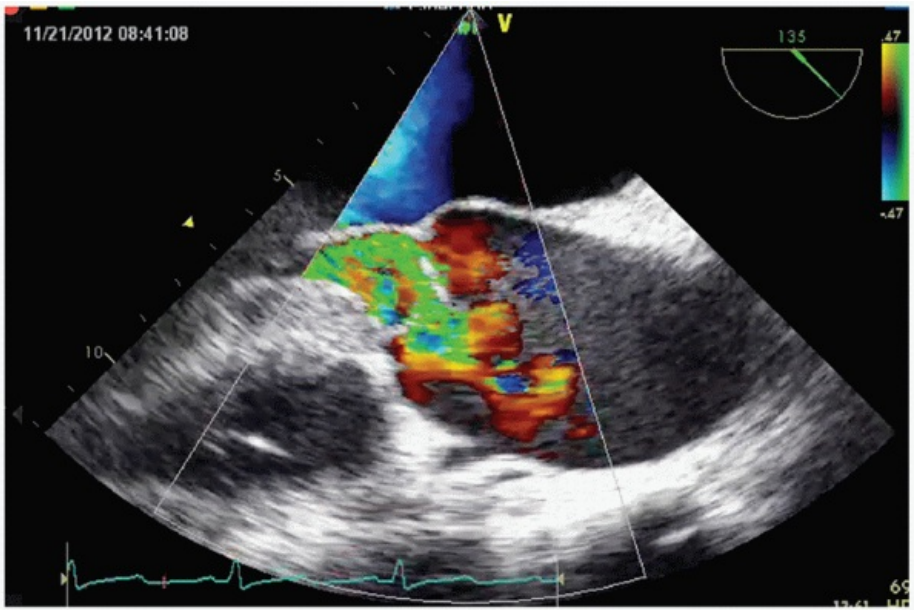


FIGURE 7.17 Transesophageal echocardiographic findings of moderate aortic regurgitation (midesophageal aortic valve long-axis view; color flow Doppler).

Mitral Regurgitation

In the presence of MR, ventriculography will demonstrate the reflux of dye from the LV into the left atrium. Severe MR is diagnosed when dye refluxes into the pulmonary veins. Color Doppler echocardiography permits similar quantification. Estimation relies on an estimation of regurgitant jet area as compared with the left atrium area and through analysis of pulmonary venous flow profiles (Fig. 7.19, Video 7.4).

In every case, color Doppler echocardiography is often useful in identifying the cause of the valvular lesion, its extent of involvement within and around the valve, and the associated hemodynamic changes. Therefore, for many valvular lesions, it may be sufficient for the diagnosis. Catheterization, however, is often performed to assess the presence of concomitant coronary artery disease, especially in patients of advanced age.

Baumgartner H, Hung J, Bermejo J, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendation for clinical practice. *J Am Soc Echocardiogr*. 2009;22(1):1-23.

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Zoghbi WA, Enriquez-Sarano M, Foster E, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr*. 2003;16(7):777-802.

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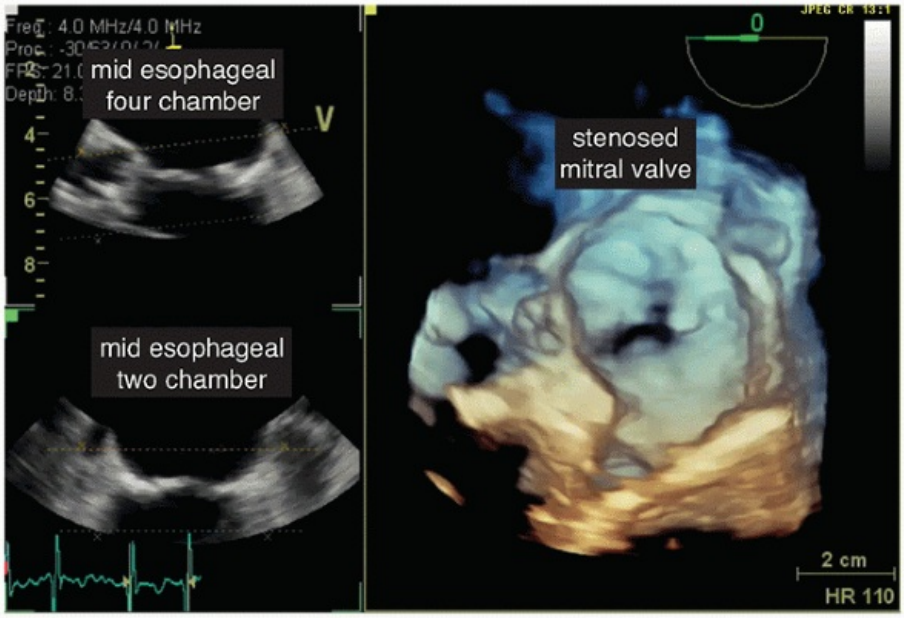


FIGURE 7.18 Transesophageal echocardiographic findings of severe mitral stenosis with twodimensional view **(left panel)** and three-dimensional view **(right)**.

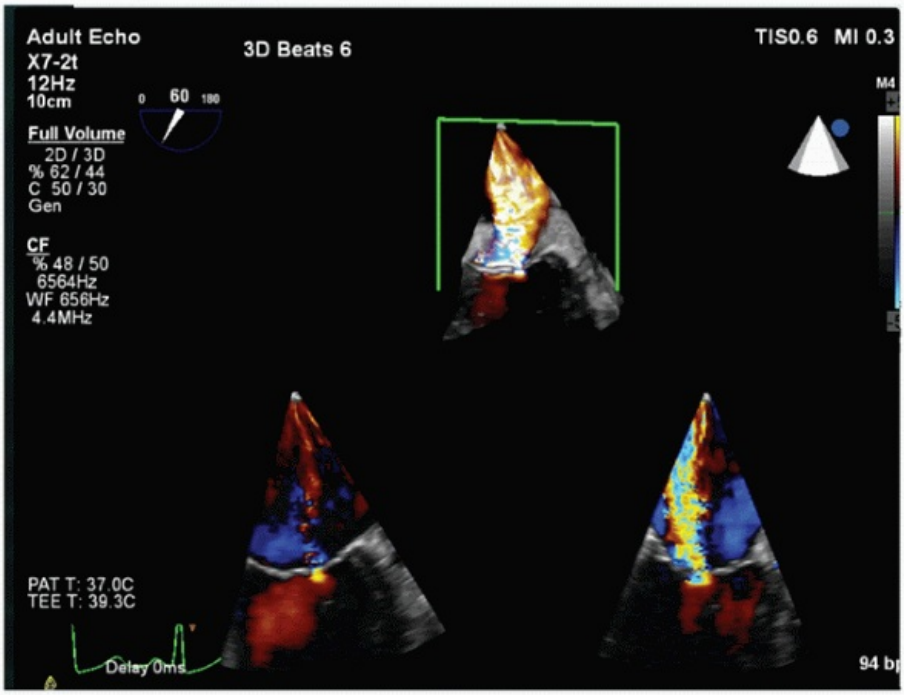


FIGURE 7.19 Transesophageal echocardiographic findings of moderate mitral regurgitation (color flow Doppler) with three-dimensional view **(top)** and two-dimensional view **(bottom)**.

B. Preoperative Evaluation and Preparation

B.1. What are the presenting signs and symptoms of the four valvular lesions listed previously?

See Table 7.2.

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Aortic Stenosis

The triad of angina, syncope, and congestive heart failure represents the progression of symptoms associated with AS. These symptoms correlate directly with mortality; the 50% survival data for these symptoms are 5, 3, and 2 years from the onset of these symptoms, respectively. Angina results from both increased demand for and a decrease in supply of coronary blood flow. Increased muscle mass from LV hypertrophy and the high energy requirements to generate increased (high) systolic pressure combine to increase demands for coronary blood flow. In addition, insufficient supply secondary to decreased perfusion gradients and a decrease in coronary vasculature relative to the increased myocardial mass add up to diminish relative myocardial blood supply. Therefore, up to one-third of patients with AS can have angina in the absence of significant coronary artery disease.

Aortic Insufficiency

Patients with AI have variable clinical presentations, primarily depending on the rapidity with which the LV volume overload develops. When the volume increase occurs gradually as in chronic AI, there is usually a long asymptomatic period. The onset of fatigue and dyspnea signals either reduced cardiac output or increased LVEDP, indicative of impairment of LV contractile function. When AI occurs acutely, the ventricular compliance is unchanged; increased LV diastolic volumes from regurgitant flow, therefore, lead to rapid rises in LVEDP and the clinical picture of congestive failure.

Mitral Stenosis

In MS, the slow and progressive obstruction to flow across the MV leads to gradual increase in left atrial pressure and volume. Symptoms of pulmonary congestion result from elevations in left atrial pressures and *not* from poor LV systolic function. Atrial fibrillation develops secondary to atrial dilation.

Mitral Regurgitation

The time course for the development of MR determines the severity of the symptoms. When the volume of regurgitant flow from the LV to the left atrium increases gradually, the left atrium compensates by gradual dilatation. In contrast, the onset of acute MR can lead to rapid increases in left atrial pressures, severe pulmonary congestion, and congestive heart failure.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1076-1111.

Frogel J, Galusca D. Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery. *Anesthesiol Clin*. 2010;28:67-85.

Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63(22):e57-e185.

TABLE 7.2 The Signs and Symptoms for the Various Valvular Lesions

LESION		SIGNS AND SYMPTOMS
AS		Angina, syncope, dyspnea/CHF
AI		
	Chronic	Fatigability, dyspnea
	Acute	Severe pulmonary edema, CHF

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MS		Pulmonary congestion, AFib
MR		
	Chronic	DOE, PND, AFib
	Acute	Severe pulmonary edema, CHF

AFib, atrial fibrillation; AI, aortic insufficiency; AS, aortic stenosis; CHF, congestive heart failure; DOE, dyspnea on exertion; MR, mitral regurgitation; MS, mitral stenosis; PND, paroxysmal nocturnal dyspnea.

B.2. What is the New York Heart Association classification of heart failure?

The New York Heart Association heart failure classification is based on the severity of symptoms, specifically dyspnea and fatigue. The classes are the following:

Class I—no symptoms (fatigue, palpitations, dyspnea or angina) during ordinary physical activity; no limitations of physical activity

Class II—symptoms with ordinary activity but comfortable at rest; slight limitation of physical activity

Class III—symptoms with less than ordinary activity but comfortable at rest; marked limitation of physical activity

Class IV—symptoms at rest; inability to carry on any physical activity without discomfort

Raphael C, Briscoe C, Davies J, et al. Limitations of the New York Heart Association functional classification system and self-reported walking distances in chronic heart failure. *Heart*. 2007;93(4):476-482.

B.3. Discuss the role of premedication for patients with the four different valvular lesions.

The role of premedication is to allay the anxiety of the impending surgical procedure, thereby controlling the sympathetic outflow that may accompany the stress response. Acute changes in heart rate, venous return, and systemic resistance can have particularly profound effects on patients with valvular heart disease.

Patients with AS may benefit from premedication by preventing unnecessary increases in heart rate. Concern must be taken to ensure adequate venous return and preservation of sinus rhythm (see later discussion).

Patients with AI can similarly benefit from premedication because any increases in afterload, which may accompany sympathetic stimulation, can increase regurgitant volume. Drug doses should be adjusted based on the severity of debilitation and degree of systemic hypoperfusion.

Patients with MS should be premedicated with caution. Elevations in carbon dioxide resulting from opioid-induced hypoventilation can dramatically elevate pulmonary pressures further compromising right ventricle output. Equally important, venodilation may excessively diminish filling pressures.

Patients with MR can respond similarly to those with MS, particularly when pulmonary hypertension is present. However, elevations in systemic pressure from stress can also compromise forward LV output. Proper premedication can be delivered by careful dose selection and the provision of supplemental oxygen.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1076-1111.

B.4. How would you premedicate the patient with severe AS and MR?

Premedication of a patient with severe AS and MR must be approached with caution. The patient should receive supplemental oxygen. A light premedication could be provided with small doses of benzodiazepines by mouth. However, it

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would preferable to titrate in small intravenous doses of sedation (midazolam 0.5 mg) while the patient is closely monitored in the operating room or holding area and with oxygen supplementation. It is important to remember that there may be significant delay in the onset of sedation secondary to pooling in the pulmonary circulation, and adequate waiting periods must be observed to avoid inadvertent overdose, which may herald respiratory depression, pulmonary hypertension, and systemic hypotension. In the elderly, use of benzodiazepines has been linked to postoperative delirium, which can be quite severe and difficult to treat as well as increase length of stay and resource utilization.

C. Intraoperative Management

C.1. Outline the hemodynamic management goals for each of the four valvular lesions. What are the anesthetic goals with respect to heart rate and rhythm, preload, afterload, and contractility?

Table 7.3 summarizes the hemodynamic goals with respect to heart rate and rhythm, preload, afterload, and contractility.

Aortic Stenosis

Patients with AS depend on LV filling occurring through a well-timed atrial contraction. Similarly, LV hypertrophy renders the LV stiff and adequate preload is required. Reducing vascular tone will do little to relieve the fixed afterload increases from a stenotic AV but rather lower diastolic coronary perfusion gradients and should be avoided. Patients with AS experiencing angina may require the administration of an α-agonist such as phenylephrine rather than nitroglycerin to increase coronary perfusion pressure.

Aortic Insufficiency

The severity of AI is determined by the size of the regurgitant orifice, the diastolic pressure gradient between the aorta and LV, and duration of diastole. Elevated heart rates decrease the time spent in diastole and can lead to a decrease in heart size. Afterload reduction can lessen the regurgitant driving forces, but therapeutic maneuvers to accomplish this may be limited by resulting systemic hypotension.

Mitral Stenosis

Patients with MS can swiftly deteriorate in the setting of rapid heart rates. The decreased filling time necessitates the marked elevation of left atrial pressures, and pulmonary edema can rapidly ensue. Whereas LV contractility is generally preserve in MS, use of β-blockade does result in decreased RV contractility, which in the setting of pulmonary hypertension can further compromise the cardiac output and systemic blood pressure. However, the loss in RV contractility is more than offset by the beneficial effects of the reduction of heart rate. Slower heart rates permit adequate time for transfer of blood from the left atrium to the LV across the stenotic MV to occur. In addition, the pressure gradient across the MV is also reduced, thereby lowering left atrial pressure and diminishing pulmonary congestion. Because there is some variability in the individual response, the use of short-acting β-blockers such as esmolol is prudent because an adverse response should be catastrophic.

Mitral Regurgitation

Patients with MR can rapidly deteriorate with marked increases in systemic blood pressure. As with AI, slightly rapid heart rates (80 to 90 beats per minute) should result in smaller LV volumes. However, tachycardia should be avoided in patients with ischemic (functional) MR.

Frogel J, Galusca D. Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery. *Anesthesiol Clin.* 2010;28:67-85.

TABLE 7.3 Hemodynamic Goals for the Various Valvular Lesions

	HEMODYNAMIC GOALS			
LESIONS	**HR AND RHYTHM**	**PRELOAD**	**AFTERLOAD**	**CONTRACTILITY**

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AS	60-70, sinus	Full	Maintain	—
AI	80-90	Maintain	Lower	May need support
MS	60-70	Full	—	—
MR	80-90, sinus if possible	Maintain	Lower	May need support

AI, aortic insufficiency; AS, aortic stenosis; HR, heart rate (beats per minute); MR, mitral regurgitation; MS, mitral stenosis.

C.2. What are the hemodynamic goals for this patient with the combination of severe AS and MR?

In this patient with combined AS and MR, therapy benefiting AS may exacerbate the severity of the MR. Early aggressive intervention is the key to these combined lesions. A lower margin for error usually exists because minor hemodynamic aberrations can rapidly lead to cardiac collapse. A good rule of thumb is to prioritize the management based on the character of the paramount symptoms. Patients with AS and MR who present with syncope or angina are best managed for their AS, whereas patients with dyspnea and pulmonary edema are best managed for their congestive symptoms. It is prudent to maintain the patient's own usual hemodynamics. TEE evaluation of LV performance can be helpful in separating pulmonary congestion secondary to left heart failure from that secondary to decreased diastolic left ventricular compliance from AS.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1076-1111.

Frogel J, Galusca D. Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery. *Anesthesiol Clin*. 2010;28:67-85.

C.3. How would you monitor this patient with severe AS and MR?

In addition to the standard American Society of Anesthesiologists recommended monitors, the patient should have a radial artery and a pulmonary artery catheter. Following induction of anesthesia and endotracheal intubation, a TEE probe would be inserted to confirm the valvular pathology and to assess ventricular function. Following valve replacement, the TEE probe would be used to check for adequacy of valvular function and the absence of paravalvular leaks and to assess postbypass ventricular function.

American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Practice guidelines for perioperative transesophageal echocardiography. An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology*. 2010;112(5):1084-1096.

C.4. Should the patient have a pulmonary artery catheter placed before induction?

Volume status may be particularly difficult to assess in patients with valvular heart disease yet of critical importance in the management of these patients. Patients with stenotic lesions depend on adequate filling pressures for diastolic filling of the ventricle. Patients with the volume overload lesions of AI and MR can benefit from the careful reductions in pulmonary pressure guided by the simultaneous assessment of cardiac performance. In these capacities, the pulmonary artery catheter is useful. Patients with current hemodynamic stability, without severe respiratory distress, can be safely anesthetized before placement of the pulmonary artery catheter. In all, there is no evidence that use of the pulmonary artery

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catheter improves outcome in the setting of surgery.

American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Practice guidelines for perioperative transesophageal echocardiography. An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology*. 2010;112(5):1084-1096.

C.5. Is a pulmonary artery catheter with pacing capabilities indicated?

Patients with AS can become severely compromised with the loss of atrial kick or the presence of slow junctional rhythms. Patients with AI or MR can experience LV dilation in the setting of slow heart rates. In such cases, a pulmonary artery catheter with atrial and ventricular pacing capacity can be useful. In patients with intact conduction systems, rate manipulation can often be achieved pharmacologically. Transesophageal atrial pacing is another option; transthoracic pacing elicits a ventricular response only and does not permit atrial stimulation. Transthoracic pacing is indicated when the ability to rapidly open the pericardium and obtain epicardial pacing is limited. This occurs in the setting of reoperations or with patients having a history of inflammatory pericardial disease. Pacing will be limited to capture of

the ventricle alone. The loss of atrial contraction can lead to under filling and hemodynamic compromise in patients dependent on the added volume from atrial systole. One of the other pacing modalities is best in this setting.

Crystal E, Connolly SJ, Sleik K, et al. Interventions on prevention of postoperative atrial fibrillation in patients undergoing heart surgery: a meta-analysis. *Circulation*. 2002;106(1):75-80.

Maisel WH, Epstein AE. The role of cardiac pacing: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. *Chest*. 2005;128(suppl 2):36S-38S.

Risk SC, Brandon D, D'Ambra M, et al. Indications for the use of pacing pulmonary artery catheters in cardiac surgery. *J Cardiothorac Vasc Anesth*. 1992;6:275-279.

Trankina MF, White RD. Perioperative cardiac pacing using an atrioventricular pacing pulmonary artery catheter. *J Cardiothorac Anesth*. 1989;3(2):154-162.

C.6. What anesthetic technique would you employ? Why?

For the patient undergoing CPB and AV replacement, general anesthesia with endotracheal intubation is the obvious choice. Both narcotics and inhalation anesthetics can be safely administered. Recent anesthetic technique for cardiac surgery has focused on the use of techniques permitting earlier tracheal extubation, so-called “fast tracking.” Anesthetic combinations using smaller total narcotic doses, inhalation anesthetics, and short-acting intravenous sedatives such as propofol are gaining popularity. For uncomplicated valve replacements with good ventricular function, the advantages of early tracheal extubation can be safely achieved. In complicated cases with longer bypass periods, poor ventricular function, or postbypass bleeding, the hemodynamic stability of a high-dose narcotic technique may be advantageous.

Howie MB, Black HA, Romanelli VA, et al. A comparison of isoflurane versus fentanyl as primary anesthetics for mitral valve surgery. *Anesth Analg*. 1996;83:941-948.

Tuman KJ, McCarthy RJ, Spiess BD, et al. Comparison of anesthetic techniques in patients undergoing heart valve replacement. *J Cardiothorac Anesth*. 1990;4:159-167.

C.7. What muscle relaxant would you use for this patient?

Muscle relaxants can alter hemodynamics both from the effects of histamine release, including vasodilatation and bronchospasm, and through effects on rhythm. Although slowing of heart rates usually benefits the patient with angina, it may have severe consequences in patients with valvular heart disease. A high-dose narcotic anesthesia usually results in

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bradycardia secondary to the vagotonic actions. Hemodynamically “neutral” relaxants such as vecuronium, rocuronium, or cisatracurium could be used, but their intermediate duration of action offers little, if any, advantage in this setting.

Therefore, it is important to choose that combination of agents that will promote hemodynamic stability in a particular patient with his or her unique hemodynamic presentation. In this patient, the judicious use of any muscle relaxant would be indicated.

Fleming N. Con: the choice of muscle relaxants is not important in cardiac surgery. *J Cardiothorac Vasc Anesth*. 1995;9:772-774.

Hemmerling TM, Russo G, Bracco D. Neuromuscular blockade in cardiac surgery: an update for clinicians. *Ann Card Anaesth*. 2008;11(2):80-90.

Hudson RJ, Thomson IR. Pro: the choice of muscle relaxants is important in cardiac surgery. *J Cardiothorac Vasc Anesth*. 1995;9:768-771.

C.8. What are the usual TEE findings in a patient with AS or MR? How do you grade the severity of AS by TEE? How do you quantify the severity of MR? What is the impact of AS on the severity of MR?

The *echocardiographic* severity of AS is usually determined by AV area and transaortic valve pressure gradient. Normal AV area is 2.5 to 3.5 cm^2. Moderate stenosis is when the AV area is within the range of 1.0 to 1.5 cm^2 and severe AS when the AV area is less than 1.0 cm^2. A patient with a large peak pressure gradient (usually more than 40 mm Hg) in the absence of excessively high cardiac output is usually considered to have severe AS as well. In the setting of low cardiac outputs, the pressure gradient may not be that great (20 to 30 mm Hg), and

determination of AV area is required. The *clinical* severity of AS is determined by a combination of echocardiographic and clinical factors. Even a patient with less than severely stenosed AV may be considered to have severe AS if his daily activities of life are reduced, he experiences symptoms, or left ventricular systolic dysfunction is present.

MR is graded by the amount of blood regurgitated backward into the left atrium during systole. Doppler color flow permits the estimation of this flow. Common methods for MR quantification include calculation of the area of the regurgitant orifice (effective orifice area) or the width of the MR jet (vena contracta) and by analysis of pulmonary vein flow profiles. It is important to remember that the amount of regurgitant blood flow in the setting of MR is determined by the amount of time spent in systole, the size of the MV defect, and the pressure gradient across the defect. Therefore, MR severity by Doppler color flow is load-dependent. The lower systemic pressure or relative hypovolemia due to the anesthetic state can often mask more severe degrees of MR, which are found in the awake state.

The LV pressures are increased in the setting of AS. Therefore, the gradient across the MV is increased often leading to more severe MR. Following replacement of the stenotic AV and elimination of the obstruction to systolic flow, LV pressures are markedly reduced. In cases of functional MR without major structural defects in the MV apparatus, the MR will be less severe following replacement of AV.

Mahmood F, Matyal R. A quantitative approach to the intraoperative echocardiographic assessment of the mitral valve for repair. *Anesth Analg*. 2015;121(1):34-58.

Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63(22):e57-e185.

C.9. What special considerations particular to cardiopulmonary bypass (CPB) operations do you have for each of the four lesions? Focus on these concerns with respect to the induction and prebypass, bypass, and postbypass periods.

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Aortic Stenosis

Critical to the management of a patient with AS is the avoidance of hypotension. Low blood pressure can initiate a cascade of events leading to cardiac arrest. Hypotension decreases the gradient for coronary perfusion with resultant ischemia. Ischemia leads to diminished cardiac output and decreased blood pressure further compromising coronary perfusion. The occurrence of cardiac arrest in a patient with AS is particularly catastrophic because closedchest cardiac massage will provide little gradient for blood flow across a stenotic AV.

Patients with AS are particularly dependent on their atrial kick for adequate ventricular filling volume and can rapidly become hypotensive and ischemic following the onset of supraventricular tachycardia or atrial fibrillation. These rhythms are not uncommon during atrial cannulation. Therefore, it is of particular importance that every preparation for the initiation of CPB be made before atrial manipulation. Increased muscle mass of ventricular hypertrophy can be more difficult to adequately protect with cardioplegia. Careful attention to surface cooling, myocardial temperature measurement, and the use of retrograde cardioplegia can be helpful. Following AV replacement, hypertension from LV output now unopposed by any valvular lesion can result in stress on suture lines and excessive bleeding. It is important to remember that the compliance of the LV is unchanged by surgery and still critically dependent on adequate preload and sinus rhythm.

Aortic Insufficiency

Patients undergoing AV replacement for AI can often present difficult management decisions. The usual treatment measures for hypotension (α-agonist) may have deleterious effects by increasing regurgitant volume. The use of combined α- and β-agonists (ephedrine, epinephrine, or infusions of dopamine or dobutamine) may be required. Although it would serve to lessen regurgitant volume, afterload reduction is beneficial in only a subset of patients with AI. Those patients with elevated LVEDP, reduced ejection fraction, diminished cardiac output, and systemic hypertension usually benefit from afterload reduction. In contrast, those patients without the previously mentioned constellation may experience a decrease in forward cardiac output secondary to diminished preload from reduced venous return.

Systemic hypotension usually limits the utility in the acute setting. The presence of AI makes initiation of CPB a critical period. Periods of bradycardia or ventricular fibrillation can lead to rapid volume overload of the LV through the incompetent AV. Pacing, electrical defibrillation, and/or cross-clamping should be performed to prevent ventricular distention. Similarly, myocardial protection is compromised by AI. Generation of adequate root pressures is usually not obtainable; hence, delivery of cardioplegia requires aortotomy and cannulation of the coronary ostia. Use of retrograde cardioplegia is advantageous. Following AV replacement, the ventricle no longer has the lower pressure/impedance outflow afforded by the low aortic diastolic pressure. Inotropic support is often required. As with AS, the presence of an aortic suture line necessitates rapid response to hypertension to avoid bleeding and dissection.

Mitral Stenosis

Patients undergoing MV replacement for MS are particularly challenging. Marked elevations in pulmonary vascular resistance can be present with associated right-sided heart failure. Stasis in the left atrium necessitates careful echocardiographic examination for the presence of atrial thrombi. Manipulation of the heart before cross-clamping should be avoided. Following replacement, the chronically underfilled, underworked LV may be unable to handle the new volume load. Inotropic support is often required for RV failure and occasionally to improve LV function. Afterload reduction and improved systemic perfusion through an IABP may be beneficial.

Mitral Regurgitation

Similarly, patients with MR may have pulmonary hypertension and right-sided heart failure. In contrast to AI, almost all patients with MR can be greatly benefited by afterload reduction, both pharmacologically and through an IABP. Diminution of LV systolic pressure through afterload reduction decreases the pressure gradient from the LV to the left atrium during systole, with resultant decreased regurgitant volume.

Prebypass assessment can be misleading. Preserved ejection fractions and elevated stroke volumes may mask marked LV systolic dysfunction. It should be remembered that much of the LV volume is ejected into the low-pressure/impedance outflow path of the left atrium. This route is no longer available after valve replacement. Following MV replacement, dysfunctional ventricles may be unable to provide adequate forward flow into the systemic circuit with its elevated vascular resistance and usually necessitate the use of inotropic support.

Patients previously in atrial fibrillation without marked atrial enlargement often revert to or can be converted to sinus rhythm following valve replacement. The capacity of maintaining a person in sinus rhythm dramatically decreases when the diameter of the atrium is more than 5 cm.

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Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1076-1111.

C.10. The patient cannot be weaned from CPB following an AV replacement and MV replacement. What are the possible causes?

The adequacy of myocardial preservation should be considered. LV hypertrophy without or with accompanying coronary artery disease increases myocardial oxygen demands. Prolonged cross-clamp time necessitated by dual valve replacement can lead to inadequate and/or nonhomogeneous myocardial protection. In addition, there may be residual effects from the cardioplegia solution. Therefore, some degree of postbypass LV dysfunction can be anticipated. Inotropic support may be required. It is important to remember that although the obstruction to LV ejection is acutely relieved by replacement of the stenotic valve, LV compliance is largely unchanged. Adequate preload still depends on sinus rhythm and sufficient LV filling pressures (pulmonary artery occlusion pressure [PAOP] or LVEDP). Elevations in pulmonary vascular resistance may render estimation of left atrial pressure through the pulmonary artery catheter inaccurate. In this setting, placement of a left atrial catheter is indicated. TEE may prove invaluable in identifying surgically correctable causes for inability to wean from CPB. Evaluation of LV filling and contractility can help resolve the situation of low cardiac output and high filling pressures. A small underfilled LV with hyperdynamic contractility and a dilated, overfilled, hypokinetic LV can both give the same hemodynamic parameters

but obviously require different pharmacologic interventions. Abnormal valve seating may compromise flow into the coronary ostia and return to bypass with valve repositioning or coronary artery bypass grafting may be indicated. Similarly, perivalvular leaks or aortic dissections can be readily identified. Iatrogenic injury to the circumflex artery, although rare, can occur during MV annuloplasty or replacement. The course of the circumflex artery along the posterior path of the MV annulus makes it a potential target for errant valve stitches. New regional wall motion abnormalities in the inferior-lateral territory may help to make this unusual diagnosis or influence the decision to pursue diagnostic testing, such as emergent cardiac catheterization. The coronary sinus can also be damaged during MV repair and replacement as the suture line is placed in the lateral mitral annulus. TEE may demonstrate abnormal echodensities in the area of the atrioventricular groove, and color flow Doppler can demonstrate high-velocity flow jets from the chambers to the sinus.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1076-1111.

Ender J, Selbach M, Borger MA, et al. Echocardiographic identification of iatrogenic injury of the circumflex artery during minimally invasive mitral valve repair. *Ann Thorac Surg*. 2010;89:1866-1872.

C.11. How would you diagnose right-sided heart failure and pulmonary hypertension? How would you treat it?

Right-sided heart failure is diagnosed by the elevations in right-sided filling pressures, specifically central venous pressure. Careful examination is required to rule out tricuspid insufficiency as the cause of the central venous pressure elevation. A high central venous pressure indicates the inability of the right heart to adequately propel the venous return volume into the pulmonary circulation. Elevation in pulmonary artery pressures is indicative of pulmonary hypertension. The combination of high central venous pressure and high pulmonary artery pressures indicates severe right-sided heart failure. This scenario can be difficult to manage. Attempts to elevate systemic perfusion pressure with α-agonists can worsen pulmonary hypertension. Administration of vasodilators to lower pulmonary pressures results in systemic hypotension. In this setting, it is often prudent to return to CPB, relieve ventricular distention, and improve myocardial perfusion. During this “rest period,” adjustments in inotropic therapy, ventilation, and cardiac rhythm can be instituted. Optimization of acid-base status and hemoglobin concentration should also be performed. Separation from bypass can then be reattempted.

Typical inotropic agents effective in this setting are those with high degrees of β-adrenergic potency and potent vasodilation in the pulmonary vasculature. Commonly employed agents include dobutamine, epinephrine, prostaglandin E_1, and the phosphodiesterase-III (PDE-III) inhibitors amrinone and milrinone. It is not uncommon to require the administration of α-agonists to counteract the systemic vasodilating effects of prostaglandin E_1 and the PDE-III agents. Some selective pulmonary vasodilating action and systemic vasoconstricting effects can often be achieved by

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administration of pulmonary vasodilating agents such as prostaglandin E_1 through the right-sided access (central venous pressure or pulmonary artery catheter) and infusion of the α-agonists through the left arterial line, thereby minimizing vasoconstriction of the pulmonary arterial bed.

Nitric oxide is a potent, inhaled pulmonary vasodilator. Its half-life in the systemic circulation is extremely short, permitting its administration to the pulmonary vasculature with minimal systemic hypotensive effects. Nitric oxide can selectively and effectively dilate the pulmonary vasculature. The exact method of delivery, scavenging of waste gases, and high cost remain as obstacles to its clinical application.

Bar-Yosef S, Schroeder RA, Barbeito A, et al. Assessment of the right ventricular function. In: Savage RM, Aronson S, Shernan SK, eds. *Comprehensive Textbook of Intraoperative Transesophageal Echocardiography* . 2nd ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2011:156-167.

Body SC, Hartigan PM, Shernan SK, et al. Nitric oxide: delivery, measurement, and clinical application. *J Cardiothorac Vasc Anesth*. 1995;9:748-763.

Kieler-Jensen N, Houltz E, Ricksten SE. A comparison of prostacyclin and sodium nitroprusside for the treatment of heart failure after cardiac surgery. *J Cardiothorac Vasc Anesth*. 1995;9:641-646.

C.12. How does an intra-aortic balloon pump (IABP) work to benefit the failing heart?

An IABP is a catheter with a large balloon (40 to 60 mL) at its tip. It is positioned in the thoracic aorta distal to the left subclavian artery origin and proximal to the takeoff of the renal vessels. It is timed to inflate during diastole to increase diastolic perfusion pressure to the coronary arteries, great vessels, and major abdominal organs and to deflate just before systole, creating a void in volume within the aorta and thus a low pressure with resultant decrease in afterload. The decreased afterload increases stroke volume and hence forward cardiac output. It is a unique modality that can improve coronary perfusion pressures while reducing myocardial oxygen demand.

Baskett RJ, Ghali WA, Maitland A, et al. The intraaortic balloon pump in cardiac surgery. *Ann Thorac Surg*. 2002;74:1276-1287.

Kucuker A, Cetin L, Kucuker SA, et al. Single-centre experience with perioperative use of intraaortic balloon pump in cardiac surgery. *Heart Lung Circ*. 2014;23(5):475-481.

C.13. What role does the IABP have in this setting?

An IABP may be useful because unlike any pharmacologic maneuver it is capable of increasing mean pressure during diastole critical for coronary perfusion while lowering afterload to systolic LV ejection. Myocardial dysfunction secondary to inadequate protection during bypass can be reduced by decreased afterload and augmentation of diastolic pressures through IABP counterpulsation. Studies have shown superior survival among patients with isolated cardiac artery bypass graft (CABG) treated with IABP compared with patients undergoing non-CABG cardiac surgeries. The IABP can only aid patients in whom ventricular function can recover in a relatively short time. Outside of this population, ventricular assist devices may be more appropriate.

Baskett RJ, Ghali WA, Maitland A, et al. The intraaortic balloon pump in cardiac surgery. *Ann Thorac Surg*. 2002;74:1276-1287.

C.14. What role does TEE play in the placement, timing, and demonstration of efficacy of an IABP?

The thoracic aorta and aortic arch can be clearly imaged by TEE. Imaging of the takeoff of the left subclavian artery facilitates optimal positioning of the IABP. In addition, before insertion, the aorta can be evaluated for dissection or the presence of severe atheromatous disease, both contraindications to IABP insertion. TEE can demonstrate the efficacy of

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an IABP by showing enhanced ventricular emptying during systole and filling during diastole.

Klopman MA, Chen EP, Sniecinski RM. Positioning an intraaortic balloon pump using intraoperative transesophageal echocardiogram guidance. *Anesth Analg*. 2011;113(1):40-43.

C.15. How would you properly time the IABP cycle?

Inflation should occur just following the dicrotic notch and deflation before the upstroke in the aortic pressure curve. Augmentation in pressures during diastole and mean pressures should occur. Diastolic pressure (the lowest pressure in the cardiac cycle) should in fact fall. Peak pressure generated by the LV or systolic pressure should fall while the balloon generated pressure during ventricular diastole (augmented pressure) should increase.

Baskett RJ, Ghali WA, Maitland A, et al. The intraaortic balloon pump in cardiac surgery. *Ann Thorac Surg*. 2002;74:1276-1287.

Cheung AT, Savino JS, Weiss SJ. Beat-to-beat augmentation of left ventricular function by intraaortic counterpulsation. *Anesthesiology*. 1996;84:545-554.

C.16. What are the contraindications to the use of an IABP?

The most common contraindications are severe AI and severe aortic disease, atheromatous, aneurysmal, or a dissection. Although often listed as absolute contraindications, there are reports of the effective use of IABP in these settings. TEE can be helpful in evaluating the

effect of an IABP on overall ventricular function. End-systolic areas should decrease, and end-diastolic areas should at least not increase but may decrease as well.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24(4):335-341.

C.17. What is the role for ventricular assist devices?

Ventricular assist devices are used in the management of chronic heart failure after exhausting medical therapy. These devices can be used as a bridge to transplantation or as a destination therapy in those who do not qualify for transplantation. The short-term use of ventricular assist devices includes patients with refractory heart failure in the immediate postoperative setting. Historically, the operative mortality associated with postcardiotomy assist devices was very high. Newer machines utilize smaller cannulas and have smaller, more efficient pumps. The magnetically suspended centrifugal pumps are associated with minimal trauma to red blood cells or pump failures. The use of these devices is rapidly expanding, and early indications are improved mortality for patients experiencing postcardiotomy shock with recoverable myocardium. Ventricular assist devices are used for right, left, and biventricular support.

Bhama JK, Kormos RL, Toyoda Y, et al. Clinical experience using the Levitronix Centrimag System for temporary right ventricular mechanical circulatory support. *J Heart Lung Transpl*. 2009;28:971-976.

DeRobertis F, Birks EJ, Rogers P, et al. Clinical performance with the Levitronix Centrimag short-term ventricular assist device. *J Heart Lung Transplant*. 2006;25:181-186.

Noon GP, Lafuente JA, Irwin S. Acute and temporary ventricular support with BioMedicus Centrifugal Pump. *Ann Thorac Surg*. 1999;68:650-654.

D. Postoperative Management

D.1. In the intensive care unit (ICU) 4 hours later, the patient became

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hypotensive with a low cardiac output. How could you distinguish between cardiac tamponade and pump failure? How would the TEE images differ?

The differentiation between cardiac tamponade and primary pump failure in the immediate postbypass-ICU setting can be difficult. Elevations in filling pressures, systemic hypotension, and low cardiac output are consistent with both diagnoses. The classic teaching of equalization of cardiac pressures seen in a "fluid" tamponade may not be present because areas of focal compression from clot can markedly reduce filling of only one chamber in the absence of an intact pericardium. Echocardiography can be beneficial in this setting by permitting visualization of chamber volume and function. The TEE approach has particular advantage over TTE in the postoperative setting in which the usual transthoracic window may be obscured by dressings and drainage tubing. Focal compression of the cardiac chambers from a clot or pericardial effusion can readily be distinguished from a volume-overloaded, failing heart with poor myocardial contractility. When the diagnosis is not clear, however, surgical re-exploration may be indicated. (See Chapter 12, Cardiac Tamponade.)

Bommer WJ, Follette D, Pollock M, et al. Tamponade in patients undergoing cardiac surgery: a clinicalechocardiographic diagnosis. *Am Heart J*. 1995;130:1216-1223.

Chuttani K, Tischler MD, Pandian NG, et al. Diagnosis of cardiac tamponade after cardiac surgery: relative value of clinical, echocardiographic, and hemodynamic signs. *Am Heart J*. 1994;127(4 pt 1):913-918.

Flynn BC, Spellman J, Bodian C, et al. Inadequate visualization and reporting of ventricular function from transthoracic echocardiography after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2010;24:280-284.

Price S, Prout J, Jaggar SI, et al. 'Tamponade' following cardiac surgery terminology and echocardiography may both mislead. *Eur J Cardio Surg*. 2004;26:1156-1160.

D.2. Would you extubate this patient early in the ICU? Why?

No. This patient has undergone a double valve replacement. In this more complex procedure, coagulopathy and postoperative bleeding, hypothermia from incomplete and nonuniform rewarming, and pulmonary hypertension are not uncommon occurrences in the immediate postoperative period. Sedation, paralysis, and mechanical ventilation can reduce the oxygen

requirements during this early phase of recovery, minimize pulmonary hypertension secondary to hypercarbia, and permit reestablishment of core temperatures.

Cheng DC. Pro: early extubation after cardiac surgery decreases intensive care unit stay and cost. *J Cardiothorac Vasc Anesth*. 1995;9:460-464.

Guenther CR. Con: early extubation after cardiac surgery decreases intensive care unit stay and cost. *J Cardiothorac Vasc Anesth*. 1995;9:465-467.

D.3. What are the advantages and disadvantages of early extubation?

The advantages of early extubation are both medical and financial. Early extubation can lessen the adverse sequelae from prolonged endotracheal intubation, including epithelial damage, decreased ciliary motility, and diminished mobilization of secretions. Positive pressure ventilation can have adverse effects on venous return. Nevertheless, the overwhelming drive toward early extubation is cost and patient comfort. Early extubation can decrease cost by decreasing ICU staff requirements, decreasing the cost of sedatives, lessening the duration of ICU stays, and improving operating room use by lessening cancellation of cases secondary to blocked ICU beds.

The potential advantages of early extubation, both financial and physiologic, must be weighed against the potential disadvantages of early extubation. The potential for respiratory compromise leading to hypoxemia, hypercarbia, ischemia, and the potential for infarction and neurologic injury is real. Any savings realized from early extubation can be rapidly lost by one adverse event. Success relies on careful integration of all players in the care of the patient undergoing cardiac

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surgery, from the management of intraoperative anesthetic techniques to the organization of the ICU and staff and the provision of postoperative analgesia. Equally important to the success of an early extubation program is appropriate patient selection.

Cheng DC. Pro: early extubation after cardiac surgery decreases intensive care unit stay and cost. *J Cardiothorac Vasc Anesth*. 1995;9:460-464.

Guenther CR. Con: early extubation after cardiac surgery decreases intensive care unit stay and cost. *J Cardiothorac Vasc Anesth*. 1995;9:465-467.

Kogan A, Ghosh P, Preisman S, et al. Risk factors for failed "fast-tracking" after cardiac surgery in patients older than 70 years. *J Cardiothorac Vasc Anesth*. 2008;22:530-535.

E. Alternative Treatments

E.1. What are the percutaneous options for MV repair?

In 1991, a surgical correction of MR was described using a technique of suturing the middle portions of the two mitral leaflets together. The resultant double orifice valve is an adequate solution for many MV lesions. Based on this principle, a percutaneous treatment for MR has emerged.

Sherlock KE, Muthuswamy G, Basu R, et al. The Alfieri stitch: the advantages for mitral valve repair in difficult circumstances. *J Card Surg*. 2011;26(5):475-477.

E.2. How is percutaneous MV repair performed?

The MitraClip is a small, polyester fabric-covered cobalt-chromium clip that is applied to the mitral leaflets to mimic the surgical procedure described earlier. The device is delivered percutaneously via a transfemoral venous approach and a transseptal puncture, and favorable results are associated with reduction of MR to less than moderate. General anesthesia is typically used.

Buzzatti N, Taramasso M, Latib A, et al. Transcatheter mitral repair and replacement: state of the art and future directions. *J Heart Valve Dis*. 2014;23(4):492-505.

Feldman T, Kar S, Rinaldi M, et al. Percutaneous mitral repair with the MitraClip system: safety and midterm durability in the EVEREST (endovascular valve edge-to-edge repair study) cohort. *J Am Coll Cardiol*. 2009;54:686-694.

Guarracino F, Baldassarri R, Ferro B, et al. Transesophageal echocardiography during MitraClip® procedure. *Anesth Analg*. 2014;118(6):1188-1196.

E.3. What are the percutaneous options for AV repair and replacement?

Surgical valve replacement is the treatment of choice for severe AS. For those patients at very high risk for surgery, alternative treatments may be preferable. Aortic balloon valvuloplasty has been a nonsurgical option since the 1980s. Although it is far less invasive than surgery, high complication rates and in-hospital mortality have reserved this treatment for a select population. In addition, high restenosis rates make this a short-lived solution. Percutaneous AV replacement is emerging as another alternative to surgery in the high-risk population.

Billings FT IV, Kodali SK, Shanewise JS. Transcatheter aortic valve implantation: anesthetic considerations. *Anesth Analg*. 2009;108:1453-1462.

Klein AA, Skubas NJ, Ender J. Controversies and complications in the perioperative management of transcatheter aortic valve replacement. *Anesth Analg*. 2014;119(4):784-798.

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E.4. How is percutaneous AV replacement performed?

Currently, two prosthetic devices are used in the United States. The percutaneous devices are bioprosthetic valves mounted in nitinol stents. The valves may be delivered by retrograde (femoral artery, axillary artery or directly in the aorta) or antegrade (transapical) approaches. After balloon valvuloplasty, the valve stent is deployed. Rapid ventricular pacing is used to decrease cardiac translation and minimize ejection pressure during deployment. TEE and fluoroscopic guidance are used. Complications of these procedures include injury to the access site or artery, aortic dissection, atherosclerotic embolic events, and renal injury secondary to angiographic contrast exposure. The most frequent complication is residual AI, which if more than mild has adverse long-term outcome.

Klein AA, Skubas NJ, Ender J. Controversies and complications in the perioperative management of transcatheter aortic valve replacement. *Anesth Analg*. 2014;119(4):784-798.

E.5. What anesthetic techniques and monitors are used?

General anesthesia is mostly used to allow for simultaneous TEE examination and in the case of thoracotomy for the transapical approach. Large-bore central venous access is necessary in the event of vascular injury or to administer vasoactive medications. Pulmonary artery catheters are frequently used in percutaneous atrial valve replacement procedures. Alternatively, local infiltration and intravenous sedation may be used for these procedures. In these cases, TTE examination is performed for evaluation at the conclusion of the procedure. Radial artery catheters are placed before induction for continuous monitoring and for arterial blood gases analysis.

Billings FT IV, Kodali SK, Shanewise JS. Transcatheter aortic valve implantation: anesthetic considerations. *Anesth Analg*. 2009;108:1453-1462.

Covello RD, Maj G, Landoni G, et al. Anesthetic management of percutaneous aortic valve implantation: focus on challenges encountered and proposed solutions. *J Cardiothorac Vasc Anesth*. 2009;23:280-285.

Horne A Jr, Reineck EA, Hasan RK, et al. Transcatheter aortic valve replacement: historical perspectives, current evidence, and future directions. *Am Heart J*. 2014;168(4):414-423.

Klein AA, Skubas NJ, Ender J. Controversies and complications in the perioperative management of transcatheter aortic valve replacement. *Anesth Analg*. 2014;119(4):784-798.

E.6. What is minimally invasive cardiac valve surgery?

The Society of Thoracic Surgeons database considers “any procedure not performed with a full sternotomy and CPB support” a minimally invasive procedure. The practical applications of “mini-valve surgery” include partial sternotomy, thoracotomy, and video-assisted and robot-assisted procedures. The downside to minimally invasive approaches include difficulty converting to a sternotomy in the case of cannula displacement or aortic dissection and complications of femoral artery cannulation (including arterial dissection, infection, and hematoma). The anesthetic management varies from standard sternotomy cases, including single-lung ventilation for thoracotomy approaches and transjugular coronary sinus catheters, to provide retrograde cardioplegia. Intraoperative TEE is especially critical

in these cases to monitor for cardiac distention, removal of air, and cannula placement. There is clearly a significant learning curve to provide an equivalent surgical outcome with a “mini” versus traditional strategy. In successful procedures, patients enjoy improved cosmesis and decreased bleeding, wound infection, pain, and hospital length of stay. Unfortunately, in high-risk patients, the increased time of aortic cross-clamping and CPB may be deleterious. Also, complications are extremely morbid, including aortic dissection and death. Mini-valve surgery is limited to patients with an isolated valve disease.

Schmitto JD, Mokashi SA, Cohn LH. Minimally-invasive valve surgery. *J Am Coll Cardiol*. 2010;56:455-462.

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Chapter 8

Pacemakers, Implantable Cardioverter-Defibrillators, and Cardiac Resynchronization Therapy Devices

Alan Cheng

Fun-Sun F. Yao

A 63-year-old woman was scheduled for urgent open cholecystectomy. She underwent a dual-chamber permanent pacemaker (PPM) implantation 10 years ago for sick sinus syndrome and intermittent heart block. Over time, she developed systolic heart failure from greater amounts of ventricular pacing that resulted in an upgrade to a cardiac resynchronization therapy-defibrillator (CRT-D) 9 months ago. Her blood pressure was 110/68 mm Hg, and her heart rate was regular at 60 beats per minute. An electrocardiogram (ECG) obtained on admission demonstrated atrioventricular (AV) sequential pacing.

A. Medical Disease and Differential Diagnosis

1. What are the indications for PPMs?
2. What is sick sinus syndrome? What is chronotropic incompetence?
3. How would you diagnose first-, second-, and third-degree AV block, bifascicular block (right bundle branch block [RBBB] with left anterior fascicular hemiblock or left posterior fascicular hemiblock), and trifascicular block?
4. Is it necessary to insert a temporary pacemaker before general anesthesia for an asymptomatic patient with bifascicular or trifascicular block?
5. What are the three-letter and five-letter identification codes of the North American Society of Pacing and Electrophysiology (NASPE) and British Pacing and Electrophysiology Group (BPEG) generic (NBG) code for pacemaker classification?
6. How many modes of pacing are available in modern PPMs? How do they work? What is the difference between DDD pacing and DDI pacing?
7. The patient was mechanically hyperventilated during surgery and her pacemaker gradually increased her heart rate. What feature of the PPM is accounting for this?
8. What are the advantages and disadvantages of atrial pacing only? What are the disadvantages of right ventricular pacing only?
9. What are the indications for and complications associated with AV sequential PPMs?
10. How would you know if the patient's PPM was atrially, ventricularly, or atrioventricularly sequentially pacing?
11. During a new PPM implantation, what are the acceptable values for modern pacemaker leads in terms of pacing thresholds, amplitude of sensed intrinsic activity and impedance?
12. What is a biventricular PPM or CRT device? What are the indications for such a device?
13. What are the usual lifespans of PPMs and implantable cardioverter-defibrillators (ICDs)?

14. What is an ICD? How does it work? What is a subcutaneous ICD?
15. What are the indications for ICDs?
16. What is the NASPE and BPEG generic defibrillator (NBD) code?

B. Preoperative Evaluation and Preparation

1. How would you preoperatively evaluate the patient described earlier?
2. How do you determine whether the patient has a cardiac implantable electronic device (CIED) and define what type of

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CIED?

3. How do you determine whether the patient is dependent on pacing function of the CIED?
4. How do you know if the implanted PPM or ICD is working?
5. What information would you like to obtain from interrogating this device?
6. How do you preoperatively prepare the patient for surgery and anesthesia?
7. Would you recommend reprogramming this device to asynchronously pace before surgery? What would you recommend regarding the ICD functions of the device?

C. Intraoperative Management

1. How would you monitor this patient?
2. What drugs and equipment would you like to have on hand in the operating room?
3. How would you set up the transcutaneous external pacer and defibrillator?
4. Had this patient's ICD been implanted the day before surgery, would you consider avoiding certain inhalational gases for anesthesia?
5. Electromagnetic interference (EMI) from electrocautery results in significant noise on your cardiac monitor. You recall that EMI also can inhibit pacing function from the PPM. In this pacemaker-dependent patient, how can you determine whether inappropriate inhibition of the PPM is occurring?
6. What are the potential responses of pacemakers and ICDs to electrocautery?
7. How would you prevent the effects of EMI on the pacemaker or ICD from the electrocautery?
8. What are the effects of a magnet over pacemakers and ICDs?
9. In the middle of surgery, the patient developed ventricular tachycardia. What would you do?
10. What precautions should be taken when a patient with a CIED is undergoing extracorporeal shock wave lithotripsy (ESWL)?
11. Is electroconvulsive therapy (ECT) contraindicated in patients with pacemakers or ICDs?
12. Is magnetic resonance imaging (MRI) contraindicated in patients with a CIED?
13. What precautions should be taken during radiofrequency ablation for a patient with a CIED?
14. During surgery, the patient developed frequent premature ventricular complexes and some of these resulted in rapid ventricular pacing (see Fig. 8.6). What is accounting for the pacemaker's behavior?

D. Postoperative Management

1. How would you monitor this patient in the postanesthesia care unit?
2. How would you confirm that the CIED is functioning properly after surgery?

A. Medical Disease and Differential Diagnosis

A.1. What are the indications for PPMs?

Artificial pacing is generally indicated for the treatment of symptomatic bradycardia of any origin. The two main indications for permanent pacing are failure of impulse formation and

failure of cardiac conduction. Clinically, sick sinus syndrome and complete heart block are the most common indications for pacemakers. The following conditions are class I and IIA indications for a PPM:

- Sinus node dysfunction with documented symptomatic bradycardia, symptomatic chronotropic incompetence, or symptomatic sinus bradycardia secondary to required drug therapy for medical conditions
- Sinus node dysfunction for heart rates less than 40 beats per minute when a clear association between symptoms consistent with bradycardia and the actual presence of bradycardia has not been documented
- Recurrent syncope caused by spontaneous carotid sinus hypersensitivity or greater than 3-second episode of

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ventricular asystole induced with carotid sinus pressure

- Third-degree or advanced second-degree AV block associated with bradycardia with symptoms or ventricular arrhythmias presumed secondary to AV block
- Asymptomatic third-degree or advanced second-degree AV block in patients with sinus rhythm and documented periods of asystole greater than 3 seconds, escape rate less than 40 beats per minute, or an escape rhythm that is below the AV node (as suggested by a wide QRS complex)
- Ventricular pauses of greater than 5 seconds in patients with persistent atrial fibrillation
- Third-degree or advanced second-degree AV block resulting from catheter ablation or cardiac surgery
- First- or second-degree AV block associated with symptoms similar to those of pacemaker syndrome or hemodynamic compromise
- Chronic bifascicular block with advanced second-degree AV block or intermittent thirddegree AV block
- Chronic bifascicular block with alternating left bundle branch block (LBBB) and RBBB conduction
- High-risk patients with congenital long QT syndrome or those with documented sustained pause-dependent ventricular tachycardia
- New York Heart Association (NYHA) class III or class IV heart failure symptoms despite optimal medical therapy in patients with dilated cardiomyopathy (ejection fraction [EF] less than 35%), QRS duration greater than 120 milliseconds and sinus rhythm (e.g., biventricular pacing)

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 10th ed. Philadelphia, PA: Saunders; 2015:721-747.

A.2. What is sick sinus syndrome? What is chronotropic incompetence?

Sick sinus syndrome describes an array of clinical disorders resulting from irreversible sinus node dysfunction. This may be manifested by episodes of sinus arrest, sinus pause, or bradycardia secondary to inadequate sinus node automaticity. As a result, episodes of tachyarrhythmias from ectopic atrial foci can occur as well. The diagnosis is made when a correlation is made between a patient's symptoms and electrocardiographic evidence of bradycardia. Hence, extended ambulatory cardiac telemetry such as 24/48-hour Holter or event monitoring is helpful to make a diagnosis. When episodes of tachycardia and bradycardia coexist, it is often referred to as *tachy-brady* syndrome. This is one of the most common indications for pacemakers and is characterized by the following:

- Unexpected persistent severe sinus bradycardia
- Episodes of sinus arrest or exit block
- Episodes of atrial fibrillation, atrial tachycardia, or atrial flutter
- Slow return to sinus rhythm following cardioversion (prolonged sinus node recovery time)

Chronotropic incompetence is loosely defined as the inability to achieve at least 80% to 85% of an individual's maximum predicted heart rate (MPHR) at peak exercise. Use of

medications including β-blockers, calcium channel blockers, and antiarrhythmic medications can confound this diagnosis. In these instances, most people have used a modified definition of failure to achieve at least 62% of the MPHR. The presence of chronotropic incompetence has been shown to increase mortality and morbidity especially in those with heart failure. Rate-adaptive pacing is often used in these instances and has been shown to increase peak oxygen consumption during exercise. It is important to point out that not all patients with sick sinus syndrome have chronotropic incompetence and not all patients with chronotropic incompetence have sick sinus syndrome.

Dobrzynski H, Boyett MR, Anderson RH. New insights into pacemaker activity: promoting understanding of sick sinus syndrome. *Circulation*. 2007;115:1921-1932.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 10th ed. Philadelphia, PA: Saunders; 2015:662-684.

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A.3. How would you diagnose first-, second-, and third-degree AV block, bifascicular block (right bundle branch block [RBBB] with left anterior fascicular hemiblock or left posterior fascicular hemiblock), and trifascicular block?

First-degree AV block is characterized by a PR interval of greater than 0.20 seconds during normal sinus rhythm (Fig. 8.1). Second-degree AV block is subdivided into two types. Mobitz type I, or Wenckebach block, is characterized by a progressively lengthening PR interval, which occurs until a P wave is not conducted down the AV node and a QRS complex is dropped. The PR interval of the first beat after the blocked P wave is almost always shorter than the PR interval of the beat prior to being blocked. The site of block is usually in the AV node, and the natural history of Mobitz I may or may not involve progression toward complete heart block. Mobitz type II block is characterized by a loss of AV conduction with no progressive lengthening of the PR interval before the sudden dropping of one or more QRS complexes. Additionally, the PR interval of the first beat after the blocked P wave is usually the same as the PR interval of the beat prior to the blocked P wave. The site of block is typically below the AV node and within the His bundle or in the Purkinje system. The natural history of Mobitz II block is often progression toward complete heart block over time. Thirddegree AV block, also called *complete heart block*, occurs when all electrical activity from the atrium fails to progress into the His-Purkinje system. The site of block can lie in either the AV node or the His-Purkinje system. The atrial and ventricular contractions have no relation with each other, with the atrial rate almost always faster than the ventricular rate. As a result, the QRS complexes seen result from an ectopic focus either from the ventricular myocardium or in an area of the AV node/His-Purkinje system below the site of block. Therefore, the QRS complex may appear wide or narrow, respectively, and typically occur with a rate of 40 to 60 beats per minute.

The term *bifascicular block* often refers to block in the right bundle and one of the two major fascicles of the left bundle. RBBB with left anterior hemiblock is present when the ECG shows an RBBB with a left axis deviation (usually greater than -60 degrees) in the absence of an inferior myocardial infarction. Complete RBBB with right axis deviation (greater than 90 degrees) is indicative of RBBB and left posterior hemiblock in the absence of a lateral myocardial infarction or evidence of right-sided heart failure. The term *trifascicular block* is used to describe first-degree AV block in the presence of bifascicular block.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 10th ed. Philadelphia, PA: Saunders; 2015:662-684.

A.4. Is it necessary to insert a temporary pacemaker before general anesthesia for an asymptomatic patient with bifascicular or trifascicular block?

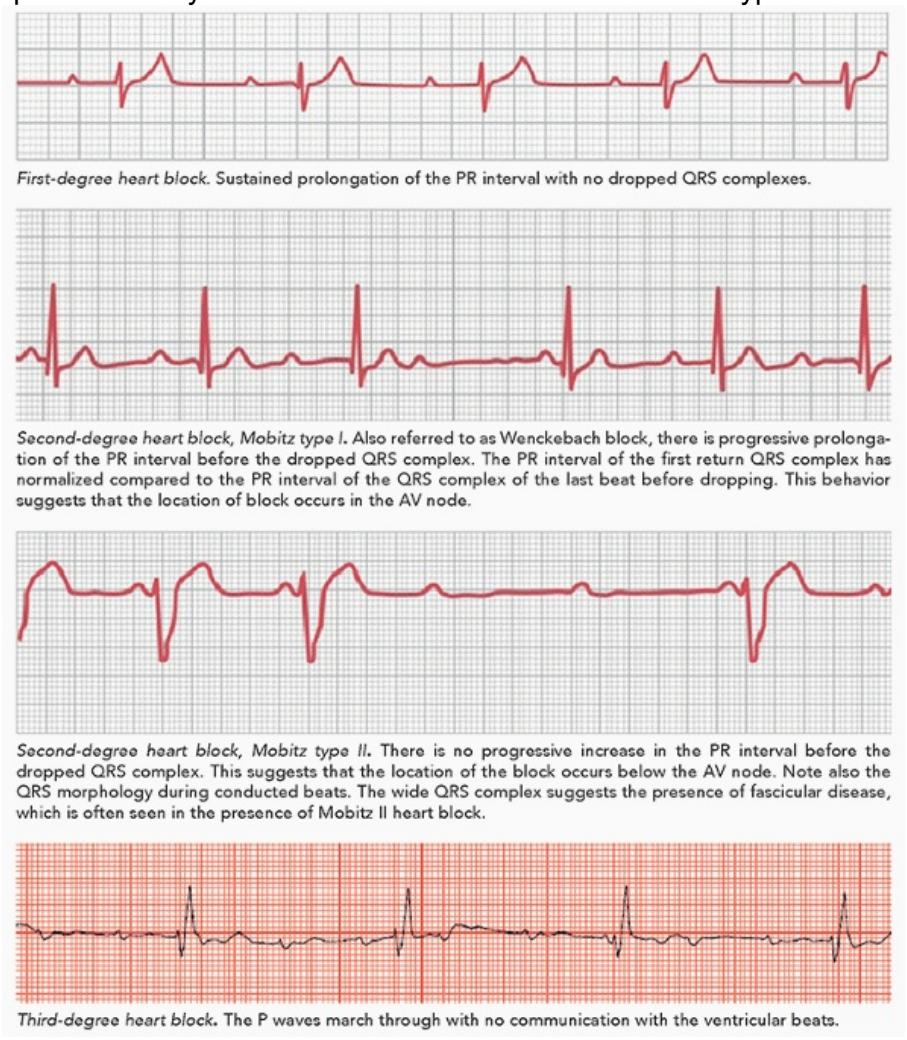
The risk for progression to complete heart block in asymptomatic patients with bifascicular block is low. Further, no clinical characteristics have been identified that accurately predict the risk of development of complete heart block. Therefore, routine PPM implantation in patients with asymptomatic bifascicular block is not recommended. Observations made in the perioperative period have suggested that development of complete heart block during general

anesthesia is also rare; therefore, it is generally not recommended that patients undergo temporary pacemaker insertion before general anesthesia. However, it is advisable to have an external pacemaker available in the operating room. The term *trifascicular block* is somewhat of a misnomer because, in truth, if all three fascicles (i.e., right bundle, left anterior fascicle, left posterior fascicle) were blocked, the patient would be in complete heart block. Although it is generally agreed that individuals with trifascicular block have a higher risk for sudden death, there is no single clinical variable that predicts a higher risk for complete heart

block during surgery. Small case series have shown that the development of intraoperative complete heart block in asymptomatic patients with trifascicular block is uncommon. Therefore, routine temporary pacemaker insertion before general anesthesia in these patients is not recommended.

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First-degree heart block. Sustained prolongation of the PR interval with no dropped QRS complexes.

Second-degree heart block, Mobitz type I. Also referred to as Wenckebach block, there is progressive prolongation of the PR interval before the dropped QRS complex. The PR interval of the first return QRS complex has normalized compared to the PR interval of the QRS complex of the last beat before dropping. This behavior suggests that the location of block occurs in the AV node.

Second-degree heart block, Mobitz type II. There is no progressive increase in the PR interval before the dropped QRS complex. This suggests that the location of the block occurs below the AV node. Note also the QRS morphology during conducted beats. The wide QRS complex suggests the presence of fascicular disease, which is often seen in the presence of Mobitz II heart block.

Third-degree heart block. The P waves march through with no communication with the ventricular beats.

FIGURE 8.1 Atrioventricular heart block.

Gauss A, Hübner C, Radermacher P, et al. Perioperative risk of bradyarrhythmias in patients with asymptomatic chronic bifascicular block or left bundle block: does an additional first degree atrioventricular block make any difference? *Anesthesiology*. 1998;88:679-687. Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 10th ed. Philadelphia, PA: Saunders; 2015:685-720.

A.5. What are the three-letter and five-letter identification codes of the North American Society of Pacing and Electrophysiology (NASPE) and British Pacing and Electrophysiology Group (BPEG) generic (NBG) code for pacemaker classification?

Given the complexity of current pacemaker systems, the Intersociety Commission for Heart Disease Resources established a classification code in the 1970s that is now widely accepted. The original nomenclature involved a three-letter identification code, as shown in the first three columns of Table 8.1. In 1980, this code was extended to five letters; the last two letters can be deleted when not applicable. In 1987, this five-letter coding system become known as the NBG pacemaker code after being adopted by both the NASPE (now known as the *Heart Rhythm Society*) and BPEG. The first letter describes the chamber(s) that the pacemaker can pace, the second letter describes the chamber(s) that it senses, and the third letter describes the response of the pacemaker to sensed intrinsic activity. The last two letters describe additional features such as rate responsiveness that are commonly omitted when not used. For example, a VVI pacing mode paces in the ventricle, can sense intrinsic activity in the ventricle, and inhibits pacing when it senses intrinsic activity. A VOO pacing mode paces in the ventricle but does not sense intrinsic activity nor does it inhibit pacing—it simply paces regardless of the heart's electrical activity.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac

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implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247-261.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 10th ed. Philadelphia, PA: Saunders; 2015:721-747.

A.6. How many modes of pacing are available in modern PPMs? How do they work? What is the difference between DDD pacing and DDI pacing?

Modern pacemakers are programmable into one of three modes of pacing: asynchronous pacing, single-chamber demand pacing, and dual-chamber AV sequential demand pacing.

TABLE 8.1 NASPE/BPEG Generic Pacemaker Identification Code[a]

LETTER I CHAMBER(S) PACED	LETTER II CHAMBER(S) SENSED	LETTER III MODE OF RESPONSE	LETTER IV PROGRAMMABILITY RATE MODULATION	LETTER V ANTITACHYARRHYTHMIA FUNCTION(S)
O = None	O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	T = Triggered	P = Single programmable	P = Pacing
V = Ventricle	V = Ventricle	I = Inhibited	M = Multiprogrammable	S = Shock
D = Dual (A + V)	D = Dual (A + V)	D = Dual (T + I)	C = Communicating	D = Dual (P + S)
			R = Rate modulation	

[a]Although the pacemaker identification coding involved the use of five letters, few modern pacemakers have antitachyarrhythmia functions. Therefore, most pacemakers are currently described by the first four letters of the coding system. BPEG, British Pacing and Electrophysiology Group; NASPE, North American Society of Pacing and Electrophysiology.

Asynchronous or fixed-rate (e.g., AOO, VOO, DOO [see section A.5 for details]) modes pace at a programmable preset rate that is independent of the inherent heart rate. They can be atrial, ventricular, or dual-chamber. Competition, pacemaker syndrome, and rarely induction of ventricular arrhythmias are the potential complications when pacing occurs in the presence of intrinsic myocardial electrical activity. Ventricular tachyarrhythmias in those with structural heart disease can theoretically occur because the pacing spike can potentially be delivered during a time when the myocardium is vulnerable to arrhythmogenesis, but this is extremely rare.

Single-chamber demand pacing (e.g., AAI, VVI) paces at a preset rate only when the spontaneous heart rate drops below the programmed preset rate. For example, if this patient's device was programmed to VVI 70, the device would pace in the ventricle only when the native ventricular rate fell below 70 beats per minute. Once the native ventricular rate resumed above 70 beats per minute, the device would sense this activity and inhibit further pacing. Single-chamber demand pacing in the atrium functions in a similar way but is rarely used alone in the United States.

Dual-chamber AV sequential pacing requires two pacemaker leads, one in the right atrium and one in the right ventricle.

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The atrium is stimulated to contract first; then, after an adjustable PR interval (also referred to as the *AV interval*), the ventricle is stimulated to contract if no intrinsic ventricular activity is sensed by the ventricular pacing lead. For example, if this patient's device was programmed to DDD 70 with an AV interval of 200 milliseconds, the device would begin pacing the atrium first if the intrinsic sinus rate fell below 70 beats per minute. After the atrium has been paced, the device will wait for 200 milliseconds to sense intrinsic ventricular activity. If it does not see intrinsic activity within 200 milliseconds, it will then pace in the ventricle as well. DDD pacemakers can also pace in the ventricle in response to intrinsic atrial activity. For example, if the intrinsic atrial rate was 80 beats per minute, the device would inhibit pacing in the atrium because the base rate was set to 70 beats per minute. But because it is a dual-chamber device programmed to inhibit and trigger pacing in both chambers (i.e., the third "D" in the coding sequence), it will wait 200 milliseconds from the time of the intrinsic atrial activity and watch for intrinsic ventricular activity. If it sees intrinsic ventricular activity (i.e., the atrial signal conducted down the AV node and to the ventricle), it will inhibit ventricular pacing. If it does not see intrinsic ventricular activity occurring within 200 milliseconds from the intrinsic atrial activity, the pacemaker will then "trigger" the ventricular pacing lead to pace the ventricle. Dual-chamber pacemakers programmed to DDI differ slightly from devices programmed to DDD, and the main difference is that AV sequential pacing occurs only when atrial pacing is present. This is in contrast to DDD pacing in which AV sequential pacing is preserved regardless of whether atrial pacing or atrial sensing is occurring. Suppose we have a dual-chamber pacemaker programmed to DDI 70 with an AV interval of 200 milliseconds. If the sinus rate fell below 70 beats per minute, the atrial pacing lead would pace the atrium. After a 200-millisecond interval, if intrinsic ventricular activity was seen by the ventricular lead, then the ventricular lead would be inhibited from pacing the ventricle. If ventricular activity was not seen after 200 milliseconds, the ventricular lead would pace the ventricle. Suppose now that the sinus rate is 80 beats per minute. Because the DDI pacemaker is programmed to 70 beats per minute, no atrial pacing is occurring. Because DDI pacemakers do not track atrial sensed events, ventricular pacing would not be "triggered" after 200 milliseconds by these atrial sensed events and only occur if the *ventricular* rate fell below the preset rate of 70 beats per minute.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 10th ed. Philadelphia, PA: Saunders; 2015:721-747.

A.7. The patient was mechanically hyperventilated during surgery and her pacemaker gradually increased her heart rate. What feature of the PPM is accounting for this?

All modern pacemakers have the ability to adjust the pacing rate according to the patient's level of activity in an effort to obtain a more physiologic response to exercise. This is known as *rate-response* (adaptive) pacing and is denoted by an "R" in the fourth position of the NBG coding schema. This is often applied in patients with chronotropic incompetence or those with permanent atrial fibrillation who have undergone AV node ablation. Various

activity-detecting systems have been developed to create a reliable rate-responsive pacemaker (e.g., muscle movement, respiratory rate, minute ventilation, central venous temperature, QT interval, myocardial contractility [dP/dt], oxygen saturation and pH in mixed venous blood, and ventricular depolarization gradient), but currently, PPMs used in the United States rely on sensors of motion or changes in minute ventilation through measurements of intrathoracic impedance. Because of the latter phenomenon, patients undergoing general anesthesia who are subjected to mechanical hyperventilation (e.g., neurosurgery) can experience an increase in the rate of pacing. Although it is generally not required to disable rate-responsive features before surgery, pacemaker-induced changes in heart rate resulting from intraoperative hyperventilation or significant motion may sometimes be mistaken for inadequate anesthesia. Hence, it is important that the anesthesia team be aware of the programmed settings of the pacemaker. If reprogramming the device to disable rate-responsive features is not readily available, a magnet may be placed over the pacemaker site to temporarily convert it to asynchronous pacing. Although the response to a magnet may be programmed off in some pacemakers, all properly functioning pacemakers within the United States have magnet-responsive features activated as a default.

Ellenbogen KA, Kay GN, Lau CP, et al, eds. *Clinical Cardiac Pacing, Defibrillation and Resynchronization Therapy*. 4th ed. Philadelphia, PA: Elsevier Saunders; 2011:156,320.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 10th ed. Philadelphia, PA: Saunders; 2015:721-747.

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A.8. What are the advantages and disadvantages of atrial pacing only? What are the disadvantages of right ventricular pacing only?

Atrial pacing only increases cardiac output by 26% over the cardiac output of ventricular pacing only because atrial contraction contributes to approximately 15% to 25% of the diastolic filling of the ventricle. It has been shown that coronary blood flow increases and coronary resistance decreases during atrial pacing only. Atrial pacing has also been shown to reduce the incidence of atrial fibrillation. Atrial pacing only is seldom used in the United States and often is implanted with the addition of a ventricular pacing lead in the event of AV block.

Ventricular pacing, occurring individually or sequentially with atrial pacing, has been shown to result in dyssynchronous left ventricular electrical activation and mechanical contraction. Under normal circumstances, electrical activation along the His-Purkinje system results in a near simultaneous activation of the entire left ventricle. This allows for efficient contraction and is said to be synchronous. When ventricular pacing is introduced, this results in activation of the right ventricle first, followed by passive activation of the left ventricular free wall. This form of contraction is said to be dyssynchronous and has been shown to potentially worsen congestive heart failure and the left ventricular EF. Prior studies have shown that individuals at greatest risk for developing reductions in EF from right ventricular pacing are those who exhibit ventricular pacing greater than 40% of the time. More recent studies have shown that individuals requiring ventricular pacing for AV block with an EF less than 50% have a 56% risk for developing a composite end point of death, urgent visit for heart failure or left ventricular dilatation over an average of 37 months.

Curtis AB, Worley SJ, Adamson PB, et al. Biventricular pacing for atrioventricular block and systolic dysfunction. *N Engl J Med*. 2013;368:1585-1593.

Healey JS, Toff WD, Lamas GA, et al. Cardiovascular outcomes with atrial-based pacing compared with ventricular pacing: meta-analysis of randomized trials, using individual patient data. *Circulation*. 2006;114:11-17.

Sweeney MO, Hellkamp AS, Ellenbogen KA, et al. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. *Circulation*. 2003;107:2932-2937.

A.9. What are the indications for and complications associated with AV sequential PPMs?

When ventricular pacing alone cannot maintain adequate cardiac output and atrial pacing alone is not justified, as in complete AV block, AV sequential pacing is indicated. Because

of the success of transvenous leads, bioengineering advances such as thinner polyurethane insulation and improved device programmability, the indications for dual-chamber pacing, have broadened. It can be used for sick sinus syndrome and all degrees of heart block. PPMs programmed to DDD pacing are the ultimate form of physiologic pacing. Programmable features include the mode of pacing, the AV delay, the maximum atrial rate that the ventricle will follow (atrial tracking), and the minimum atrial rate for sensing at which atrial pacing commences. The major advantage of such pacing is the ability to significantly increase the cardiac output under extreme stress and a reduced incidence of atrial fibrillation development. Historically, the major disadvantage of DDD pacing has been the possibility of pacemaker-mediated tachycardia (see section C.14). Another disadvantage recognized has been the development of ventricular dyssynchrony (see section A.8) as a result of right ventricular only pacing. Long-term follow-up of patients with dual-chamber pacemakers demonstrated reductions in left ventricular EFs when compared to atrial pacing alone, especially in the setting of preexisting left ventricular dysfunction.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 10th ed. Philadelphia, PA: Saunders; 2015:721-747.

Sweeney MO, Hellkamp AS, Ellenbogen KA, et al. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. *Circulation*. 2003;107:2932-2937.

A.10. How would you know if the patient's PPM was atrially,

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ventricularly, or atrioventricularly sequentially pacing?

Modern-day cardiac monitors are equipped with filters that can accentuate and highlight artificial pacing potentials. In atrial pacing, an electrical spike often appears before the P wave and the QRS complex is usually normal, provided there is normal intrinsic AV conduction. One may need to adjust the monitor so that pacing spikes are accentuated and can readily be seen. In ventricular pacing, the electrical spike is followed immediately by a widened QRS complex. In fact, most right ventricular pacing leads are positioned at the right ventricular apex. Because of this location, pacing would result in a QRS complex that has a QS pattern in lead V1 and a QS pattern in the inferior limb leads (II, III, and aVF). In AV sequential pacing, there are two spikes, one before the P wave and another preceding the QRS complex.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 10th ed. Philadelphia, PA: Saunders; 2015:721-747.

A.11. During a new PPM implantation, what are the acceptable values for modern pacemaker leads in terms of pacing thresholds, amplitude of sensed intrinsic activity and impedance?

Modern-day PPMs have a maximal pacing output of 7.5 V at 1.5 milliseconds, and current device manufacturers recommend that pacing outputs should be ideally programmed to at least twice the voltage threshold or three times the pulse width threshold. Hence, pacing thresholds of newly implanted leads should theoretically not exceed 3.75 V at 0.5 millisecond. Most implanting physicians aim for values well below this and will often move the lead during the implant if the value is above 2 V at 0.5 millisecond. It is common to see fluctuations in the pacing thresholds during the first few weeks after a pacing lead has been implanted. There is an initial sharp rise in the pacing threshold during the first 2 weeks because of tissue reaction around the tip of the electrode despite the presence of steroid embedded at the tip. The threshold then returns to levels similar to what were seen at the time of implant. In the chronic state, pacing thresholds remain essentially at the same level in 80% of patients. For the ventricular lead, the intrinsic R waves should be at least 5 to 6 mV in amplitude. For the atrial lead, the intrinsic P waves should be at least 1 mV in amplitude. Impedances for atrial or ventricular leads should be between 250 and 1,300 ohms, depending on the type of lead implanted. These are general guidelines.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 10th ed. Philadelphia, PA: Saunders; 2015:721-747.

A.12. What is a biventricular PPM or CRT device? What are the indications for such a device?

It has long been recognized that individuals with interventricular conduction abnormalities have a predilection toward impaired left ventricular systolic function. In fact, one of the more common interventricular conduction delays seen in patients with congestive heart failure is LBBB. On a mechanistic level, individuals with LBBB demonstrate ventricular dyssynchrony, a phenomenon whereby the left ventricle contracts in a stepwise process. Unlike normal individuals where the left ventricular septum and the left ventricular lateral free wall contract nearly simultaneously, patients with LBBB have a delay in the activation of the left lateral free wall. As a result, there is marked impairment in left ventricular systolic function and increased myocardial work and oxygen consumption. One approach to correct this dyssynchrony is to “resynchronize” the heart through the use of a biventricular pacemaker/ICD. These devices are capable of pacing both the left ventricular septum (through a pacemaker lead in the right ventricle) and the left ventricular lateral free wall simultaneously (through a pacemaker lead in the coronary sinus), thereby allowing for activation of the entire left ventricle at the same time. Candidates for implantation of a biventricular device include individuals on optimal heart failure medications with

- Sinus rhythm, EF ≤35%, LBBB with QRS >120 milliseconds, NYHA II to IV symptoms
- Sinus rhythm, EF ≤35%, non-LBBB with QRS >150 milliseconds, NYHA III to IV symptoms
- Patients requiring >40% of ventricular pacing with EF ≤35%

Jarcho JA. Biventricular pacing. *N Engl J Med*. 2006;355:288-294.

Tracy CM, Epstein AE, Darbar D, et al. 2012 ACCF/AHA/HRS focused update of the 2008 guidelines for

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devicebased therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Circulation*. 2012;126:1784-1800.

A.13. What are the usual lifespans of PPMs and implantable cardioverterdefibrillators (ICDs)?

Modern-day pacemakers are lithium-powered and can on average last 7 to 10 years. The lifespan of current ICDs relies not only on the battery but also on the high-voltage capacitor. Hence, typical lifespans are 5 to 8 years.

Ellenbogen KA, Kay GN, Lau CP, et al, eds. *Clinical Cardiac Pacing, Defibrillation and Resynchronization Therapy*. 4th ed. Philadelphia, PA: Elsevier Saunders; 2011:178-183.

A.14. What is an ICD? How does it work? What is a subcutaneous ICD?

An ICD system consists of a pulse generator and leads for tachyarrhythmia detection and therapy. ICDs provide antitachycardia and antibradycardia pacing, synchronized (cardioversion) or nonsynchronized (defibrillation) shocks, telemetry, and diagnostics including stored event electrograms and history logs. Essentially, the pulse generator is a self-powered computer within a hermetically sealed titanium casing (can). A battery with high power density is used to power the pulse generator, circuitry, and aluminum electrolytic storage capacitors. Most ICD designs use two capacitors in series to achieve a maximum voltage for defibrillation. A major challenge in ICD design is the large range of voltages that must be controlled in a very small package. Modern devices can charge up to 41 joules of energy.

ICDs use transvenous lead systems for sensing, pacing, and shocks. Epicardial leads are still used in infants and small children. Ventricular demand pacing for bradycardia is a standard feature of all ICDs. Modern-day ICDs have all the capabilities of modern-day pacemakers, including rate-adaptive pacing and automatic mode switching. The response of ICDs to magnets differs from that of a pacemaker (see section C.8).

Current ICDs have many programmable features, but essentially, they measure each cardiac R-R interval and categorize the rate as normal, too fast (short R-R interval), or too slow.

When the device detects a sufficient number of short R-R intervals within a period of time (all programmable), it will declare a tachycardia episode. The internal computer will decide between antitachycardia pacing (less energy use, better tolerated by patient) and shock based on its programmed algorithm. If shock is chosen, an internal capacitor is charged that takes approximately 5 to 13 seconds depending on the amount of energy to be delivered and age of the device. Most devices are programmed to reconfirm ventricular tachycardia or ventricular fibrillation after charging to prevent inappropriate shock therapy. Typically, ICDs deliver no more than six shocks per episode. Once therapy is delivered, the ICD will redetect to determine whether or not the therapy successfully terminated the arrhythmia. A tachycardia episode is considered terminated when sinus rhythm has been restored for a certain period (varies by manufacturer).

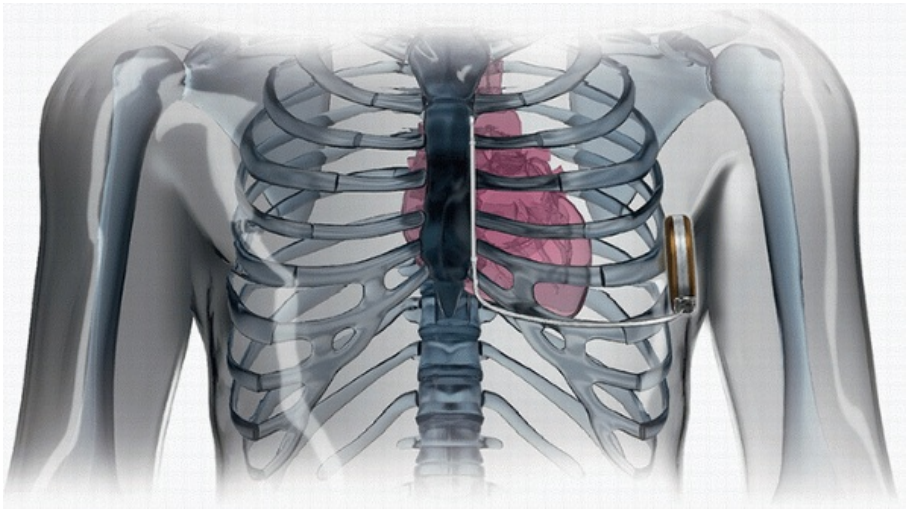


FIGURE 8.2 The subcutaneous ICD. ICD can is implanted along the left midaxillary line, and the lead is tunneled across the left lower chest to the xiphoid process. The lead is then directed superiorly along the left sternal border so

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that the lead's defibrillator coil is alongside the sternum. Defibrillation vector involves the can to the coil. (Reproduced with permission from Boston Scientific Corporation. EMBLEM S-ICD system. http://www .bostonscientific.com/en-US/products/defibrillators/emblem-s-icd-system.html. Accessed September 12, 2015.)

The subcutaneous ICD was approved for use in the United States on September 28, 2012. Unlike traditional ICD systems, this device does not require implantation of transvenous leads within the heart.

The ICD can is implanted along the left midaxillary line, and the defibrillator lead is tunneled across the left base of the chest to the xiphoid process. From there, the lead is then tunneled superiorly along the left sternal border toward the sternal notch so that the defibrillator coil is positioned alongside the sternum (Figs. 8.2 and 8.3). The vector for defibrillation is defined with the can as the cathode and the defibrillator coil as the anode. These systems are unique and provide a solution to patients who have vascular issues or may not want indwelling transvenous leads. Because defibrillation occurs from the chest wall, the amount of energy required for defibrillation is higher with current systems being able to generate a maximum of 80 joules. Because the amount of energy needed is higher, the current generation of subcutaneous ICDs are larger and the battery longevity shorter. Additionally, these systems differ from traditional ICDs in that they do not provide pacing support or deliver antitachycardia pacing.

Bardy GH, Smith WM, Hood MA, et al. An entirely subcutaneous implantable cardioverter defibrillator. *N Engl J Med*. 2010;363:36-44.

Burke MC, Gold MR, Knight BP, et al. Safety and efficacy of the totally subcutaneous implantable defibrillator: 2-year results from a pooled analysis of the IDE study and EFFORTLESS registry. *J Am Coll Cardiol*. 2015;65(16):1605-1615.

A.15. What are the indications for ICDs?

Initially, ICDs were indicated for hemodynamically significant ventricular tachycardia or ventricular fibrillation. Newer indications include the following and continue to evolve:

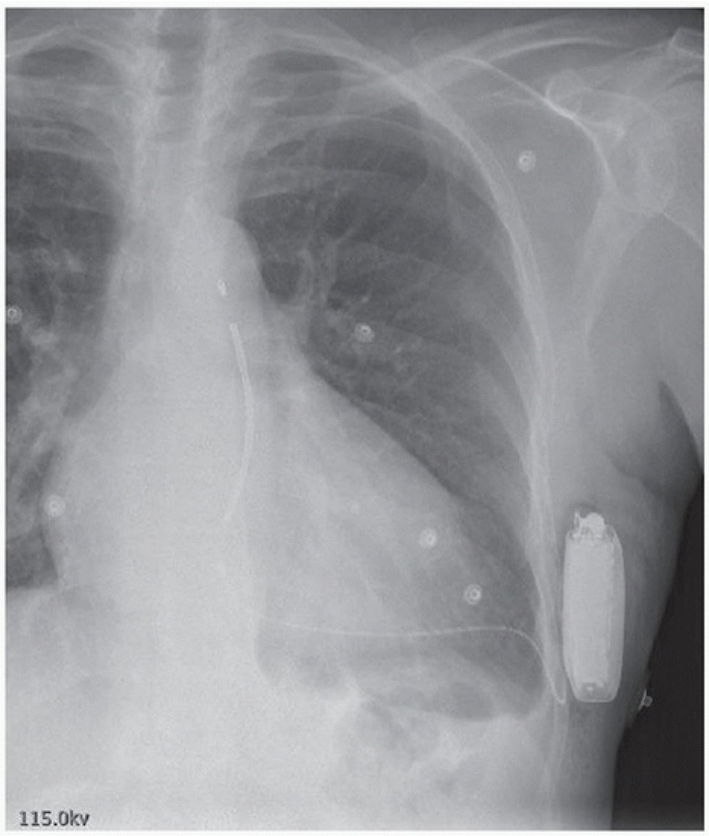


FIGURE 8.3 Chest x-ray of implanted subcutaneous ICD.

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- Survivors of cardiac arrest because of ventricular tachycardia/ventricular fibrillation not resulting from a transient or reversible cause
- Spontaneous or induced at electrophysiology study sustained ventricular tachycardia in the presence of structural heart disease
- Syncope of undetermined origin with clinically relevant, hemodynamically significant sustained ventricular tachycardia or ventricular fibrillation-induced at electrophysiology study
- Ischemic cardiomyopathy (EF ≤30%) without a recent myocardial infarction (within the last 40 days) or revascularization in the past 3 months
- Ischemic or nonischemic dilated cardiomyopathy (EF ≤35%) with NYHA class II or III heart failure symptoms
- Inherited channelopathies including Brugada syndrome (RBBB and ST-segment elevation leads V1 to V_3), catecholaminergic polymorphic ventricular tachycardia, long QT syndrome, short QT syndrome, idiopathic ventricular fibrillation
- Inherited or acquired high-risk states including arrhythmogenic right ventricular dysplasia, hypertrophic cardiomyopathy, cardiac sarcoidosis, or Chagas cardiomyopathy.

Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 Guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2008;117:e350-e408.

Tracy CM, Epstein AE, Darbar D, et al. 2012 ACCF/AHA/HRS focused update of the 2008 guidelines for devicebased therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2012;60:1297-1313.

TABLE 8.2 NASPE/BPEG Generic Defibrillator Code

LETTER I	LETTER II	LETTER III	LETTER IV
SHOCK CHAMBER(S)	**ANTITACHYCARDIA PACING CHAMBER(S)**	**TACHYCARDIA DETECTION**	**ANTIBRADYCARDIA PACING CHAMBER(S)**
O = None	O = None	E = Electrogram	O = None
A = Atrium	A = Atrium	H = Hemodynamic	A = Atrium
V = Ventricle	V = Ventricle	(not yet available)	V = Ventricle
D = Dual (A + V)	D = Dual (A + V)		D = Dual (A + V)

BPEG, British Pacing and Electrophysiology Group; NASPE, North American Society of Pacing and Electrophysiology.

A.16. What is the NASPE and BPEG generic defibrillator (NBD) code?

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Like pacemakers, ICDs have a generic code to indicate lead placement and function. The NBD code is shown in Table 8.2. The most robust form of identification, referred to as the “label form,” replaces the fourth letter of the NBD with the appropriate generic pacemaker code.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247-261.

B. Preoperative Evaluation and Preparation

B.1. How would you preoperatively evaluate the patient described earlier?

Preoperative evaluation should include the routine systemic workup, paying particular attention to cardiovascular disorders. The comprehensive evaluation includes complete blood count, urinalysis, coagulation screening with prothrombin time and partial thromboplastin time, serum electrolytes, blood urea nitrogen, blood sugar, chest radiograph, and ECG. Special attention should be paid to the history, symptoms, and signs of myocardial infarction, congestive heart failure, and arrhythmia. Serum electrolytes, especially potassium level, must be in the normal range. For the patient with a CIED, recent guidelines have recommended that all CIEDs be properly interrogated within 3 to 6 months before surgery. This evaluation should include the following:

- Establish whether a patient has a CIED.
- Define the type of CIED.
- Determine dependency on pacing function of the CIED.
- Determine CIED function and programming details.
- Determine magnet behavior and whether CIED requires reprogramming on the day of surgery to avoid inappropriate device behavior from EMI.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247-261.

Crossley GH, Poole JE, Rozner MA, et al. The Heart Rhythm Society (HRS)/American Society of Anesthesiologists (ASA) Expert Consensus Statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: facilities and patient management. *Heart Rhythm*. 2011;8:1114-1154. Salukhe TV, Dob D, Sutton R. Pacemakers and defibrillators: anesthetic implications. *Br J Anaesth*. 2004;93:95-104.

B.2. How do you determine whether the patient has a cardiac implantable electronic device (CIED) and define what type of CIED?

Determining whether a patient has a CIED should be based on (1) a focused history including but not limited to the patient interview, medical records review, review of available chest

radiograph, ECG, or any available monitor or rhythm strip information and (2) a focused physical examination (e.g., checking for scars, palpating for device).

Defining the type of device is accomplished by (1) obtaining the manufacturer's identification card from the patient or other source, (2) ordering chest radiography studies if no other data are available, or (3) referring to supplemental resources (e.g., manufacturer's databases, pacemaker clinic records, consultation with a cardiologist).

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac

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Implantable Electronic Devices. *Anesthesiology*. 2011;114:247-261.

B.3. How do you determine whether the patient is dependent on pacing function of the CIED?

Pacemaker dependency is not defined by an absolute amount of pacing seen over time. Rather, it is defined by how functionally dependent a patient is without pacing support. For instance, a patient with a dual-chamber pacemaker may not pace 100% of the time. But during periods of pacing, if pacing were to be temporarily discontinued and the patient develops light-headedness or presyncope, then s/he would be considered functionally dependent. Functional dependency on pacing support may be determined by one or more of the following: (1) a verbal history or an indication in the medical record that the patient has experienced a bradyarrhythmia that has caused syncope or other symptoms requiring CIED implantation, (2) a history of successful AV nodal ablation that resulted in CIED placement, or (3) a CIED evaluation that shows clinically evidenced hemodynamic compromise when the pacing function of the CIED is temporarily disabled or programmed to the lowest programmable rate.

For emergency surgery, an ECG or rhythm strip should be examined for pacing spikes. If pacing spikes are noted before most or all of either P wave or QRS complexes, then the patient should be treated as if pacemaker-dependent. All pacemaker-dependent patients and patients with ICDs should have transcutaneous pacing and defibrillator pads placed during surgery. A magnet should always be available, and its use is recommended in the pacemakerdependent patient as well as the patient with an ICD. Regardless of the type of device, interrogation of the CIED under the direction of a physician knowledgeable in the function of devices should occur as soon as possible.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247-261.

B.4. How do you know if the implanted PPM or ICD is working?

The CIED function is ideally assessed by interrogating the device, and this is the recommended approach. But if interrogating the device is not an option, one can slow the intrinsic heart rate to a rate below that of the pacemaker by carotid massage or the Valsalva maneuver. Carotid massage to slow the heart rate should be used cautiously because it could result in an arteriosclerotic plaque embolizing to the cerebral circulation. If the rate does not slow down enough for the pacemaker to take over the ventricle, the device can be tested by placing a magnet over it that will temporarily program it to a fixed-rate pacing mode. In this mode, pacing spikes march through the rhythm strip with no regard for the intrinsic electrical activity of the heart. The rate at which the pacemaker will pace in the presence of a magnet varies among device manufacturers and is dependent on the battery life. Once the magnet is removed, the device returns to its normal programming. Of note, placing a magnet over an ICD does not temporarily program the device to pace asynchronously. The magnet on an ICD will only temporarily disable the ICD therapies and will have no effect on the pacing function.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247-261.

B.5. What information would you like to obtain from interrogating this device?

Device interrogations provide information on the status and current programmed settings of a PPM or ICD. The important primary information for anesthesiologists include (1) battery life, (2) programmed pacing mode such as VVIR and DDDR, (3) pacemaker dependency, (4) intrinsic rhythm, (5) behavior to a magnet, (6) prior recorded arrhythmic events, and (7) pacemaker lead parameters (including pacing threshold, ability to sense intrinsic activity, and lead impedance).

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac

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Implantable Electronic Devices. *Anesthesiology*. 2011;114:247-261.

B.6. How do you preoperatively prepare the patient for surgery and anesthesia?

Preparation for patient safety and proper maintenance of the device during a procedure includes the following:

- Determining whether EMI is likely to occur during the planned procedure as well as the location of the EMI
- Properly positioning the electrocautery grounding pad so the path of conduction across the device is minimized to the fullest extent
- Determining whether reprogramming the CIED pacing function to an asynchronous pacing mode or disabling any special algorithms, including rate-adaptive features, is needed
- Suspending antitachyarrhythmia functions if present
- Advising the surgeon performing the procedure to minimize prolonged bursts of monopolar cautery or consider use other less EMI-generating sources of energy including bipolar electrocautery or ultrasonic (harmonic) scalpel
- Ensuring the availability of temporary pacing and defibrillation equipment
- Evaluating the possible effects of anesthetic techniques and of the procedure on CIED function and patient-CIED interactions

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247-261.

B.7. Would you recommend reprogramming this device to asynchronously pace before surgery? What would you recommend regarding the ICD functions of the device?

Given the number of patients with CIEDs, recommending that all patients undergo reprogramming immediately before surgery is untenable and would significantly compromise perisurgical throughput. Moreover, reports have described individuals with ICDs or PPMs who later expired because the device was not reactivated before discharge after surgery. These issues raise the need for proper triaging of patients who truly need their devices reprogrammed before surgery. The patient in this example has a CRT-implantable cardioverter defibrillator. It is likely that the patient is functionally dependent on the CIED. Furthermore, the location of the EMI delivered in this case is close to the device system and therefore would likely result in inappropriate inhibition of pacing or sensing of EMI that the device would inappropriately mark as ventricular fibrillation. Given functional dependency on the device and the location of the EMI delivered, reprogramming the device would be recommended to deactivate the ICD and pace asynchronously before surgery for the following reasons:

- Electrocautery during surgery may inhibit pacing function.
- A magnet cannot convert the pacemaker in an ICD system to asynchronous mode pacing. A magnet placed over an ICD only disables tachycardia detection and therapy of the ICD. This is true of all devices used in the United States. One notable exception are ICDs manufactured by ELA/Sorin Medical (Cedex, France), which, in the presence of a magnet, will

not only disable tachycardia detection therapy but also convert pacing to a fixed rate at 96 beats per minute.

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C. Intraoperative Management

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C.1. How would you monitor this patient?

Intraoperative monitoring should include both continuous ECG and continuous peripheral pulse monitoring. Peripheral pulse can be monitored by palpation of the pulse, auscultation of heart sounds, pulse plethysmography or oximetry, a tracing of arterial wave form, or ultrasound peripheral pulse monitoring.

Arterial line and central venous pressure or pulmonary artery pressure monitoring may be used only if the patient has poor ventricular function. The artifact filter on the ECG monitor should be disabled to detect the pacing spikes. The ECG monitor should be set in diagnostic mode instead of monitoring mode.

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Crossley GH, Poole JE, Rozner MA, et al. The Heart Rhythm Society (HRS)/American Society of Anesthesiologists (ASA) Expert Consensus Statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: facilities and patient management. *Heart Rhythm*. 2011;8:1114-1154.

C.2. What drugs and equipment would you like to have on hand in the operating room?

A complete array of drugs and equipment must be immediately available for cardiopulmonary resuscitation. The minimal requirements include ECG monitor, a transcutaneous external pacing and direct current (DC) defibrillator, and the usual drugs for resuscitation.

Atlee JL, Bernstein AD. Cardiac rhythm management devices (part I): indication, device selection, and function. *Anesthesiology*. 2001;95:1265-1280.

C.3. How would you set up the transcutaneous external pacer and defibrillator?

We prefer applying defibrillating electrodes such as ZOLL® Pads to paddles because the electrodes can be placed before surgery at the desired positions and connected to a defibrillator/pacemaker for pacing and defibrillation. The electrodes should be placed as far (more than 6 in. or 15 cm) from a CIED as possible. The three recommended electrode placements are as follows:

- *Anteroposterior placement*. The right arm (RA) electrode placed under the left scapula and the left leg (LL) electrode at apex of the heart (as shown in Fig. 8.4).
- *Apex-anterior placement*. The RA electrode placed under the right clavicle and the LL electrode at the apex of the heart (Fig. 8.5A).
- *Apex-posterior placement*. The RA electrode placed over the right scapula and the LL electrode at the apex of the heart (Fig. 8.5B,C).

It is important to remember that the presence of a CIED should not deter standard resuscitation efforts.

Stone KR, McPherson CA. Assessment and management of patients with pacemakers and implantable cardioverter defibrillator. *Crit Care Med*. 2004;32(suppl 4):S155-S165.

C.4. Had this patient's ICD been implanted the day before surgery, would you consider avoiding certain inhalational gases for anesthesia?

It has been reported that nitrous oxide could cause pacemaker malfunction by increasing gas in the prepectoral pacemaker pocket. Despite air evacuation with antibiotic solution before

closure of the prepectoral pocket, a small amount of air remains entrapped in the pocket. In general, this small amount of

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air should have no clinical significance. Nitrous oxide is 35 times more soluble in blood than nitrogen. When nitrous oxide is used for anesthesia, the amount of nitrous oxide diffused from blood to the air pocket is much more than the amount of nitrogen diffused from the air pocket to blood. Therefore, this causes an expansion of the gas in the pocket that leads to loss of anodal contact and pacing system malfunction. It is advisable not to use nitrous oxide in a patient with a newly implanted pacemaker.

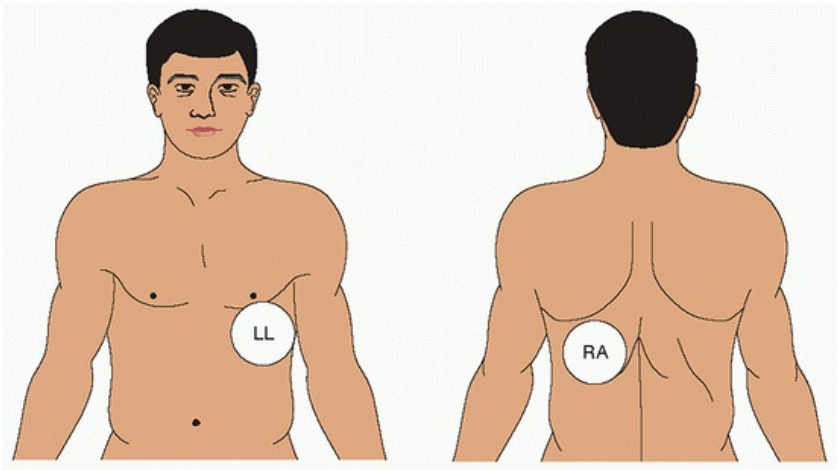


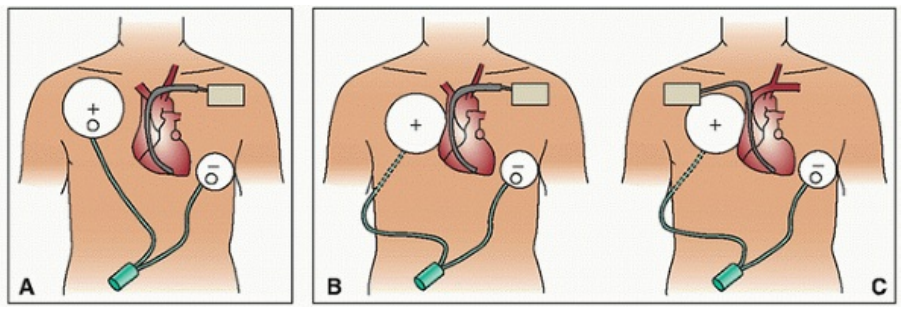
FIGURE 8.4 Anteroposterior placement of defibrillating electrodes. The right arm (RA) electrode is placed under the left scapula, and the left leg (LL) electrode is placed at the apex of the heart.

Lamas GA, Rebecca GS, Braunwald NS, et al. Pacemaker malfunction after nitrous oxide anesthesia. *Am J Cardiol*. 1985;56:995.

C.5. Electromagnetic interference (EMI) from electrocautery results in significant noise on your cardiac monitor. You recall that EMI also can inhibit pacing function from the PPM. In this pacemaker-dependent patient, how can you determine whether inappropriate inhibition of the PPM is occurring?

During electrocautery, the ECG is frequently useless because of interference. The best monitor available to determine if inhibition is taking place is a hand on the pulse. The precordial or esophageal stethoscope, pulse oximeter, or blood pressure is also acceptable.

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FIGURE 8.5 Placement of defibrillating electrodes. **A**. Apex-anterior placement with both pads placed anteriorly. **B** and **C**. Apex-posterior placement shown with the device in the left prepectoral region **(B)** and the right pectoral region **(C)**. (Adapted from Ellenbogen KA, Kay GN, Wilkoff BL, eds. *Clinical Cardiac Pacing and Defibrillation*. 2nd ed. Philadelphia, PA: Saunders; 2000:944.)

C.6. What are the potential responses of pacemakers and ICDs to electrocautery?

The responses of pacemakers to electrocautery or other EMI include the following:

- Inhibition of pacing
- Asynchronous pacing
- Reset to backup mode
- Myocardial burns, rare
- Ventricular fibrillation, rare

The responses of ICDs include the following:

- Inhibition of pacing
- Asynchronous pacing
- Inappropriate tachy therapy
- Inhibition of tachy therapy

Salukhe TV, Dob D, Sutton R. Pacemakers and defibrillators: anesthetic implications. *Br J Anaesth*. 2004;93:95-104. Stone KR, McPherson CA. Assessment and management of patients with pacemakers and implantable cardioverter defibrillator. *Crit Care Med*. 2004;32(suppl 4):S155-S165.

C.7. How would you prevent the effects of EMI on the pacemaker or ICD from the electrocautery?

The safest way to prevent intraoperative EMI response is appropriate reprogramming. The following precautions should be taken to minimize the effects of electrocautery:

- Place the cautery grounding plate as close to the operative site and as far from the CIED as possible to make sure that the current pathway does not pass through or near the CIED system. For some cases, the grounding plate might need to be placed on a site different from the thigh (e.g., the superior posterior aspect of the shoulder contralateral to the CIED generator position for a head and neck case).
- Do not use cautery within 15 cm of the pacemaker because it may interfere with the battery circuitry. If in contact with a break in the insulation of the electrode, it may cauterize the myocardium at the electrode tip, rendering it insensitive to pacing impulses.
- Limit cautery use to 1-second bursts every 10 seconds to prevent repetitive asystolic periods (if possible).
- If the pacemaker is inhibited by the cautery, place a high-powered magnet over the demand nonprogrammable pacemaker to convert it to fixed-rate mode.
- Using bipolar electrocautery forceps or ultrasonic (harmonic) scalpel reduces EMI.

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Salukhe TV, Dob D, Sutton R. Pacemakers and defibrillators: anesthetic implications. *Br J Anaesth*. 2004;93:95-

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104.

Stone KR, McPherson CA. Assessment and management of patients with pacemakers and implantable cardioverter defibrillator. *Crit Care Med*. 2004;32(suppl 4):S155-S165.

C.8. What are the effects of a magnet over pacemakers and ICDs?

The effect of placing a magnet over a pacemaker or ICD can vary quite considerably depending on the device manufacturer, model, and individual programmed modes. This information may be obtained by consulting the device manufacturer's representative. Most pacemakers will switch to a fixed-rate pacing mode when a magnet is placed. However, the response of a pacemaker to a magnet placement may also include the following:

- Asynchronous pacing without rate responsiveness
- No response
- Brief (10 to 100 beats) asynchronous pacing
- Continuous or transient loss of pacing

The response of an ICD to magnet placement is different from the response of a pacemaker. Magnets will disable tachyarrhythmia detection and therapy that, except in some Guidant-Boston Scientific devices, are reenabled when the magnet is removed. Magnets generally will, with a few exceptions, not affect the pacing mode or rate of ICDs. Therefore, the pacemaker in an ICD can be inappropriately inhibited by electrocautery even when a magnet is placed.

It is important to remember that some early generation Guidant-Boston Scientific ICDs are permanently disabled when a magnet is placed for more than 30 seconds. The ICD will not be reactivated when the magnet is removed. To reactivate the Guidant-Boston Scientific ICDs, the magnet has to be reapplied over the ICD for more than 30 seconds and then removed. If a magnet is to be used during surgery, the magnet effects should be tested in the operating room before surgery to ensure that the desired effects will occur during surgery.

Crossley GH, Poole JE, Rozner MA, et al. The Heart Rhythm Society (HRS)/American Society of Anesthesiologists (ASA) Expert Consensus Statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: facilities and patient management. *Heart Rhythm*. 2011;8:1114-1154.

Salukhe TV, Dob D, Sutton R. Pacemakers and defibrillators: anesthetic implications. *Br J Anaesth*. 2004;93:95-104.

C.9. In the middle of surgery, the patient developed ventricular tachycardia. What would you do?

For a patient with an ICD and magnet-disabled therapies:

- Advise the surgeon performing the procedure to terminate all sources of EMI.
- Remove the magnet to reenable antitachycardia therapies.
- Observe the patient and the monitors for appropriate CIED therapy. This can be delayed for as long as 10 to 12 seconds as the ICD is charging.
- If the activities mentioned in the preceding text do not restore ICD function, proceed with emergency external defibrillation.

For a patient with an ICD and programming-disabled therapies:

- Advise individual performing the procedure to terminate all sources of EMI while magnet is removed.
- Reenable therapies through programming if the programmer is immediately available and ready to be used.
- Observe the patient and the monitors for appropriate CIED therapy.
- If the activities mentioned in the preceding text do not restore ICD function, proceed with emergency external defibrillation.

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For external defibrillation (see also section C.3):

- Position defibrillation/cardioversion pads or paddles as far as possible from the CIED generator.
- If it is technically impossible to place the pads or paddles in locations that help to protect the CIED, defibrillate/cardiovert the patient in the quickest possible way and be prepared to provide pacing through other routes.
- Use a clinically appropriate energy output.

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C.10. What precautions should be taken when a patient with a CIED is undergoing extracorporeal shock wave lithotripsy (ESWL)?

ESWL is no longer contraindicated for patients with pacemakers. The only exception to this general statement is the abdominally placed pacemaker generators. Because these generators are in the blast path of the shock wave, such patients should not be treated with ESWL. Nevertheless, most transvenous pacemaker generators are placed in a pectoral location that

is at a safe distance from the blast path. Consider preoperative disabling of atrial pacing if the lithotripsy system triggers on the R wave. Avoid focusing the lithotripsy beam near the pulse generator.

Although most pacemakers are not affected by ESWL, sometimes it may cause pacemaker malfunctions that include the following:

- Switching to magnet mode
- Reaching upper rate limit
- Pacing irregularity
- Oversensing of asynchronous shocks
- Damage to rate-sensing piezoelectric crystal
- Intermittent inhibition of ventricular output in dual-chamber pacemaker
- EMI

There may be a rate increase in a rate-response (adaptive) pacemaker after ESWL shocks. Therefore, special precautions should be taken preoperatively. The type of pacemaker, indications for its placement, degree of patient dependence, and pacemaker programmability must be determined before lithotripsy. A dedicated pacemaker programmer should be available in the lithotripsy suite should pacemaker malfunction be caused by the shock waves. In addition, an alternative means of pacing, such as transcutaneous pacing, should also be available in case the pacemaker becomes permanently damaged. Low-energy shock waves (less than 16 kV) should be used initially; then the energy level is gradually increased while pacemaker function is monitored carefully. It is best to disable tachycardia detection of an ICD during ESWL and to thoroughly test the ICD following the procedure.

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C.11. Is electroconvulsive therapy (ECT) contraindicated in patients with pacemakers or ICDs?

It is advisable to consult with the ordering physician, the patient's cardiologist, a cardiac rhythm management device (CIED) service, or the device manufacturer. ECT appears safe for patients with pacemakers or ICDs because little current flows within the heart due to the high impedance of body tissues. Nevertheless, the seizure and succinylcholine

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fasciculations may generate sufficient myopotentials for pacemaker inhibition (unipolar devices) or ventricular tracking (adaptive-rate devices). Therefore, it is advisable to program the pacemaker to a nonsensing (asynchronous) mode for pacemaker-dependent patients either by reprogramming prior to the procedure or using a magnet during the case. It is also important to keep in mind that a magnet placed over an ICD will only disable tachytherapies and will not cause the ICD to pace asynchronously. An external pacemaker should also be available. Current guidelines also suggest that all ICDs should be programmed so that tachycardia detection is disabled before ECT and reprogrammed to its original programmed parameters prior to discharge.

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C.12. Is magnetic resonance imaging (MRI) contraindicated in patients with a CIED?

MRIs are generally contraindicated in patients with a CIED, but certain newer generation generators and leads have been engineered to be labeled as “MRI conditional.” Hence, patients with these newer devices systems can undergo MRI scanning if clinically indicated. If MRI must be performed, consult with the ordering physician, the patient's cardiologist or electrophysiologist, the diagnostic radiologist and the CIED manufacturer. MRIs can cause rapid pacing, inhibition, resetting of DDD pacemakers, and transient reed switch malfunction

with asynchronous pacing. Serious malfunction with no output or rapid pacing may occur because pulsed energy from MRIs can enter the lead by capacitive coupling and cause rapid ventricular pacing. All CIEDs being exposed to MRIs should be checked before and after MRI scanning.

Jung W, Jäckle S, Zvereva V. MRI and implantable cardiac electronic devices. *Curr Opin Cardiol*. 2015;30(1):65-73.

Roguin A, Schwitter J, Vahlhaus C, et al. Magnetic resonance imaging in individuals with cardiovascular implantable electronic devices. *Europace*. 2008;10:336-346.

C.13. What precautions should be taken during radiofrequency ablation for a patient with a CIED?

- Avoid contact of radiofrequency catheter with the CIED generator and leads.
- Radiofrequency current path as far away from the CIED generator and leads as possible.
- Discuss these concerns with the operator.

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C.14. During surgery, the patient developed frequent premature ventricular complexes and some of these resulted in rapid ventricular pacing (see Fig. 8.6)*. What is accounting for the pacemaker's behavior?*

Ventricular ectopy can often interfere with proper functionality of a dual-chamber pacemaker or defibrillator. In many instances, premature ventricular complexes can conduct retrograde up the AV node and result in atrial sensed events that are detected by the atrial lead. Depending on when this occurs, a dual-chamber pacemaker programmed to DDD may track this and trigger ventricular pacing, thus resulting in what is often termed *pacemaker-mediated tachycardia* (Fig. 8.6).

Current devices are equipped with algorithms that can limit the duration of these episodes. During surgery, it is important to be aware of this phenomenon and not mistake these runs of pacing induced wide complex tachycardia as ventricular tachycardia.

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Ellenbogen KA, Kaszala K, eds. *Cardiac Pacing and ICDs*. 6th ed. Hoboken, NJ: Wiley Blackwell; 2014:211-271.

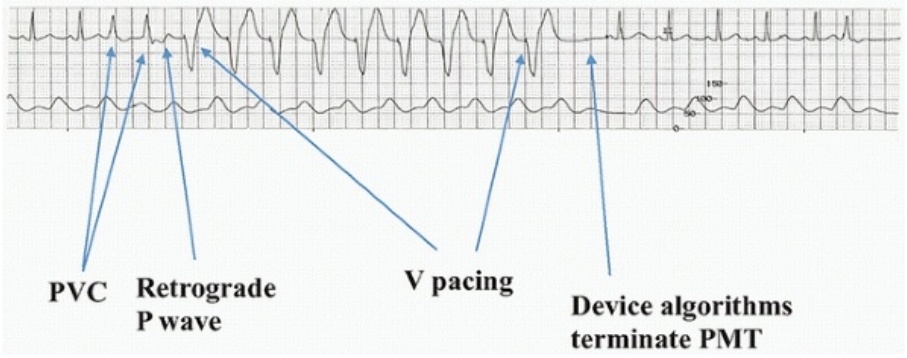


FIGURE 8.6 Rhythm strip of pacemaker-mediated tachycardia (PMT). Premature ventricular complexes (PVCs) are seen initially followed by a run of wide complex tachycardia with each QRS complex preceded by a pacing spike suggesting ventricular (V) pacing. This phenomenon occurs because the PVCs conduct through the atrioventricular node in a retrograde fashion and result in an atrial sensed event that the DDD device detects. Because of the DDD programming, ventricular pacing is triggered and the paced ventricular beat perpetuates the cycle by conducting through the atrioventricular node again in a retrograde fashion and resulting in another atrial sensed event. The tachycardia eventually terminates because the device has an anti-PMT algorithm.

D. Postoperative Management

D.1. How would you monitor this patient in the postanesthesia care unit?

Cardiac rate and rhythm should be continuously monitored throughout the immediate postoperative period. Backup pacing capability and cardioversion-defibrillation equipment should be immediately available at all times.

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Crossley GH, Poole JE, Rozner MA, et al. The Heart Rhythm Society (HRS)/American Society of Anesthesiologists (ASA) Expert Consensus Statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: facilities and patient management. *Heart Rhythm*. 2011;8:1114-1154.

D.2. How would you confirm that the CIED is functioning properly after surgery?

Postoperative interrogation and restoration of CIED function are basic elements of postoperative management. But given the robustness of modern devices, not all CIEDs require postoperative interrogation before discharge, especially in cases in which the EMI is remote from the device system. CIEDs that should be interrogated postoperatively before discharge include the following:

- CIEDs that were reprogrammed or deactivated before surgery so that baseline settings can be restored
- Patients who underwent hemodynamically embarrassing surgeries such as cardiac surgery or significant vascular surgery
- Patients who experienced significant intraoperative events, including cardiac arrest, requiring temporary pacing or cardiopulmonary resuscitation, and/or tachyarrhythmias requiring external electrical cardioversion during surgery

All other individuals should have their devices evaluated as an outpatient within the next 3 months.

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Chapter 9
Thoracoabdominal Aortic Aneurysms

Sharon McCartney
Stephen Gregory
J. Mauricio Del Rio
Mani A. Daneshmand
Madhav Swaminathan

A 68-year-old man presents for surgical repair of a thoracoabdominal aortic aneurysm (TAAA). He has a significant past medical history that includes a type A aortic dissection 12 years ago, for which he underwent a Bentall repair, poorly controlled hypertension, chronic obstructive pulmonary disease (COPD), tobacco use (45 pack-years), and stage III chronic kidney disease (CKD). His type A dissection event was complicated by end-organ ischemia, including ischemic colitis and renal failure. He has been undergoing routine surveillance of his aorta, and computed tomography (CT) reveals his aortic aneurysm has recently enlarged to 5.5 cm starting at the innominate artery and extending into the abdominal aorta, proximal to the renal arteries. Chest radiograph demonstrates thoracic aortic aneurysmal dilation, without compression of surrounding structures. Transthoracic echocardiogram demonstrates normal left and right ventricular function, trivial aortic insufficiency (AI), and trivial mitral insufficiency. Laboratory studies indicate a hemoglobin of 14.5 g per dL, hematocrit 44%, blood urea nitrogen (BUN) 22 mg per dL, and creatinine 1.8 mg per dL.

A. Pathophysiology and Differential Diagnosis

1. What is a thoracic aortic aneurysm (TAA) and how does it typically present?
2. How are TAAs classified?
3. What is the pathogenesis of aortic aneurysms and what genetic conditions predispose to their formation?
4. What are the risk factors for TAA rupture?
5. What is the natural history and medical management of thoracic aneurysms?
6. What is a thoracic aortic dissection, and how does it typically present?
7. How are thoracic aortic dissections classified?

B. Preoperative Evaluation and Preparation

1. What are the indications and timing of surgical intervention for TAAs?
2. Which patients are candidates for endovascular aortic repair, and what are the advantages to this approach?
3. What are the preoperative considerations for the anesthesiologist before TAA repair?
4. What is the preoperative management of a patient presenting with acute aortic dissection (AAD)?
5. What is the spinal cord blood supply?

C. Intraoperative Management

1. What are the surgical approaches to thoracic aneurysm repair?
2. How is the open repair performed?

3. How are the endovascular repair of TAAAs performed?
4. What are the specific considerations for anesthetic management of the patient presenting for open TAAA repair?
5. What are the specific considerations for anesthetic management of the patient presenting for endovascular TAAA

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repair?

6. What hemodynamic monitors should be used for the patient undergoing thoracic aneurysm repair?
7. What strategies are used for spinal cord protection during a TAAA repair?
8. What strategies are used for mesenteric and renal preservation?
9. What is the pathophysiology of aortic clamping and unclamping?
10. Why does coagulopathy ensue and how is it prevented/treated?

D. Postoperative Anesthetic Management

1. What are the postoperative complications after open TAAA repair?
2. What are the postoperative complications after endovascular TAAA?

A. Pathophysiology and Differential Diagnosis

A.1. What is a thoracic aortic aneurysm (TAA) and how does it typically present?

Thoracic and TAAAs are abnormal dilations of the thoracic and/or abdominal aorta to greater than 150% of its expected diameter. They can occur at any point along the aorta, including the root, arch, and descending portions with occasional extension into branching vessels. The dimensions that define normal aortic size are determined by patient age, gender, and body surface area.

One of the greatest challenges in the care of patients with thoracic aortic disease is identifying them prior to the onset of a catastrophic aortic event. Despite their propensity for life-threatening complications, TAAs are often clinically silent and are often diagnosed during imaging for an unrelated disorder. When symptoms do occur, they are often nonspecific, and diagnosis requires a high index of clinical suspicion. Symptoms of TAAs frequently result from compression of adjacent structures. Patients may exhibit hoarseness from recurrent laryngeal nerve compression, stridor from bronchial or tracheal compression, dyspnea from lung compression, dysphagia from esophageal compression, and facial edema from superior vena cava (SVC) compression. Pain in the neck, jaw, back, shoulders, or abdomen may also be present. Additionally, new-onset heart failure symptoms may occur as aortic enlargement results in progressive AI (Fig. 9.1).

Once identified, dedicated imaging with either CT (Fig. 9.2) or magnetic resonance imaging (MRI) should be undertaken to delineate the extent of the aneurysm, its maximum dimension, branch vessel involvement, and the presence or absence of a coexisting intramural hematoma (Fig. 9.3) or penetrating aortic ulcer. Transthoracic echocardiography (TTE) is also performed to assess for valvular disease, evaluate cardiac function, and more carefully assess the anatomy of the aortic root (Fig. 9.4).

Booher AM, Eagle KA. Diagnosis and management issues in thoracic aortic aneurysm. *Am Heart J*. 2011;162:38.e1-46.e1.

Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *J Am Coll Cardiol*. 2010;55(14):e27-e129.

A.2. How are TAAs classified?

Ascending TAAs do not follow a specific classification system but are described by the extent of the aorta that is involved, including the aortic valve (AV), aortic root, and aortic arch.

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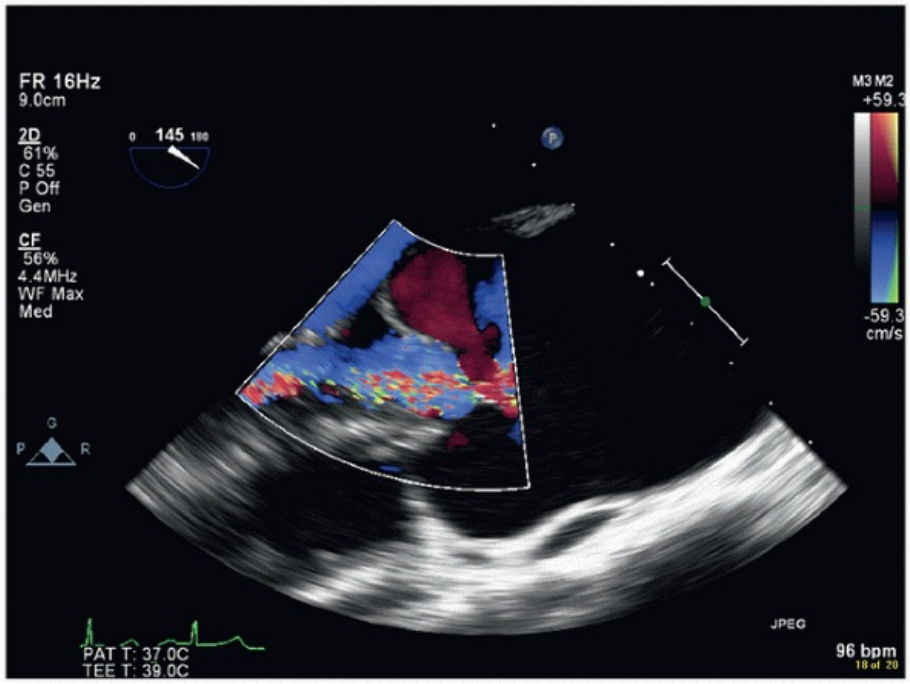


FIGURE 9.1 Midesophageal aortic valve long-axis view on TEE demonstrating moderate central aortic insufficiency secondary to ascending aortic dilatation in a young woman with Turner syndrome.

TAAAs are described using the modified Crawford classification, which subdivides TAAAs into five types according to the extent of the surgical repair required (Fig. 9.5).

- *Type I* begins distal to the left carotid artery and extends down below the diaphragm to above the renal arteries.
- *Type II* begins distal to the left carotid above the sixth intercostal space. They extend through the diaphragm and end below the renal arteries.
- *Type III* begins below the sixth intercostal space but above the diaphragm. They extend below the renal arteries.
- *Type IV* begins below the diaphragm but above the renal arteries, with extension to below the renal arteries.
- *Type V* begins above the diaphragm and end above the renal arteries.

Crawford ES, Crawford JL, Safi HJ, et al. Thoracoabdominal aortic aneurysms: preoperative and intraoperative factors determining immediate and long-term results of operations in 605 patients. *J Vasc Surg*. 1986;3:389-404.

Frederick JR, Woo YJ. Thoracoabdominal aortic aneurysm. *Ann Cardiothorac Surg*. 2012;1(3):277-285.

Hoel AW. Aneurysmal disease: thoracic aorta. *Surg Clin North Am*. 2013;93:893-910.

A.3. What is the pathogenesis of aortic aneurysms and what genetic conditions predispose to their formation?

TAAs primarily arise from focal degeneration of the elastic and muscular tissue of the aortic wall. The resulting tissue weakness predisposes the wall to dilate under the stress of high pressures within the aorta. The dilation of the aorta is associated with decreased vessel wall compliance, increased wall stress, and a propensity for subsequent rupture of the aneurysm.

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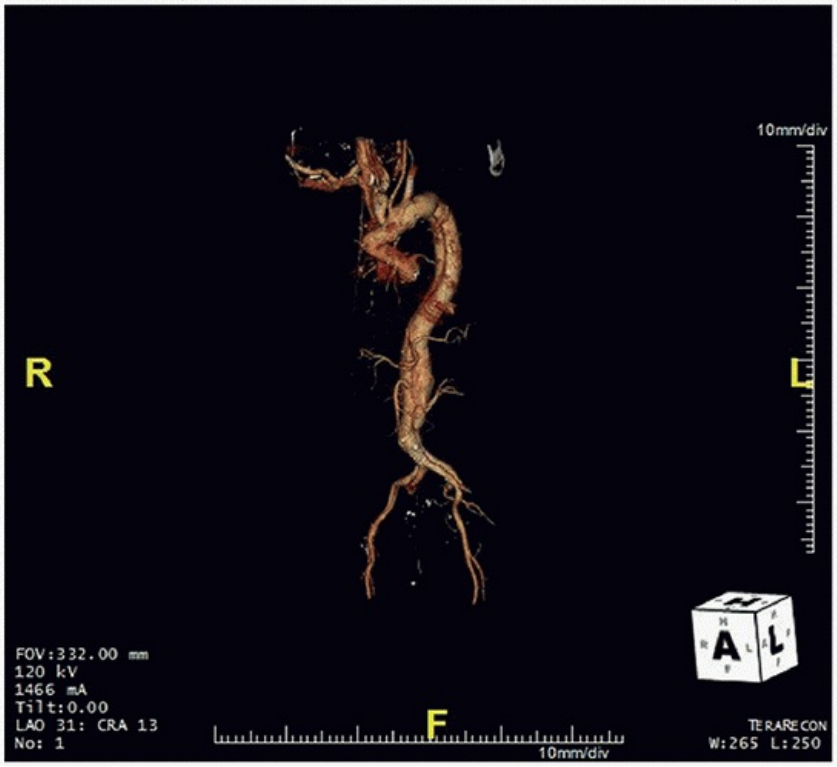


FIGURE 9.2 Three-dimensional (3D) CT reconstruction demonstrating a thoracoabdominal aneurysm that begins in the descending thoracic aorta and extends to the infrarenal aorta, above the bifurcation into the iliac arteries. Also seen in a chronic type B aortic dissection.

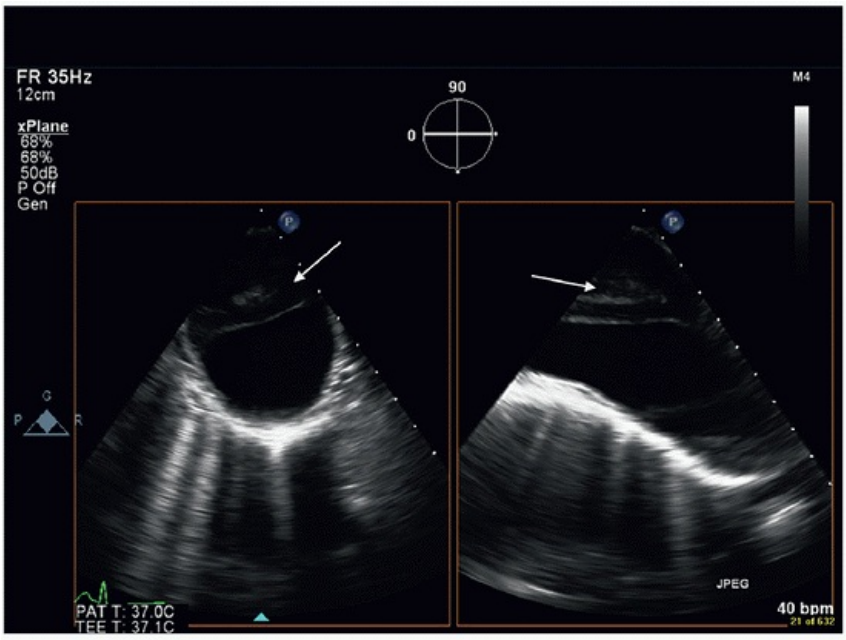


FIGURE 9.3 Descending aorta in short axis **(left)** and long axis **(right)** on TEE demonstrating an intramural hematoma *(arrow)* in a patient with a thoracoabdominal aneurysm.

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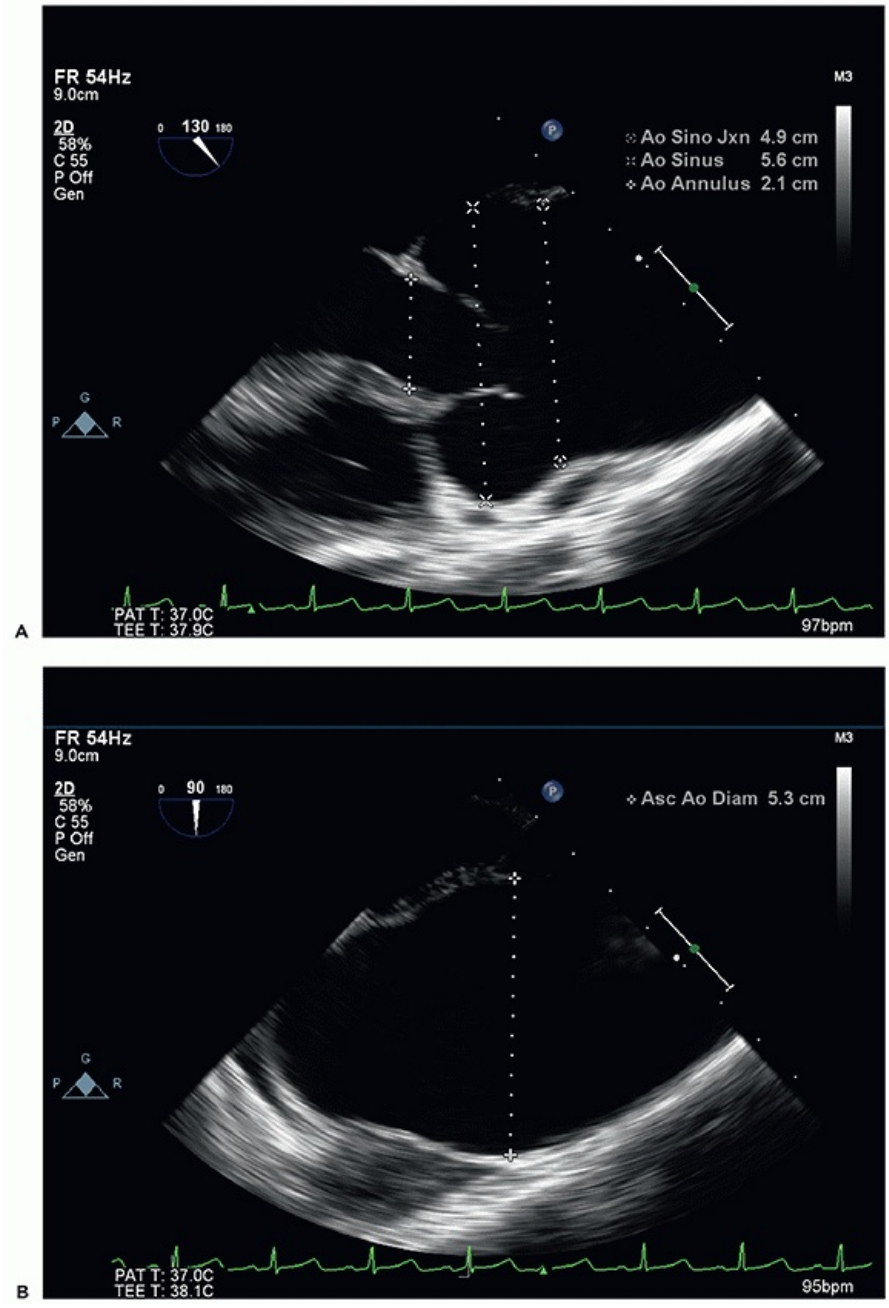
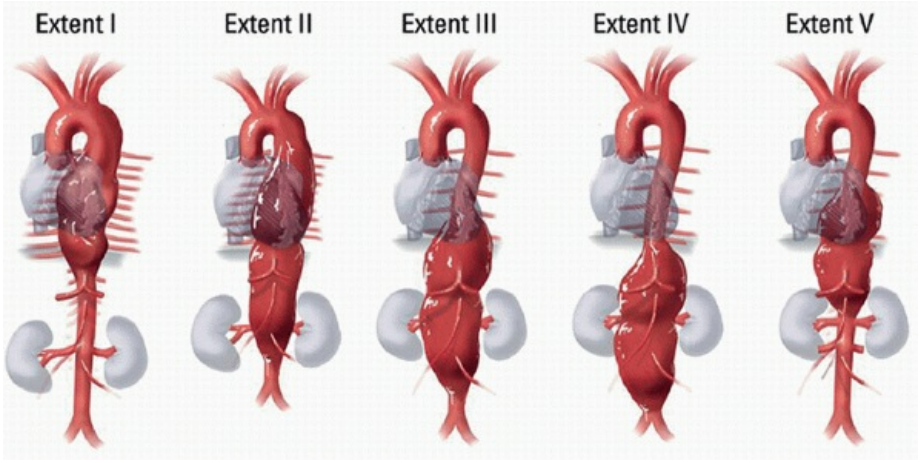


FIGURE 9.4 A. Midesophageal aortic valve long-axis view on TEE demonstrating aortic valve annulus, sinus, and sinotubular junction dimensions at mid-systole. **B.** Ascending aorta in short axis demonstrating aneurysmal enlargement with a diameter of 5.3 cm in a young woman with Turner syndrome.



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FIGURE 9.5 The modified Crawford classification of thoracoabdominal aortic aneurysms. (Used with permission from Frederick JR, Woo YJ. Thoracoabdominal aortic aneurysm. *Ann Cardiothorac Surg*. 2012;1[3]:277-285.)

Although the majority of TAAs follow a degenerative pattern, there are a number of congenital disease processes that are associated with aneurysm formation.

Marfan syndrome (MFS) is an autosomal dominant disorder caused by a mutation in the fibrillin-1 gene. Patients with MFS have characteristic overgrowth of the long bones of the arms and legs, increased finger length (arachnodactyly), and joint laxity. They can also demonstrate ocular abnormalities, most commonly lens dislocation. In addition to the musculoskeletal and ocular manifestations of MFS, patients are also at increased risk of aortic root dilation, ascending and descending aortic aneurysms, and aortic dissection. Valvular disease can also be present, with mitral regurgitation and associated pulmonary hypertension being the most common cause of MFS-related infant mortality. On a molecular level, mutations in the fibrillin-1 gene result in disordered formation of the microfibril matrix, leading to disruption of the elasticity of the aorta. More recent evidence suggests that excessive transforming growth factor *β* (TGF-*β*) signaling also plays a role in the clinical phenotype of MFS.

Vascular Ehlers-Danlos syndrome (vEDS) is the result of mutation in the COL3A1 gene coding for type III procollagen. Mutations in type III procollagen can result in a number of complications, including spontaneous intestinal or uterine rupture, fragile skin, and vascular dissection. Children may also present with inguinal hernias, pneumothoraces, or recurrent joint dislocations. Although diagnosis is often made clinically, many patients are only diagnosed after a major arterial or gastrointestinal event.

Loeys-Dietz syndrome (LDS) is a heterogeneous disease stemming from mutations in either the TGFBR1 or TGFBR2 gene, resulting in a relative increase in TGF-*β* signaling. LDS presents with characteristic craniofacial, skeletal, and cardiovascular anomalies with a broad range of phenotype. Because patients with milder disease exhibit limited skeletal features and no typical ophthalmologic manifestations of the disease, the diagnosis is often made within a family after a significant aortic event. These patients are also at risk of complicated cerebral aneurysms, and imaging of all major arterial structures is recommended after diagnosis.

Turner syndrome is a genetic disorder characterized by the lack of an X-chromosome in a female patient (45, X). Women with Turner syndrome are often short in stature, have dysfunctional ovaries, and are at increased risk of cardiovascular disease. Bicuspid AV disease is present in between 10% and 25% of women with Turner syndrome, and approximately 8% have coarctation of the aorta. The risk of AAD is also increased in women with Turner syndrome and tends to occur at a younger age and smaller aortic diameter than the general population.

Less common genetic etiologies of thoracic and thoracoabdominal aortic disease include mutations in the MYH11, ACTA2, MYLK, SLC2A10, or SMAD3 gene. Despite progress in discerning the genetic mechanisms of familial TAAs, up to 80% are without a clear molecular etiology.

There are a number of rheumatologic diseases that may affect the thoracic aorta. Takayasu arteritis, giant cell arteritis, Behçet disease, and ankylosing spondylitis have all been demonstrated to contribute to the development of aneurysmal dilation of the aorta with varying degrees of frequency.

Patients may also develop aneurysms with an infectious etiology, although this is rare. There are several mechanisms by which this can occur, including direct spread from adjacent structures, septic embolic events from bacterial endocarditis, and hematogenous seeding of the aorta from bacteremia. Although most infections are caused by bacteria, immunosuppressed patients are also susceptible to fungal and mycobacterial infection. Interestingly, HIV infection also appears to be associated with an increased risk of TAA formation.

Finally, patients with a *bicuspid AV* have a markedly increased risk of TAA formation. Aortic dilation in bicuspid AV disease most commonly involves enlargement of the ascending aorta in addition to dilation of the aortic root (Fig. 9.6). Risk factors for aneurysm development include older age, male sex, systolic hypertension, valve stenosis or regurgitation, and the specific morphology of the valve itself. Although a specific unifying gene remains elusive, bicuspid aortic disease demonstrates familial inheritance.

Boodhwani M, Andelfinger G, Leipsic J, et al. Canadian Cardiovascular Society position statement on the management of thoracic aortic disease. *Can J Cardiol*. 2014;30:577-589.

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Hoel AW. Aneurysmal disease: thoracic aorta. *Surg Clin North Am*. 2013;93:893-910.

Jondeau G, Boileau C. Genetics of thoracic aortic aneurysms. *Curr Atheroscler Rep* . 2012;14:219-226.

Jones JA, Ikonomidis JS. The pathogenesis of aortopathy in Marfan syndrome and related diseases. *Curr Cardiol Rep*. 2010;12:99-107.

Pomianowski P, Elefteriades JA. The genetics and genomics of thoracic aortic disease. *Ann Cardiothorac Surg*. 2013;2(3):271-279.

Ramanath VS, Oh JK, Sundt TM III, et al. Acute aortic syndromes and thoracic aortic aneurysm. *Mayo Clin Proc*. 2009;84(5):465-481.

Verma S, Siu SC. Aortic dilatation in patients with bicuspid aortic valve. *N Engl J Med*. 2014;370:1920-1929.

A.4. What are the risk factors for TAA rupture?

The size of a TAA is the most important predictor of rupture (Table 9.1). For every 1 cm increase in aneurysm diameter, the risk of rupture roughly doubles. The “hinge point” at which the risk of rupture increases dramatically is approximately 6 cm in diameter for ascending aneurysms and 7 cm for descending aneurysms, although 31% and 43%, respectively, of patients will have experienced rupture or dissection by the time they reach this point. Patients with COPD, advanced age, and symptomatic aneurysms appear to have an increased risk of rupture. Although women tend to develop TAAs later in life, they appear to also have an increased risk of aneurysm rupture relative to their male counterparts.

Chau KH, Elefteriades JA. Natural history of thoracic aortic aneurysms: size matters, plus moving beyond size. *Prog Cardiovasc Dis*. 2013;56:74-80.

Davies RR, Goldstein LJ, Coady MA, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. *Ann Thorac Surg*. 2002;73:17-27.

Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. *Ann Thorac Surg*. 2002;74:S1877-S1880.

Frederick JR, Woo YJ. Thoracoabdominal aortic aneurysm. *Ann Cardiothorac Surg*. 2012;1(3):277-285.

A.5. What is the natural history and medical management of thoracic aneurysms?

The location and etiology of thoracic and thoracoabdominal aneurysms determines their rate of growth and subsequent propensity for rupture. Ascending TAAs typically grow at a rate of 0.1 cm per year, whereas descending aneurysms grow slightly faster at 0.3 cm per year. The rate of growth is greater in patients with larger aneurysms, dissected aortas, and certain familial causes of TAA. The aortic size is a strong predictor of the risk of complications, with a marked increase in risk profile as the aneurysm increases to greater than 6 cm.

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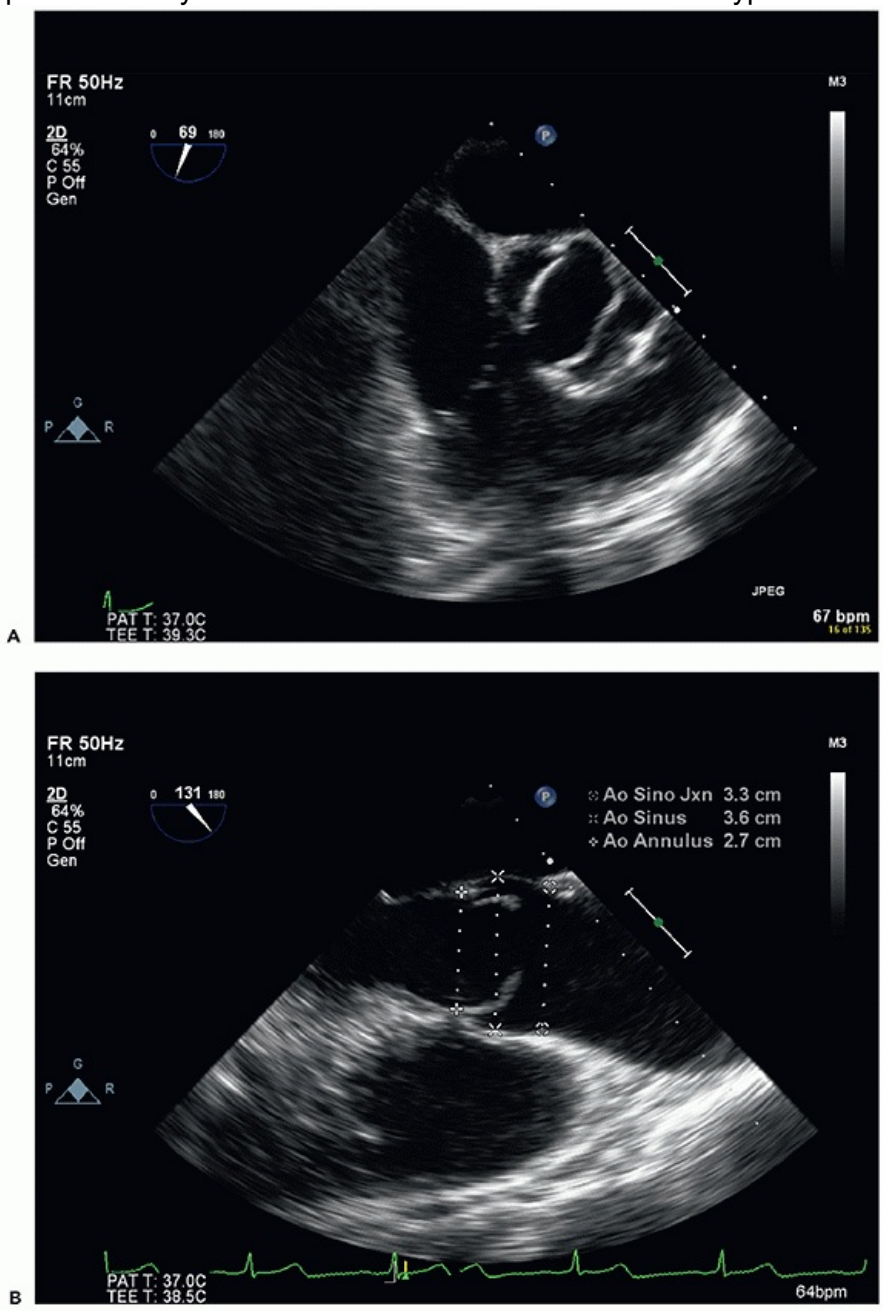


FIGURE 9.6 A. Midesophageal aortic valve short-axis view on TEE showing a bicuspid valve, with fusion of the left and right coronary cusps. **B.** Midesophageal aortic valve long-axis view on TEE demonstrating the characteristic doming of a stenotic bicuspid aortic valve and blunting of the sinotubular junction due to aortic root dilatation.

TABLE 9.1 Annual Rate of Rupture for Thoracic Aortic Aneurysms

SIZE OF ANEURYSM	ANNUAL RATE OF RUPTURE
<5 cm	2%
5-5.9 cm	3%
>6 cm	7%

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Medical therapy to slow aneurysm growth or to reduce the risk of dissection or rupture has only been modestly successful thus far. Initial therapy consists of lifestyle modifications including smoking cessation and minimization of heavy lifting to avoid significant spikes in systolic blood pressure, which may precipitate rupture or aortic dissection.

Despite a relative paucity of clinical evidence, *β*-blocker therapy is often prescribed with the goal of reducing the rate of aortic dilatation by decreasing left ventricular contractility and subsequently decreasing shear stress. Although this has been demonstrated to be beneficial in patients with MFS, evidence for its use in the broader population of patients with TAAs is still lacking. Statins have also recently been shown to be beneficial in the medical management of TAAs, with patients receiving statin therapy showing a slower rate of aneurysmal growth, a smaller percentage requiring surgery, and a decrease in the overall number of adverse events.

Angiotensin receptor blockade has shown promise in the murine model of MFS, with a small human study showing a decrease in the rate of aneurysmal growth. This data formed the basis for the ongoing MARFANSARTAN trial (Study of the Efficacy of Losartan on Aortic Dilatation in Patients with Marfan Syndrome). Current recommendations suggest aggressive blood pressure reduction with *β*-blockers and angiotensin-converting enzyme (ACE)-inhibitors or angiotensin receptor blockers to the lowest level that patients can tolerate without adverse effects.

Brooke BS, Habashi JP, Judge DP, et al. Angiotensin II blockade and aortic-root dilation in Marfan's syndrome. *N Engl J Med*. 2008;358:2787-2795.

Chau KH, Elefteriades JA. Natural history of thoracic aortic aneurysms: size matters, plus moving beyond size. *Prog Cardiovasc Dis*. 2013;56:74-80.

Danyi P, Elefteriades JA, Jovin IS. Medical therapy of thoracic aortic aneurysms. *Trends Cardiovasc Med*. 2012;22(7):180-184.

Devereux RB, Roman MJ. Aortic disease in Marfan's syndrome. *N Engl J Med*. 1999;340:1358-1359.

Stein LH, Berger J, Tranquilli M, et al. Effect of statin drugs on thoracic aortic aneurysms. *Am J Cardiol*. 2013;112(8):1240-1245.

A.6. What is a thoracic aortic dissection, and how does it typically present?

An AAD typically develops when a tear in the intimal layer of the aorta permits blood to enter into the medial layer, creating a false lumen that may rapidly expand both proximally and distally (Fig. 9.7). This can cause ischemia of the brain and viscera because the vasculature supplying these organs is occluded. Proximal dissection may cause AI, cardiac ischemia from coronary artery occlusion, or accumulation of blood in the pericardium resulting in tamponade (Fig. 9.8). Finally, the false lumen can rupture, resulting in rapid exsanguination.

Hypertension is the most common comorbid disease in patients experiencing aortic dissection, although hyperlipidemia, tobacco use, and cocaine use are other risk factors. Pregnancy can also increase the risk of AAD, with most women typically presenting during their third trimester or in the early postpartum period. There are several genetic conditions that increase the risk of AAD, including MFS, Ehlers-Danlos syndrome, familial aortic dissection, LDS, and annuloaortic ectasia. AAD can also occur iatrogenically during cardiac surgery, cardiac catheterization, and insertion of an intra-aortic balloon pump.

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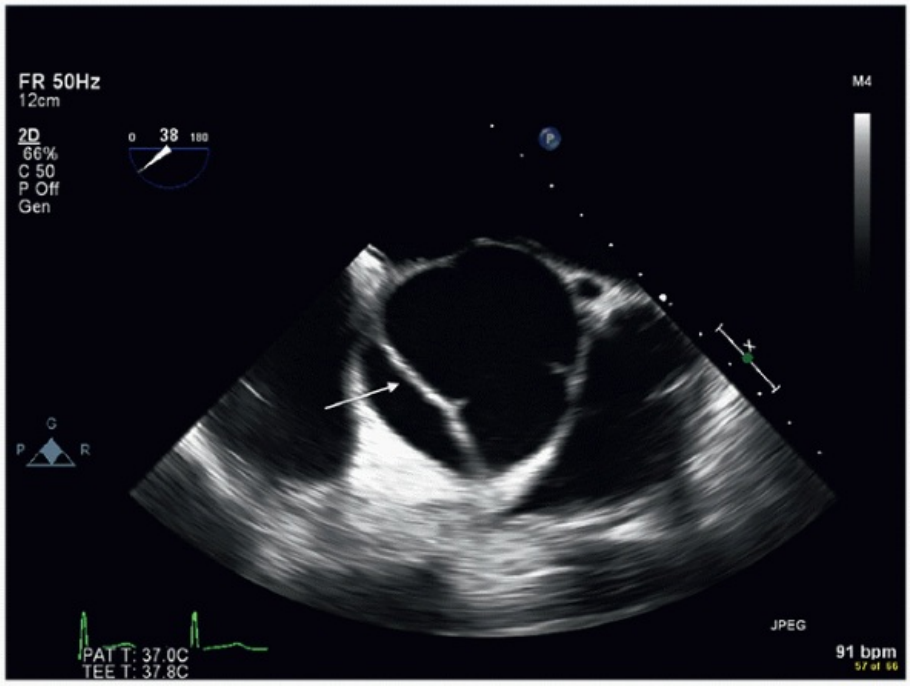


FIGURE 9.7 Midesophageal aortic valve short-axis view on TEE demonstrating an acute aortic dissection *(arrow)* that extends proximally to the aortic valve in a young patient with Marfan syndrome.

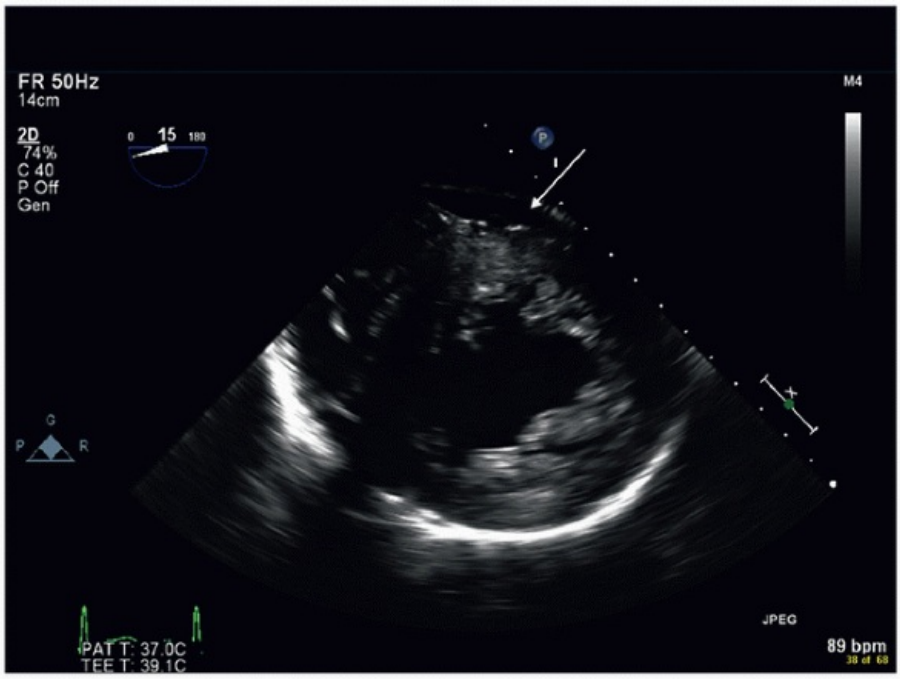


FIGURE 9.8 Transgastric midpapillary view on TEE demonstrating accumulation of blood in the posterior pericardial space *(arrow)* after acute aortic dissection.

Patients typically present with the acute onset of severe chest and back pain, although this is not a universal finding. Less commonly, patients can present with abdominal pain, syncope, or symptoms of limb or visceral malperfusion. In roughly 6% of cases, the aortic dissection is painless and presents as new-onset heart failure, stroke, or syncope. These patients tend to be diabetic, have a history of aortic aneurysm, or a history of prior cardiac surgery. Hypertension is common on initial presentation, and the diastolic murmur of AI is present in 44% of patients with a type A dissection. Hypotension is an ominous sign and portends a poor clinical prognosis.

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It is important to differentiate AAD from acute coronary syndrome (ACS) because they may have similar presentations. Symptomatically, patients with AAD typically present with acute, severe chest pain, whereas patients with ACS typically have pain that is more gradual in onset. This differentiation is important because the treatment of ACS (antiplatelet agents, anticoagulation, and occasionally thrombolytics) is potentially catastrophic in patients with aortic dissection. AAD should be in the differential diagnosis for any patient presenting with syncope; new-onset chest, abdominal, or back pain; acute heart failure; or clinical evidence of malperfusion. Diagnosis is most commonly made via spiral CT scan (Fig. 9.9) or transesophageal echocardiogram (TEE), although aortography and MRI may also be used.

Ramanath VS, Oh JK, Sundt TM III, et al. Acute aortic syndromes and thoracic aortic aneurysm. *Mayo Clin Proc*. 2009;84(5):465-481.

Tsai TT, Trimarchi S, Nienaber CA. Acute aortic dissection: perspectives from the International Registry of Acute Aortic Dissection (IRAD). *Eur J Vasc Endovasc Surg*. 2009;37:149-159.



FIGURE 9.9 CT scan demonstrating an acute aortic dissection that extends from the aortic root to the iliac arteries.

A.7. How are thoracic aortic dissections classified?

There are several systems used to classify aortic dissections that focus on anatomic or clinical factors noted on presentation (Fig. 9.10).

DeBakey Classification

The DeBakey classification system categorizes aortic dissections based on their site of origin and degree of distal extension.

Type I dissection originates in the ascending aorta and propagates to at least the level of the aortic arch and often beyond, sometimes extending as distal as the iliac arteries.

Type II dissection begins in, and is limited to, the ascending aorta. Although these occur on occasion in patients with MFS, they are the rarest form of aortic dissection. Type I and type II dissections are almost always treated surgically.

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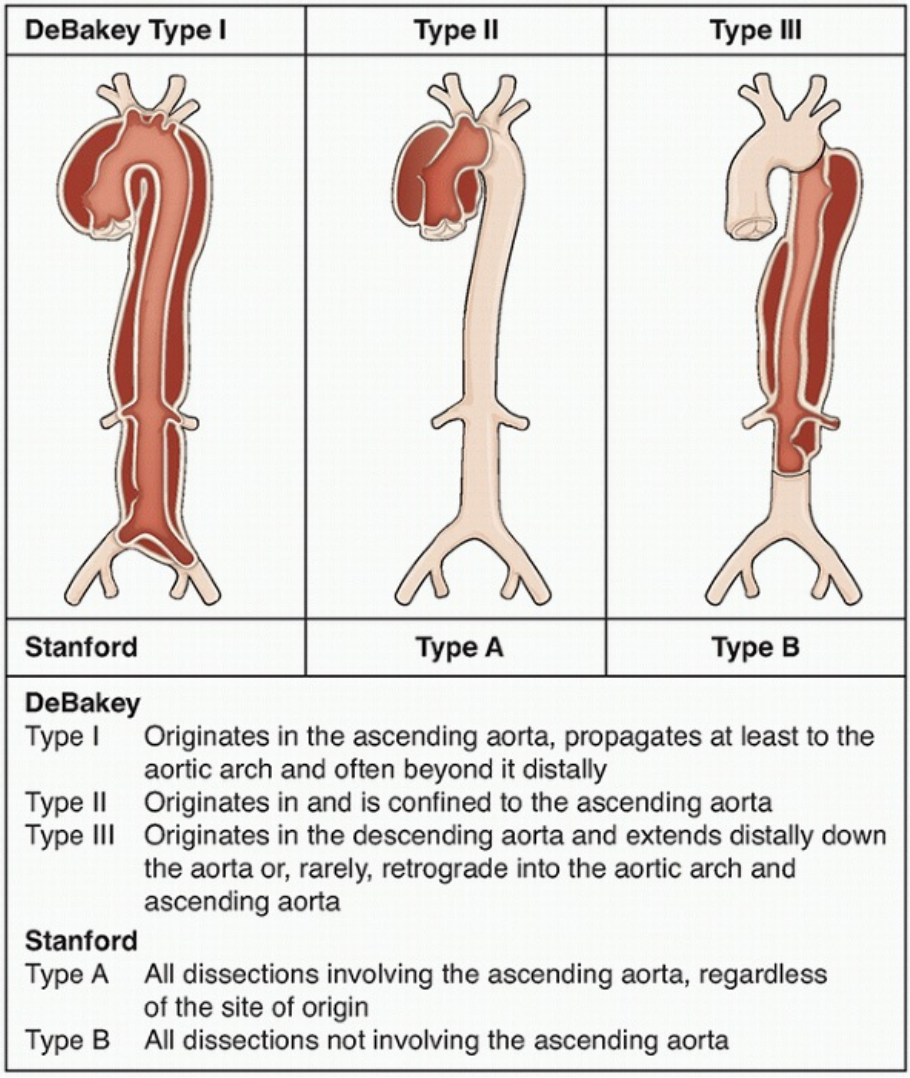


FIGURE 9.10 The Stanford and DeBakey classifications of aortic dissections. (Used with permission from Nienaber CA, Eagle KA. Aortic dissection: new frontiers in diagnosis and management: part I: from etiology to diagnostic strategies. *Circulation*. 2003;108:628-635.)

Type IIIa dissection begins beyond the origin of the left subclavian artery and is limited to the descending thoracic aorta.

Type IIIb dissection begins beyond the left subclavian origin and extend more distally beyond the diaphragm. Type III dissections are often managed medically.

Stanford Classification

The Stanford classification system is similar to the DeBakey system in that it describes aortic dissections based on their anatomic site of origin.

Stanford type A aortic dissections originate in the ascending aorta and include DeBakey type I and type II dissections.

Stanford type B aortic dissections originate in the descending aorta and include DeBakey type IIIa and IIIb dissections. These may occasionally also propagate proximally into the ascending aorta or aortic arch.

A notable limitation to both the Stanford and DeBakey classification systems is their inability to classify dissections originating in the aortic arch.

Penn Classification

More recently, patients with acute Stanford type A aortic dissection have been subcategorized according to ischemic symptoms noted on presentation in what has been termed the Penn classification. This has been successfully validated as a predictor of perioperative mortality.

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Penn Class Aa patients have no ischemic symptoms on presentation. This is the most common clinical finding in type A aortic dissection, encompassing approximately 60% of all patients. It is also associated with the best clinical outcome with a 30-day mortality of 3% and a 5-year cumulative survival approaching 85% in one cohort.

Penn Class Ab patients present with branch vessel malocclusion producing clinically significant organ ischemia. This includes patients presenting with stroke, paraplegia, renal dysfunction, mesenteric malperfusion, and occlusion of vascular supply to the extremities.

Penn Class Ac patients present with circulatory collapse with or without cardiac involvement. Class Ab and Ac patients have similar perioperative and long-term survival profiles.

Penn Class Abc patients present with symptoms of both local and generalized ischemia. These patients have the worst prognosis with a 30-day perioperative mortality of 40%. Most deaths are secondary to multisystem organ failure, hemorrhage, cardiac failure, or central nervous system (CNS) dysfunction.

Augoustides JG, Geirsson A, Szeto WY, et al. Observational study of mortality risk stratification by ischemic presentation in patients with acute type A aortic dissection: the Penn classification. *Nat Clin Pract Cardiovasc Med*. 2009;6:140-146.

Daily PO, Trueblood HW, Stinson EB, et al. Management of acute aortic dissections. *Ann Thorac Surg*. 1970;10:237-247.

DeBakey ME, Cooley DA, Crawford ES, et al. Aneurysms of the thoracic aorta; analysis of 179 patients by resection. *J Thorac Surg*. 1958;36:393-420.

Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *J Am Coll Cardiol*. 2010;55(14):e27-e129.

Kimura N, Ohnuma T, Itoh S, et al. Utility of the Penn classification in predicting outcomes of surgery for acute type A aortic dissection. *Am J Cardiol*. 2014;113(4):724-730.

Nienaber CA, Eagle KA. Aortic dissection: new frontiers in diagnosis and management: part I: from etiology to diagnostic strategies. *Circulation*. 2003;108:628-635.

B. Preoperative Evaluation and Preparation

B.1. What are the indications and timing of surgical intervention for TAAs?

Patients diagnosed with aneurysms of the thoracic aorta require frequent surveillance to assess for aneurysmal expansion. The goal is to facilitate surgical intervention prior to the onset of aortic dissection or aneurysm rupture. Important considerations include the

appropriate interval for surveillance imaging and the diameter at which surgical intervention should be recommended.

TABLE 9.2 Guidelines for Elective Intervention in Patients with Ascending or Descending Thoracic Aortic Aneurysms

Normal aorta	5.5 cm for ascending aneurysms

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	6.5 cm for descending aneurysms
Normal aorta + valvular indication	4.5 cm
Marfan syndrome	5.0 cm for ascending aneurysms 6.0 cm for descending aneurysms
Marfan syndrome + pregnancy	4.0 cm
Loeys-Dietz syndrome	4.2 cm as measured by TEE 4.4-4.6 cm as measured by CT scan

CT, computed tomography; TEE, transesophageal echocardiogram.

Patients diagnosed with thoracic and TAAAs should undergo initial CT or MRI to define the size and extent of the aneurysm. Follow-up surveillance imaging is typically performed 6 months after diagnosis, with continued follow-up imaging at an interval determined by the rate of growth. These aneurysms tend to grow slowly, with arch and ascending aneurysms growing 0.1 cm per year and descending aneurysms growing 0.3 cm per year.

Determining when to intervene depends on the underlying pathology, size, rate of expansion, and presence or absence of symptoms (Table 9.2). In patients without known connective tissue disease, surgical repair is recommended at 5.5 cm in ascending aortic aneurysms and 6.5 cm in descending aneurysms. In patients with concomitant AV disease who are scheduled to undergo AV replacement, an aneurysm should be repaired if it is greater than 4.5 cm in diameter. Patients with symptomatic aneurysms of any size should be considered for surgical intervention. Very large and very small patients may be better managed by indexing aortic diameter to body size to determine the appropriate timing of repair.

Special recommendations exist for patients with underlying connective tissue disorders, as these patients tend to suffer significant aortic events at smaller aortic diameters. Patients with MFS require frequent surveillance, with CT imaging 6 months after initial diagnosis and then annually if aortic diameter is stable. More frequent imaging may be recommended with larger aneurysms (>4.5 cm) or if significant growth is noted. Earlier repair is recommended in MFS, and patients with ascending aneurysms of greater than 5 cm in diameter or descending aneurysms of greater than 6 cm in diameter should be considered for surgical intervention. MFS patients with a family history of early aortic dissection at less than 5 cm are often referred for early correction. Finally, women with MFS considering pregnancy should be counseled for elective aortic aneurysm surgery if the aorta is greater than 4 cm in diameter. After surgery on an ascending aortic aneurysm, continued surveillance with CT imaging is necessary to evaluate for the development of aneurysms of the arch and descending aorta.

Patients with LDS also represent a population requiring early repair. Surveillance imaging is similar to patients with MFS, but operative repair is recommended earlier in the disease process. Patients with aneurysms that demonstrate an internal diameter of 4.2 cm on TEE or an external diameter of 4.4 to 4.6 cm on CT are referred for surgical intervention. Similarly, patients with a bicuspid AV with an accompanying TAA are typically repaired at 5 cm, although patients with a valvular indication for surgery are typically repaired if the aortic diameter exceeds 4.5 cm. First-degree relatives of patients with a suspected familial TAA syndrome should be screened with CT imaging at 5-year intervals.

Once the decision is made to proceed with surgery, there are several decision points that dictate the course of the operation. These include the decision to employ hypothermic circulatory arrest (HCA) or cardiopulmonary bypass (CPB) and whether to utilize an open or endovascular approach. If an endovascular approach is utilized, some patients may require additional aortic debranching procedures prior to endograft placement, depending on the extent of the aneurysm.

Overall, surgical decision making in patients with TAAs, thoracoabdominal aneurysms, and combined aneurysmal and AV disease requires a careful comparison of a patient's operative risk with his or her risk of a significant aortic event. Consideration of medical comorbidities and the underlying pathology adds additional nuance to the decision of whether to undertake a surgical repair, and, when repair is recommended, what surgical technique should be utilized.

Elefteriades JA, Botta DM Jr. Indications for the treatment of thoracic aortic aneurysms. *Surg Clin North Am*. 2009;89:845-867.

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Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *J Am Coll Cardiol.* 2010;55(14):e27-e129.

Paterick TE, Humphries JA, Ammar KA, et al. Aortopathies: etiologies, genetics, differential diagnosis, prognosis and management. *Am J Med*. 2013;126(8):670-678.

Shimizu H, Yozu R. Valve-sparing aortic root replacement. *Ann Thorac Cardiovasc Surg*. 2011;17:330-336.

B.2. Which patients are candidates for endovascular aortic repair, and what are the advantages to this approach?

Thoracic endovascular aortic repair (TEVAR) is a commonly used alternative to open repair. It is less invasive, and evidence suggests it is associated with lower rates of perioperative respiratory, renal, and neurologic complications, which facilitates shorter intensive care unit (ICU) and hospital stays with similar long-term outcomes. In recent years, aortic stent grafting has undergone a significant liberalization in its use for many aortic pathologies. In addition to repair of TAAs, many centers are now treating complicated type B aortic dissections, traumatic aortic injuries, intramural hematomas, and penetrating aortic ulcers via the endovascular approach.

Determination of whether to undertake open or endovascular approach is dependent on multiple factors, including patient age, comorbidities, life expectancy, aneurysm morphology and diameter, the presence of “landing zones” of normal aorta on either side of the aneurysm, and the experience of the operating surgeon. Relative contraindications to TEVAR include mycotic aneurysms, aneurysms secondary to connective tissue disease (MFS, Ehlers-Danlos, etc.), and aneurysms extending proximal to the left subclavian artery. Connective tissue disease presents a relative contraindication due to concern for the longevity of the endovascular repair in this patient population.

Many patients with extensive visceral involvement or multiple comorbidities now undergo “hybrid” procedures, which consist of debranching of the visceral arterial supply followed by endovascular repair of the aneurysm. Advantages of this approach include decreased visceral ischemic time, avoidance of aortic cross-clamping, and avoidance of the need for thoracotomy that accompanies an open repair.

Cao CQ, Bannon PG, Shee R, et al. Thoracic endovascular aortic repair—indications and evidence. *Ann Thorac Cardiovasc Surg*. 2011;17:1-6.

Desai ND, Burtch K, Moser W, et al. Long-term comparison of thoracic endovascular aortic repair (TEVAR) to open surgery for the treatment of thoracic aortic aneurysms. *J Thorac Cardiovasc Surg*. 2012;144(3):604-609.

Hanna JM, Andersen ND, Ganapathi AM, et al. Five-year results for endovascular repair of acute complicated type B aortic dissection. *J Vasc Surg*. 2014;59(1):96-106.

Svensson LG, Kouchoukos NT, Miller DC, et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. *Ann Thorac Surg*. 2008;85:S1-S41.

Yamaguchi D, Jordan WD Jr. Hybrid thoracoabdominal aortic aneurysm repair: current perspectives. *Semin Vasc Surg*. 2012;25(4):203-207.

B.3. What are the preoperative considerations for the anesthesiologist before TAA repair?

Surgery for TAA repair involves the potential for significant morbidity and mortality. Thorough preoperative workup is

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complications and to facilitate a coordinated anesthetic and surgical plan that provides the greatest likelihood of good clinical outcome. Particular attention should be given to the patient's cardiac, respiratory, renal, and neurologic function because these systems represent the greatest threats to morbidity and mortality. Although thoracic and thoracoabdominal aneurysm repairs represent high-risk surgical procedures at baseline, patients presenting for urgent or emergent intervention are at the greatest risk of postoperative complications. Unfortunately, these patients may also be clinically unstable and thorough preoperative workup may not be feasible.

Cardiovascular

Detailed evaluation of the patient's cardiovascular system is essential prior to undertaking complex aortic repair. Major fluid shifts, aortic cross-clamping, and the physiologic stress of intraoperative and postoperative blood loss represent a significant threat to the cardiovascular system. Major thoracic aortic surgery falls into the highest risk group for perioperative cardiac morbidity. Up to two-thirds of patients demonstrate diastolic dysfunction with aortic cross-clamping, and 30% of patients manifest some degree of cardiac dysfunction postoperatively. Hypertension is a common comorbidity, and elderly patients may also have coexisting coronary artery disease (CAD). Evidence of congestive heart failure may also be present as a result of progressive AI due to aneurysm enlargement.

Cardiac workup should at least include electrocardiogram (ECG) and a TTE, although stress testing and/or coronary angiography are routinely performed at many centers. Patients who are found to have unstable CAD, left main stenosis, or three-vessel disease are typically revascularized prior to or during the repair of the aneurysm. There is debate whether or not to perform percutaneous coronary intervention (PCI) on less complex lesions because the antiplatelet therapy that accompanies PCI may complicate surgical hemostasis. Occasionally, aneurysmal expansion can result in ischemia from compression of the coronary arteries. Patients taking antihypertensive and antianginal drugs should continue these until the time of surgery, and titrated preoperative anxiolysis is important to prevent stress-induced hypertension and tachycardia, which could precipitate aneurysm rupture. Therapeutic anticoagulation or antiplatelet agents should be discontinued or bridged with short-acting alternatives prior to surgical intervention.

Respiratory

The respiratory system also deserves special attention in the preoperative evaluation of patients undergoing thoracic aneurysm repair. Perioperative respiratory failure is the most common serious complication of thoracic and thoracoabdominal aneurysm repair, and patients with a history of smoking or COPD are at especially high risk. Pulmonary function should be evaluated preoperatively because one-lung ventilation (OLV) is important for open surgical repair of Crawford type I, II, III, and V aneurysms. Patients with very poor pulmonary reserve may require CPB because of an inability to tolerate OLV. Preoperative smoking cessation should be encouraged.

In addition to the evaluation of pulmonary mechanics, history should include consideration of positional dyspnea or stridor, which may indicate aneurysmal compression of the trachea or, more commonly, the left mainstem bronchus. Review of CT or MRI is important to determine whether significant bronchial compression is present because this may complicate airway management and double-lumen endotracheal tube placement. Finally, patients with significant preoperative respiratory dysfunction should be counseled about the possible need for prolonged postoperative mechanical ventilation, including tracheostomy placement.

Renal

Many patients also have baseline renal insufficiency, which places them at risk for subsequent postoperative renal failure. Up to 25% of patients undergoing TAAA repair develop some degree of postoperative renal insufficiency, with 8% of patients requiring hemodialysis. Although evidence for preoperative hydration is minimal, at many centers, it is common practice to admit patient the night before surgery for intravenous (IV) hydration.

Neurologic

Finally, the neurologic system deserves special consideration given the risk to both the brain and spinal cord during aneurysm repair. In an effort to minimize stroke risk, carotid and brachiocephalic angiography are often performed preoperatively, especially in patients with a prior history of stroke or transient ischemic attack. Patients should also be counseled about the risk of possible postoperative paralysis from spinal cord ischemia. Although the risk was historically much higher, the current incidence of postoperative spinal cord injury is between 2% and 6%, depending on the anatomy of the aneurysm. Onset can either be immediate or delayed. Risk factors for postoperative paralysis include preoperative

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renal dysfunction, Crawford type II aneurysm repair, and AAD. Preoperative identification and preservation of the artery of Adamkiewicz decreases the risk of paraplegia from 50% to roughly 5%.

In summary, preoperative assessment prior to thoracic aneurysm repair is important for both anesthetic and surgical planning. Although aortic surgery represents a high-risk procedure, evaluation of clinical risk factors, multisystem assessment, thoughtful preoperative testing, and, when appropriate, referral to subspecialists for medical optimization can improve perioperative outcome.

Dawson J, Vig S, Choke E, et al. Medical optimisation can reduce morbidity and mortality associated with elective aortic aneurysm repair. *Eur J Vasc Endovasc Surg*. 2007;33:100-104.

Estrera AL, Miller CC III, Huynh TT, et al. Preoperative and operative predictors of delayed neurologic deficit following repair of thoracoabdominal aortic aneurysm. *J Thorac Cardiovasc Surg*. 2003;126(5):1288-1294.

Kahn RA, Stone ME, Moskowitz DM. Anesthetic consideration for descending thoracic aortic aneurysm repair. *Semin Cardiothorac Vasc Anesth*. 2007;11:205-223.

Silvay G, Stone ME. Repair of thoracic aneurysms, with special emphasis on the preoperative work-up. *Semin Cardiothorac Vasc Anesth*. 2006;10(1):11-15.

Vaughn SB, LeMaire SA, Collard CD. Case scenario: anesthetic considerations for thoracoabdominal aortic aneurysm repair. *Anesthesiology*. 2011;115(5):1093-1102.

B.4. What is the preoperative management of a patient presenting with acute aortic dissection (AAD)?

Patients presenting with AAD will either be admitted to the ICU or will progress immediately from the emergency department to the operating room. Invasive monitoring of blood pressure in both arms, large-bore IV access, and aggressive control of blood pressure and heart rate are priorities.

Blood pressure reduction is typically accomplished with *β*-blockers and vasodilators aiming to reduce myocardial contractility and minimize further extension of the dissection. The goal systolic blood pressure and heart rate are 100 to 120 mm Hg and less than 60 beats per minute, respectively. If heart rate and blood pressure control remain inadequate after initializing *β*-blocker and vasodilator therapy, calcium channel blockers may be an additional adjunct. Hydralazine is typically not used as it may precipitate a reflex tachycardia, which can worsen the dissection. Conversely, patients who are hypotensive on presentation should be treated aggressively with vasopressors and fluid resuscitation in an effort to maintain endorgan perfusion until the patient can undergo definitive operative repair.

Stanford type A aortic dissection is typically treated as a surgical emergency, as it is a highly lethal condition with a mortality of 1% to 2% per hour after onset. After 24 hours, 20% of patients will die without surgical intervention. Conversely, patients with Stanford type B aortic dissection that is not complicated by limb ischemia, malperfusion, or rupture may be managed medically with aggressive blood pressure and heart rate reduction.

Li JZ, Eagle KA, Vaishnava P. Hypertensive and acute aortic syndromes. *Cardiol Clin*. 2013;31:493-501. Ramanath VS, Oh JK, Sundt TM III, et al. Acute aortic syndromes and thoracic aortic aneurysm. *Mayo Clin Proc*. 2009;84(5):465-481.

B.5. What is the spinal cord blood supply?

The spinal cord blood supply consists of both longitudinal and segmental components (Fig. 9.11). The longitudinal arteries include the anterior and paired posterior spinal arteries.

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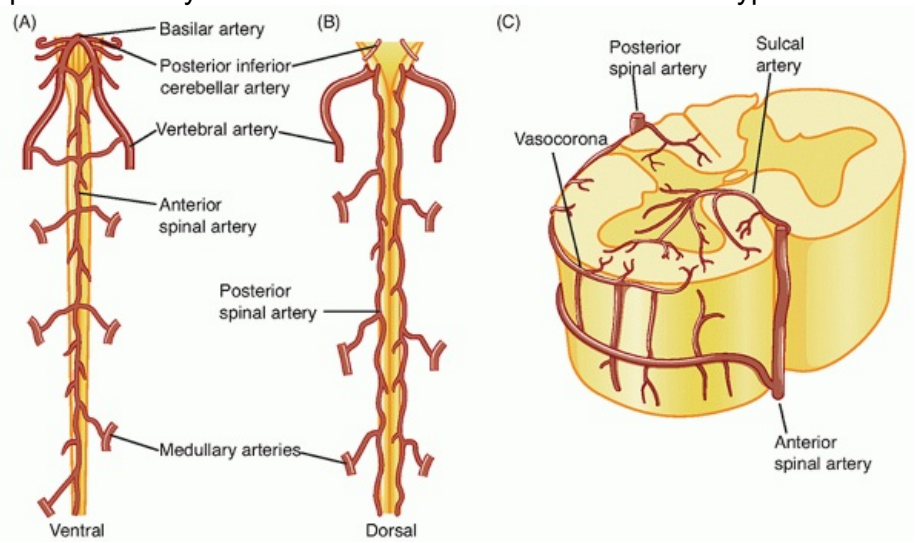


FIGURE 9.11 Spinal cord blood supply. (Used with permission from Purves D, Augustine GJ, Fitzpatrick D, et al, eds. *Neuroscience*. 2nd ed. Sunderland, MA: Sinauer Associates; 2001.)

The anterior spinal artery (ASA) arises from paired feeding vessels that originate in the vertebral arteries near the foramen magnum. It extends the length of the spinal cord and is situated in the anterior spinal sulcus. The ASA is fed by a series of radicular arteries, and the areas between these radicular contributions are watershed areas that are at the greatest risk of ischemia. The most significant of these radicular arteries is the artery of Adamkiewicz. It is a large radicular contribution that most commonly arises between T8 and L2, although it can originate as high as T5 and as low as L4. The artery of Adamkiewicz is critical to the maintenance of adequate collateral blood supply to the lower two-thirds of the spinal cord. The ASA supplies the anterior two-thirds of the spinal cord, including the corticospinal and spinothalamic tracts and is dependent on a robust collateral circulation, making it particularly susceptible to ischemic injury.

There are two paired posterior spinal arteries that originate as branches of either the vertebral or posterior inferior cerebellar arteries and descend along the posterolateral portion of the spinal cord. The posterior spinal arteries are also fed by numerous radicular arteries. The anterior and posterior spinal arteries are connected to each other via a circular anastomosis known as the vasocorona medullaris.

In addition to the longitudinal arteries, there are multiple segmental branches that arise from the posterior portion of the aorta. These include the intercostal, subcostal, and lumbar segmental arteries. These arteries travel posteriorly and branch to supply the vertebral bodies, muscle and cutaneous structures, and spinal cord. The spinal division enters through the intervertebral foramen and subdivides to supply either the vertebral and ligamentous structures or the nerve roots and dura. At some levels, the arteries supplying the nerve roots and dura also supply the spinal cord. These vessels are termed radiculomedullary arteries and play an important role in supplying accessory flow to both the anterior and posterior spinal arteries.

Santillan A, Nacarino V, Greenberg E, et al. Vascular anatomy of the spinal cord. *J Neurointerv Surg*. 2012;4:67-74.

Ullery BW, Wang GJ, Low D, et al. Neurological complications of thoracic endovascular aortic repair. *Semin Cardiothorac Vasc Anesth*. 2011;15(4):123-140.

C. Intraoperative Management

C.1. What are the surgical approaches to thoracic aneurysm repair?

Ascending Aortic Aneurysms

Proximal ascending aneurysms not only cause aortic rupture and dissection but also alter the three-dimensional conformation of the aortic root and AV complex, leading to AI (Fig. 9.1). The extent of involvement of the aortic root

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determines the surgical procedure necessary for repair (Table 9.3). When the AV and aortic root are not diseased, a graft can be implanted above the sinuses of Valsalva, called a supracoronary tube graft. The Wheat procedure is performed when the AV and proximal aorta are diseased, without dilation of the aortic root. It involves a supracoronary graft and an AV replacement but spares the sinuses of Valsalva, making coronary artery reimplantation unnecessary.

The Bentall procedure is performed when the aortic root and AV are involved in the aneurysm. The Bentall procedure involves replacement of the AV, replacement of the aortic root, and reimplantation of the coronary buttons onto the neoaorta. Modifications of the Bentall procedure have focused on resuspending the AV to the neoaorta in patients with normal AV leaflets but poor coaptation due to the dilated aortic root. Resuspension of the AV to the neoaorta can decrease AI without requiring AV replacement. This is referred to as the David procedure.

Sixty percent of aortic arch aneurysms are located in the proximal arch and involve the distal ascending aorta. Surgical options for aortic arch aneurysms include hemiarch replacement or total arch replacement with or without a distal elephant trunk. A hemiarch replacement is performed in patients whose aneurysm does not extend to the proximal descending aorta. In patients whose aneurysm extends to the proximal descending aorta, either a total arch replacement with reimplantation of the great vessels (Fig. 9.12) as a button can be performed, or the elephant trunk procedure can be performed. The elephant trunk procedure includes an aortic arch graft and reimplantation of the great vessels to the prosthetic graft, in addition to a distal 5- to 7-cm “trunk” that dangles in the proximal descending aorta and is available for grafting for current or future descending aortic aneurysms (Fig. 9.13).

Surgery for the proximal ascending aorta, including Bentall, Wheat, David, and hemiarch procedures, is performed through a median sternotomy with CPB, with or without HCA. If the procedure involves the aortic arch, HCA is necessary.

Thoracoabdominal Aneurysms

Open repair of TAAAs is the treatment of choice for appropriate surgical candidates. Open repair includes a large thoracoabdominal incision and reimplantation of branch arteries on the surrounding aorta, after resection of the diseased aorta and graft placement. Additionally, total arch replacement and elephant trunk procedures are performed by utilizing a left thoracotomy approach with the patient in the right lateral decubitus position.

TABLE 9.3 Types of Thoracic Ascending Aorta Aneurysm Repairs

AORTIC VALVE	ROOT	ASCENDING AORTA	SURGICAL APPROACH	NAME OF PROCEDURE
Normal	Normal	Aneurysmal	Supracoronary tube graft	
Diseased	Normal	Aneurysmal	AVR + supracoronary tube graft	Wheat procedure
Diseased	Aneurysmal	Aneurysmal	AVR + replacement of aortic root and reimplantation or coronary arteries	Bentall
Normal	Aneurysmal	Aneurysmal	Valve-sparing root replacement	David procedure

AVR, aortic valve replacement.

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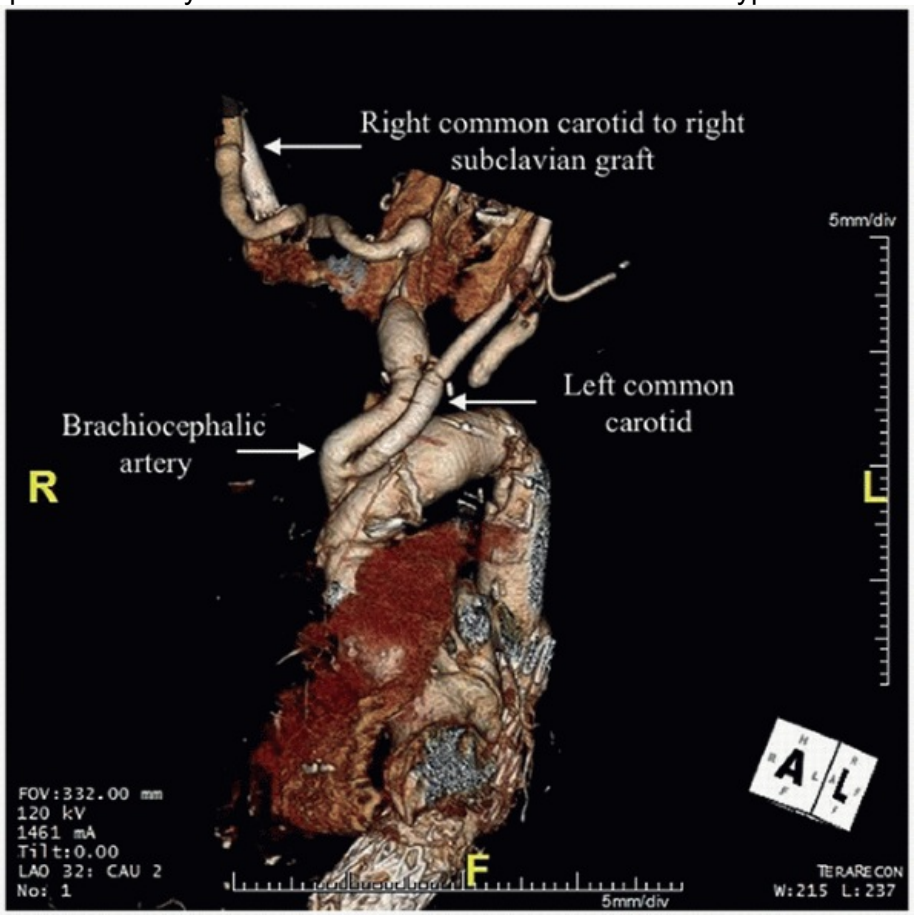


FIGURE 9.12 Three-dimensional (3D) CT reconstruction demonstrating total arch replacement with reimplantation of the great vessels. The left common carotid has been detached from the aortic arch and reimplanted to the brachiocephalic artery. Additionally, bilateral carotid to subclavian artery grafts are present (graft from left common carotid to left subclavian not shown).

Endovascular treatment of TAAAs has become common, particularly in patients with comorbid diseases precluding them from open repair. Endovascular treatment includes deployment of a stent graft into the diseased segment of the aorta via the femoral artery (Fig. 9.14). Endovascular treatment must incorporate visceral arteries in the repair. This is accomplished via application of branched or fenestrated aortic grafts, which allow perfusion of the major visceral arteries. The branched or fenestrated aortic grafts can be custom-made or commercially available.

A hybrid procedure combines an open surgical approach with an endovascular stenting procedure to expand the anatomic suitability for deployment of stent grafts into the aorta. Hybrid procedures can either be staged or performed concurrently. In patients who have transverse aortic arch aneurysms without an adequate proximal landing zone for the stent graft, a first-stage total arch replacement is performed to create a proximal landing zone using CPB and HCA. This procedure is followed by a concomitant or second-stage endovascular repair of the distal portion of the aortic aneurysm.

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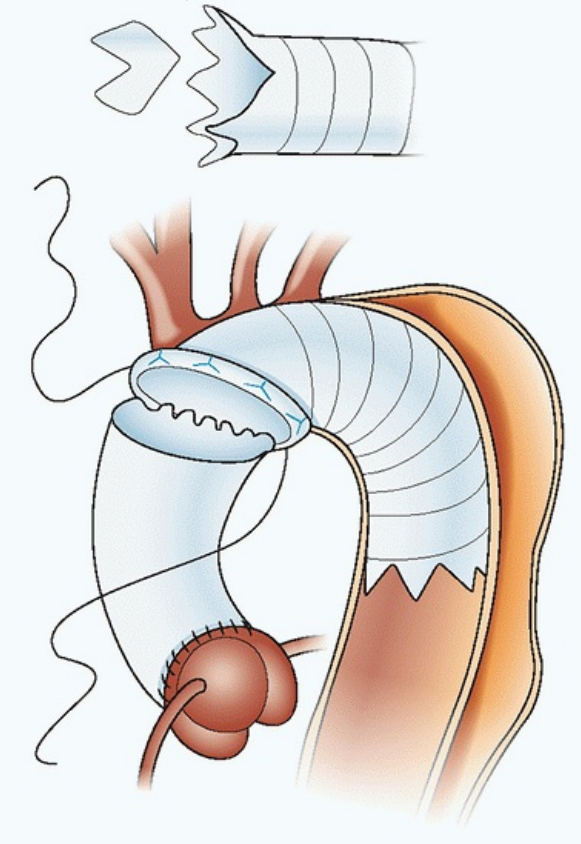


FIGURE 9.13 Illustration demonstrating the elephant trunk procedure, where an aortic graft is used to reimplant great vessels, in addition to a distal portion of the graft that dangles in the proximal descending aorta and is available for grafting for current or future descending aortic aneurysms. (Adapted from Roselli EE. We should replace the aortic arch and more in DeBakey type I dissection—a perspective from the Cleveland Clinic. *Ann Cardiothorac Surg*. 2013;2[2]:216-221.)

Aortic visceral debranching procedures allow for endovascular stenting of TAAAs that involve the visceral arteries. Open debranching procedures can revascularize the visceral and renal arteries from the iliac arteries in a retrograde fashion or from the descending thoracic aorta above the aneurysm being treated (Fig. 9.15). After open debranching, the patient undergoes endovascular stent placement in the diseased segment of the aorta to exclude the aneurysm. The hybrid procedure exploits the benefit of both techniques and provides a favorable treatment option for high-risk patients. The hybrid technique avoids the need for custom-designed fenestrated or branched grafts and avoids the dangers of occluding vital visceral vessels.

Escobar GA, Upchurch GR Jr. Management of thoracoabdominal aortic aneurysms. *Curr Probl Surg*. 2011;48(2):70-133.

Moon MR, Sundt TM III. Aortic arch aneurysms. *Coron Artery Dis*. 2002;13:85-92.

Nicolaou G, Ismail M, Cheng D. Thoracic endovascular aortic repair: update on indications and guidelines. *Anesthesiol Clin*. 2013;31:451-478.

Roselli EE. We should replace the aortic arch and more in DeBakey type I dissection—a perspective from the Cleveland Clinic. *Ann Cardiothorac Surg*. 2013;2(2):216-221.

Shimizu H, Yozu R. Valve-sparing aortic root replacement. *Ann Thorac Cardiovasc Surg*. 2011;17(4):330-336.

Ziganshin BA, Elefteriades JA. Surgical management of thoracoabdominal aneurysms. *Heart*. 2014;100: 1577-1582.

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C.2. How is the open repair performed?

Ascending Aortic Aneurysms

Position: The surgical approach is through a median sternotomy with the patient positioned supine.

Cannulation for CPB: The CPB circuit requires a venous cannula that provides blood to the CPB pump and an arterial cannula that provides blood from the CPB pump to the patient. For aortic surgery, the arterial cannula can reside in any large artery, including the femoral,

axillary, innominate, or carotid artery. Direct aortic cannulation can also be performed away from the site of the aneurysm if the anatomy allows. Arterial cannulation can be accomplished either directly or with the use of a graft anastomosis to the target artery. Direct aortic and femoral cannulations are used less frequently because they carry a risk of embolization or malperfusion in patients with aortic dissection or atherosclerosis. Commonly, the axillary or innominate arteries are used for cannulation sites because they can provide adequate arterial flow from the CPB pump during CPB and can also provide antegrade cerebral perfusion (ACP) during HCA. Cannulation of these smaller arteries is achieved with end-to-side anastomosis with a synthetic graft. The venous cannula for CPB is commonly inserted into the right atrium or femoral vein.

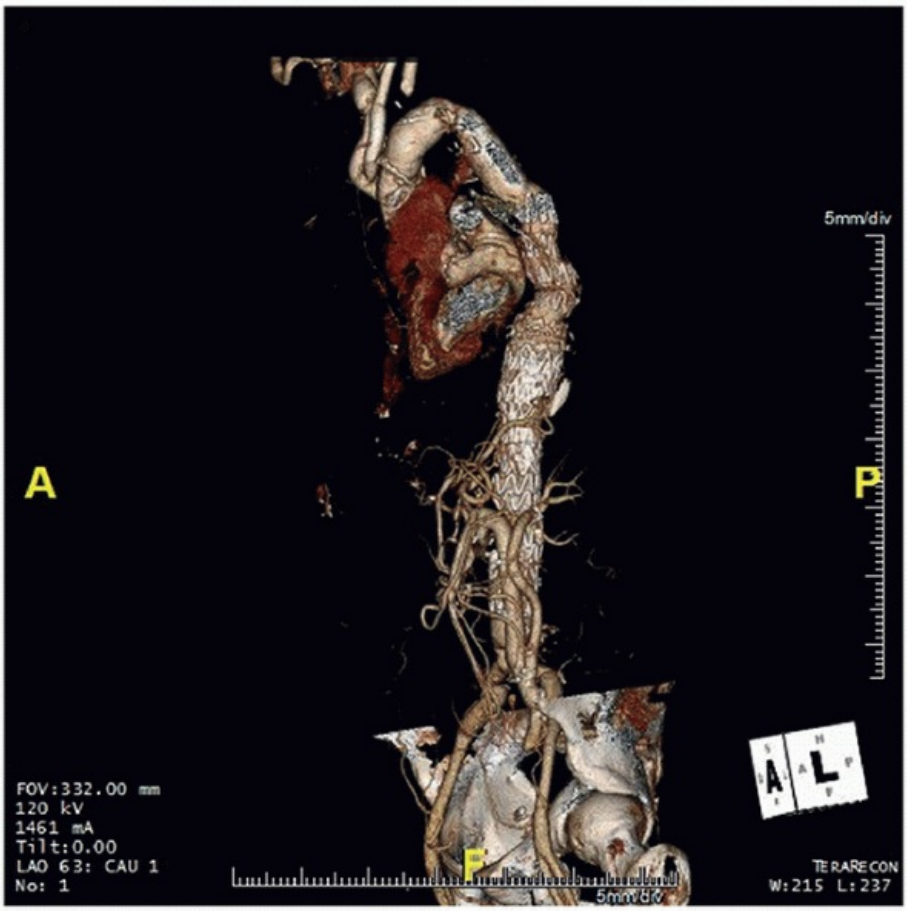


FIGURE 9.14 Three-dimensional (3D) CT reconstruction demonstrating endovascular exclusion of the descending thoracic aorta aneurysm after abdominal and arch debranching.

Hypothermic circulatory arrest: Despite advances in surgical technique, neurologic injury remains a major cause of morbidity and mortality after open aortic arch repair. Cerebral protection depends on decreasing metabolic demand and providing metabolic supply with adequate cerebral perfusion while excluding blood flow through the great vessels. Deep hypothermic circulatory arrest (DHCA) improves the ischemic tolerance of the brain

considerably by decreasing metabolic demand but also has limitations. The safe limit of DHCA at 18°C is limited to 30

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minutes, after which the brain is vulnerable to ischemia. Mild (28°C to 34°C) and moderate (20°C to 28°C) HCA have recently been advocated and are increasingly used with better outcomes than DHCA. Moderate HCA provides 10 to 20 minutes of safe circulatory arrest time. Regional cerebral perfusion has become a commonly utilized technique to both assist with metabolic supply and increase the safe duration of circulatory arrest. Regional cerebral perfusion can be achieved in either an antegrade or retrograde fashion. ACP is accomplished by cannulating the axillary artery and clamping the proximal portion of the brachiocephalic artery, which provides perfusion to the right common carotid artery without disrupting the surgical site. ACP can be either unilateral or bilateral. Commonly, a unilateral approach is performed via the right axillary artery and DHCA with unilateral ACP of less than 50 minutes is tolerated. With bilateral ACP, DHCA can be tolerated for a longer period of time, up to 160 minutes. Retrograde cerebral perfusion (RCP) can be achieved by SVC cannulation, delivering oxygenated blood via the venous system. The SVC

is clamped above the right atrium to separate this system from the venous return to the CPB pump. Debate regarding superiority of one method of regional cerebral perfusion continues. The proposed advantages of RCP include de-airing of arch vessels and decreased cerebral embolic events, whereas the disadvantage is a possible increase in transient postoperative neurologic dysfunction.



FIGURE 9.15 Three-dimensional (3D) CT reconstruction after abdominal debranching. The superior mesenteric artery (SMA), celiac artery, and renal arteries arise from a left iliac artery graft.

Thoracoabdominal Aneurysms

Position: The surgical approach is typically through the left chest, with the patient positioned in a partial right lateral decubitus position, with the shoulders at 60 degrees and the hips at 30 degrees. The patient is supported with the use of a bean bag.

Incision: A thoracoabdominal incision is the preferred approach for the majority of aneurysms. The proximal extent of the incision is dictated by the patient's body habitus and the aortic pathology. Typically, if the distal aortic arch and proximal descending aorta are to be exposed (Crawford type I and II), an incision to the fifth intercostal space is necessary. If the proximal extent of the aneurysm involves the distal thoracic aorta (Crawford type III and V), an incision to the seventh or

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eighth intercostal space is required. If the aneurysm is localized to the abdominal aorta (Crawford type IV), the proximal incision is made at the 9th or 10th intercostal space. The abdominal portion of the incision is typically limited to the retroperitoneum. Diaphragm preservation, defined as division only of the muscular portion of the diaphragm with preservation of the central tendinous portion, is performed to help improve postoperative respiratory mechanics.

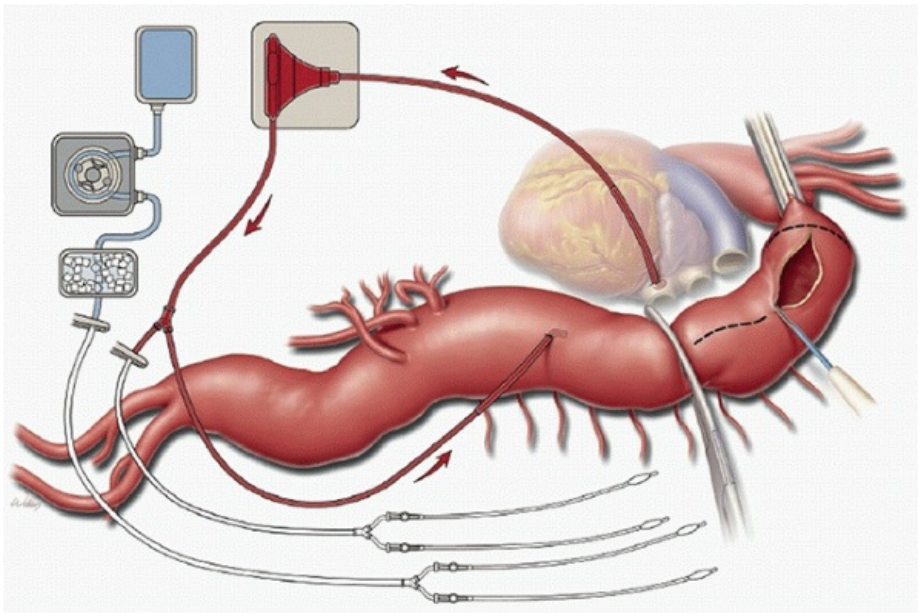
Cannulation for left-heart bypass (LHB): Open surgical procedures on the thoracoabdominal aorta require a period of ischemia to the lower portion of the body during the period of time that the aorta is cross-clamped. This poses the risk of ischemia to the spinal cord, viscera, and kidneys during complex procedures requiring long cross-clamp times. LHB is utilized to reduce the risk of ischemia to the abdominal organs and spinal cord. LHB delivers oxygen-rich blood to the lower body and viscera while permitting longer cross-clamp times for the surgeon to perform the repair. In LHB, the left atrium or pulmonary vein is cannulated and directed to the femoral artery via a centrifugal pump (Fig. 9.16). Alternatively, passive axillary artery to femoral artery bypass can be used, which is dependent on the mean arterial blood pressure (MAP) proximal to the cross-clamp. In addition to the benefit of distal aortic perfusion, atrial-femoral bypass reduces preload to the left ventricle, reducing myocardial stress during cross-clamping. The use of LHB requires less systemic heparinization (100 units per kg given 5 minutes prior to cannulation) than CPB. It also minimizes ischemia to the lower extremities, thereby decreasing the acidosis that can develop after cross-clamp release. During the period of aortic cross-clamp, flow through the LHB is maintained to provide a proximal aortic pressure of 90 mm Hg or distal aortic pressure of 70 mm Hg.

Cannulation for CPB with hypothermic circulatory arrest: Similar to ascending aorta repairs, the use of CPB with HCA obviates the need for proximal aortic cross-clamping and therefore reduces the potential for spinal cord injury. Preserved end-organ function and decreased incidence of paraplegia are some of the benefits of using CPB with HCA. Typically, a right femoral venous cannula is placed prior to right lateral positioning of the patient. Arterial cannulation can reside in the distal aortic arch, proximal descending aorta, axillary artery, or femoral artery. During circulatory arrest, antegrade or RCP may be used for neuroprotection and direct cannulation of the visceral segments with antegrade perfusion may be used for gastrointestinal protection.

Cross-clamp: The surgeon must develop an operative plan for safe aortic cross-clamping such that an adequate aortic cuff is available for proximal anastomosis and is not compromised by aortic cross-clamp placement.

Anastomoses: In type I and II repairs, the aorta is first dissected away from the esophagus to help prevent the formation of an esophageal-aortic fistula. The proximal aorta is cross-clamped and the proximal anastomosis of the graft is sewn on to the aorta in an end-to-end fashion. Intercostal arteries in the T4-T8 region are often ligated if they exhibit excessive retrograde bleeding indicative of good collateral flow. When feasible, patent intercostal arteries from T8 to L1 are reattached to the graft. The clamp is then moved distally and reapplied above the visceral vessels. The superior mesenteric artery,

renal arteries, and celiac artery are then anastomosed to the graft. Finally, the clamp is moved distally past the visceral vessels, allowing for the distal anastomosis of the graft to the descending aorta.



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FIGURE 9.16 Left-heart bypass is utilized for distal perfusion during TAAA repair. The drainage cannula is placed in the left atrium, and the outflow cannula is placed in the thoracic aorta distal to the site of aortic cross-clamping. Additional catheters are available for selective perfusion of visceral arteries with blood during operative repair. A separate line may be set up to provide cold lactated Ringer's solution through the renal arteries for renal protection. (Used with permission from de la Cruz KI, LeMaire SA, Weldon SA, et al. Thoracoabdominal aortic aneurysm repair with a branched graft. *Ann Cardiothorac Surg*. 2012;1[3]:381-393.)

Clamp and sewtechnique: The “clamp and sew” technique involves cross-clamping the proximal aorta and replacing the aneurysmal aorta with a graft. In this technique, distal aortic perfusion with the use of LHB or HCA are not utilized. The technique poses a time limit to the surgeon as the patient's organs are not being supported during cross-clamp. This technique is typically inadequate for difficult repairs.

Escobar GA, Upchurch GR Jr. Management of thoracoabdominal aortic aneurysms. *Curr Probl Surg*. 2011;48(2):70-133.

Gutsche JT, Ghadimi K, Patel PA, et al. New frontiers in aortic therapy: focus on deep hypothermic circulatory arrest. *J Cardiothorac Vasc Anesth*. 2014;28(4):1171-1175.

Levine WC, Lee JJ, Black JH, et al. Thoracoabdominal aneurysm repair: anesthetic management. *Int Anesthesiol Clin*. 2005;43(1):39-60.

Ouzounian M, LeMaire SA, Coselli JS. Open aortic arch repair: state-of-the-art and future perspectives. *Semin Thorac Cardiovasc Surg*. 2013;25:107-115.

Reed H, Berg KB, Janelle GM. Aortic surgery and deep-hypothermic circulatory arrest: anesthetic update. *Semin Cardiothorac Vasc Anesth*. 2014;18(2):137-145.

Spielvogel D, Kai M, Tang GH, et al. Selective cerebral perfusion: a review of the evidence. *J Thorac Cardiovasc Surg*. 2013;145(3 suppl):S59-S62.

C.3. How are the endovascular repair of TAAAs performed?

Position: Endovascular repair of TAAAs are performed with the patient supine for adequate access to the femoral artery.

Incision: During endovascular repair, the endograft is typically introduced via the femoral artery, although the iliac artery or infrarenal aorta may be used if the femoral artery is inadequate in size or is heavily calcified.

Deployment: Branched and fenestrated grafts are handmade for each individual case and require over a month before they can be delivered and implanted. Due to the emergent need for surgery in some patients with aortic aneurysms or dissections, commercially available endovascular grafts are often modified by the surgeon with fenestrations to accommodate the patient's anatomy.

The left subclavian artery may need to be covered by the endograft in order to achieve an adequate proximal landing zone. The proximal left subclavian artery is covered, with the distal subclavian artery gaining perfusion from collateral vessels, including the left internal mammary artery (LIMA) and vertebral artery. In some instances, occlusion is not tolerated, necessitating left carotid to subclavian bypass.

In patients with aneurysms involving the mid transverse arch, ascending aortic-based arch debranching may be performed, without the use of CPB via a median sternotomy with extension of the incision along the anterior border of the sternocleidomastoid muscle.

Escobar GA, Upchurch GR Jr. Management of thoracoabdominal aortic aneurysms. *Curr Probl Surg*. 2011;48(2):70-133.

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Hughes GC, Sulzer CF, McCann RL, et al. Endovascular approaches to complex thoracic aortic disease. *Semin Cardiothorac Vasc Anesth*. 2008;12(4):298-319.

C.4. What are the specific considerations for anesthetic management of the patient presenting for open TAAA repair?

Patients presenting for TAAA repair typically have multiple preexisting comorbid conditions, and open repair of the TAAA poses a direct and immediate threat to the cardiac, pulmonary, renal, gastrointestinal, and neurologic systems.

Induction of anesthesia should include a slow and hemodynamically stable induction, avoiding hypertension and tachycardia. Short-acting antihypertensive agents such as nitroglycerin, nicardipine, esmolol, and labetalol are useful to assist in hemodynamic stability.

Anesthetic management must seek to avoid hemodynamic changes that will increase the risk of aneurysm rupture while maintaining adequate end-organ perfusion. As surgical dissection exposes the aorta, the counterforce to the systemic blood pressure on the aneurysm wall is decreased, increasing the risk of aneurysm rupture. Prior to cross-clamp removal and reperfusion of the visceral organs and lower extremities, systemic blood pressure should be increased because removal of the cross-clamp and reperfusion can lead to profound hypotension.

Lung isolation is necessary for repair of types I, II, and some type III TAAAs. A doublelumen endotracheal tube is superior to a bronchial blocker as it provides access to the nonventilated lung for suctioning and addition of continuous positive airway pressure (CPAP) when oxygenation is inadequate. Either right- or left-sided double-lumen endotracheal tubes may be used; however, a type I or II aneurysm may distort the anatomy of the left mainstem bronchus, making a left-sided double-lumen tube difficult to place.

If motor evoked potentials (MEPs) are being monitored, either succinylcholine or a shortacting nondepolarizing neuromuscular blocker should be used to facilitate tracheal intubation and then discontinued. Anesthetic maintenance may be achieved using a low concentration of volatile anesthetic, combined with an infusion of propofol or narcotic. If MEPs are not being monitored, neuromuscular blockers can be used with inhalation agents and narcotics.

Some institutions will institute a wake-up test prior to transportation to the ICU. If this is performed, anesthetic management must take this into consideration. During the wake-up test, the patient is asked to move his lower extremities. After completion of the wake-up test, the patient is resedated and the double-lumen endotracheal tube is changed to a single-lumen endotracheal tube.

Escobar GA, Upchurch GR Jr. Management of thoracoabdominal aortic aneurysms. *Curr Probl Surg*. 2011;48(2):70-133.

Levine WC, Lee JJ, Black JH, et al. Thoracoabdominal aneurysm repair: anesthetic management. *Int Anesthesiol Clin*. 2005;43(1):39-60.

C.5. What are the specific considerations for anesthetic management of the patient presenting for endovascular TAAA repair?

Endovascular treatment of thoracic aneurysms is typically less invasive than open surgical repair, but preparation for possible open repair must be undertaken. General and regional anesthetic techniques have been described, but general anesthesia remains the primary choice because TEE and neuromonitoring can occur when the patient is under general anesthesia. Hemodynamic stability must be sought, avoiding hypertension and tachycardia. During deployment of the stent, transient balloon occlusion of the aorta may result in significant transient hemodynamic instability, particularly if the patient has poor cardiac function. Vasopressors and inotropes must be available to treat hemodynamic instability.

Although the risk of spinal cord ischemia is lower in endovascular procedures, it does occur. Cerebrospinal fluid (CSF) drains may be placed selectively in patients considered high risk for spinal cord ischemia for neuroprotection. Neuromonitoring of somatosensory evoked potentials (SSEPs) and MEPs may be used. If MEPs are used for neuromonitoring, this may necessitate the use of a total IV anesthetic.

Blood loss during the endovascular surgery may be difficult to quantify, necessitating frequent hemoglobin checks.

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Escobar GA, Upchurch GR Jr. Management of thoracoabdominal aortic aneurysms. *Curr Probl Surg*. 2011;48(2):70-133.

Hughes GC, Sulzer CF, McCann RL, et al. Endovascular approaches to complex thoracic aortic disease. *Semin Cardiothorac Vasc Anesth*. 2008;12(4):298-319.

C.6. What hemodynamic monitors should be used for the patient undergoing thoracic aneurysm repair?

In addition to the standard monitoring recommended by the American Society of Anesthesiologists, there are additional monitors that should be applied to the patient undergoing open repair of a TAA. Electrocardiographic monitoring with ST-segment analysis is essential because the incidence of intraoperative myocardial ischemia and arrhythmias is significant. During open repair of TAAs, systemic blood pressure should be measured with the use of an arterial line. During repair of Crawford type I and II aneurysms, the arterial catheter should be placed in the right radial artery because flow to the left subclavian artery may be disrupted from the proximal aortic cross-clamp. Left radial monitoring may be useful to determine the patency of the left subclavian artery but should not be used independently because left subclavian flow can be altered. If distal aortic perfusion through bypass or a shunt is performed, a femoral arterial line is inserted to monitor distal perfusion pressure. A femoral arterial line is also useful in determining the pressure gradient across the surgical repair by comparing the femoral blood pressure to the radial blood pressure. During ascending aortic repairs, bilateral arterial catheters are used. The left radial arterial line is used to monitor the systemic pressure reliably prior to and during CPB, whereas the right radial arterial catheter will measure the blood pressure during HCA with ACP. The right radial arterial catheter is not used during other intraoperative periods because the presence of an axillary aortic cannula can make the readings unreliable.

The potential for rapid blood loss during repair is significant; therefore, large-bore IV access should be obtained. The ability to transfuse blood products rapidly with a rapid infusion device should be available. Left upper extremity IV access should be avoided during aortic arch repairs because the left innominate vein may be injured or ligated during the procedure. Pulmonary artery (PA) catheters are often used to allow hemodynamic monitoring and assess cardiac output, but the routine use of PA catheters during these procedures varies among different institutions.

TEE should be used in all open thoracic aorta repairs, unless contraindications exist. TEE can assess the extent and severity of aortic disease, evaluate valvular and functional abnormalities, and assist with cannula placement. TEE should also be used in endovascular thoracic aorta procedures for cardiac monitoring, procedural guidance, and endovascular

graft leak detection. During balloon occlusion of the aorta, TEE can monitor the cardiac performance and guide vasoactive therapies.

Hughes GC, Sulzer CF, McCann RL, et al. Endovascular approaches to complex thoracic aortic disease. *Semin Cardiothorac Vasc Anesth*. 2008;12(4):298-319.

Levine WC, Lee JJ, Black JH, et al. Thoracoabdominal aneurysm repair: anesthetic management. *Int Anesthesiol Clin*. 2005;43(1):39-60.

C.7. What strategies are used for spinal cord protection during a TAAA repair?

Spinal cord injury with resultant paraplegia remains one of the most serious complications of surgical procedures on the descending and thoracoabdominal aorta despite major advances in surgical technique. Several components of TAAA surgery impart risk to the spinal cord. Temporary occlusion of the aorta with a cross-clamp, permanent deletion of intercostal arteries, and embolization of air or particulate matter to the aorta may contribute to the development of spinal cord injury. Several techniques have been instituted to minimize the risk of postoperative paraplegia.

Left-Heart Bypass

LHB is commonly used to provide distal aortic perfusion during aortic cross-clamp and repair (Fig. 9.16). During LHB, the arterial inflow cannula typically resides in the femoral artery and provides antegrade flow to the lower extremities with retrograde flow to the visceral organs and spinal cord. The venous cannula resides in the left atrium or pulmonary veins

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and drains oxygenated blood. LHB circuits can be equipped with or without an oxygenator.

Intraoperative Neuromonitoring

Neuromonitoring of SSEPs and MEPs has been instituted at various centers as a means of timely diagnosis of ischemia and modification of the surgical technique when ischemia occurs. SSEPs monitor the dorsal column of the spinal cord by stimulating the posterior tibial nerve and recording the responses from the somatosensory cortex. MEPs monitor the function of the corticospinal tract and anterior horn motor neurons by stimulating the motor cortex or cervical spinal cord and recording the response from the anterior tibial muscle. Unfortunately, monitoring of SSEPs produces a significant amount of false-positive results, and relying on SSEPs alone for determining the need for revascularization does not affect the incidence of postoperative neurologic injury. Current guidelines state that the use of neurophysiologic monitoring with SSEPs and MEPs may be considered.

Cerebrospinal Drainage

During aortic cross-clamp and surgical retraction, CSF pressure may acutely increase. Additionally, the spinal cord may suffer from spinal cord reperfusion injury, whereby spinal canal edema forms following reperfusion. Spinal cord perfusion pressure is the difference between MAP and CSF pressure. The rationale for CSF drainage is based on this premise, as decreasing the compartment pressure of the spinal cord should improve spinal cord perfusion pressure. Studies have shown that reducing the CSF pressure to less than 15 mm Hg is beneficial, and meta-analysis supports the use of CSF drainage as an adjunct to prevent paraplegia. The current guidelines recommend the use of CSF drainage in open and endovascular thoracic aortic repair in patients at high risk of spinal cord ischemia.

Hypothermia

Mild hypothermia to 32°C may provide neuronal protection by reducing excitatory neurotransmitter release, decreasing free oxygen radical production, decreasing postischemic edema, and stabilizing CNS blood flow.

Moderate systemic hypothermia has been associated with improved neurologic outcomes after TAAA surgery. Hypothermia is achieved via passive heat loss during surgery or active cooling by heat exchangers on bypass circuits. Current guidelines state that the use of moderate hypothermia is reasonable for protection of the spinal cord.

Some institutions implement regional hypothermia to avoid the detrimental effects of systemic hypothermia on the coagulation system. Epidural cooling can be instituted with the

insertion of a T12-L1 epidural catheter and an L3-L4 intrathecal thermistor catheter, selectively cooling the spinal cord after aortic cross-clamp. The spinal cord is cooled at the T8-L1 region, a watershed area with variation in collateral supply most susceptible to ischemic injury. The thermistor catheter allows measurement of temperature and CSF pressure. After full TAAA reconstruction is completed, epidural cooling is stopped.

Similar to ascending aortic aneurysms, HCA may be used during repair of TAAAs. The use of HCA obviates the need for an aortic cross-clamp and the use of LHB to protect the spinal cord and viscera.

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Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *J Am Coll Cardiol*. 2010;55(14):e27-e129.

Levine WC, Lee JJ, Black JH, et al. Thoracoabdominal aneurysm repair: anesthetic management. *Int Anesthesiol Clin*. 2005;43(1):39-60.

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Ziganshin BA, Elefteriades JA. Surgical management of thoracoabdominal aneurysms. *Heart*. 2014;100: 1577-1582.

C.8. What strategies are used for mesenteric and renal preservation?

Over the past few decades, strategies have been developed to minimize ischemic damage to downstream organs while the aorta is clamped. One strategy is the use of a passive shunt to provide distal aortic perfusion. Passive shunting is uncommonly utilized due to the popularity of mechanical circulatory support and the inability to adjust flow rates through the shunt.

LHB, as previously described, is now a common approach to maintain distal aortic perfusion. The advantage of LHB is that flow rates can be adjusted to help provide stable hemodynamics. The disadvantage of LHB is that it is associated with increased incidence of postoperative renal dysfunction. Selective visceral perfusion may be used in combination with LHB, perfusing the four branching arteries with cold blood or crystalloid.

Femoro-femoral CPB with a range of protective hypothermia strategies, from mild (34°C) to profound (18°C), have been described to provide end-organ protection. Separate roller pumps may be used to selectively perfuse the celiac artery, superior mesenteric artery, and renal arteries during CPB. Lastly, HCA may be combined with CPB to avoid aortic crossclamping and preserve end-organ function.

Selective renal artery perfusion can be performed by infusion of a cold (4°C) crystalloid or blood solution into the renal artery ostia during aortic cross-clamp occlusion, achieving renal hypothermia. Mannitol and methylprednisolone may also be added to the perfusate. Mannitol decreases renal oxygen demand and steroids stabilize cell membranes during ischemia. Mannitol also assists in maintaining urine output during the cross-clamp period. Additives such as histidine-tryptophan-ketoglutarate have recently shown promise in decreasing renal dysfunction. Current guidelines support the use of either cold crystalloid or blood perfusion to the kidneys but do not recommend the use of furosemide, mannitol, or dopamine solely for renal protection.

As concomitant atherosclerotic disease is commonly present in this patient population, the renal and visceral arteries often contain occlusive disease. Endarterectomy and balloonexpandable stent placement may be beneficial in decreasing postoperative renal dysfunction.

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C.9. What is the pathophysiology of aortic clamping and unclamping?

Aortic Clamping

Hemodynamics: As for any major vascular surgery, it is imperative to be familiar with the pathophysiology of aortic cross-clamping to understand and treat the hemodynamic disturbances appropriately. The most reliable response to aortic

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cross-clamping is systemic arterial hypertension. This is due to both an increase in afterload and redistribution of the blood volume. Blood volume redistributes after aortic cross-clamping, with a decrease in venous capacitance below the clamp, expelling blood from the splanchnic and nonsplanchnic vascular beds, and an increase in venous capacitance above the clamp. The increase in upper body blood volume results in increased filling pressures. Central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), and left ventricular enddiastolic pressure (LVEDP) all increase with aortic cross-clamp placement. Differences in hemodynamic responses are observed with occlusion of different levels of the aorta and may be the result of different degrees and patterns of blood volume distribution. Supraceliac cross-clamp application results in the most consistent redistribution of blood flow, whereas infraceliac aortic cross-clamp has inconsistent effects on blood flow redistribution and preload.

Oxygen consumption: Oxygen consumption in the part of the body distal to the aortic occlusion decreases. Paradoxically, oxygen uptake above the aortic occlusion also decreases. The reason for the decrease in oxygen consumption above the cross-clamp is unclear but may be related to sympathetic discharge from the adrenal glands, arteriovenous shunting, or blood volume redistribution and proximal hypervolemia. Mixed venous oxygen saturation increases during aortic cross-clamp, indicating decreased extraction. Plasma levels of epinephrine and norepinephrine significantly increase after thoracic aorta cross-clamping.

Coronary blood flowand contractility : Aortic cross-clamping is associated with increases in preload and afterload, leading to an increase in myocardial oxygen demand. In an intact coronary blood supply, an increase in demand would lead to coronary artery vasodilation and a concomitant increase in oxygen supply. When coronary blood flow increases, the subendocardium is perfused and contractility will increase in response to aortic cross-clamping. In the presence of inadequate coronary blood flow, the LVEDP increases, the subendocardium is not perfused, and cardiac output decreases.

Level and duration of aortic cross-clamp: The level of the aortic cross-clamp affects the hemodynamic response observed. Changes in MAP, filling pressures, ejection fraction, and wall motion are minimal during infrarenal aortic cross-clamping but exaggerated during supraceliac aortic cross-clamping. With increased duration of aortic cross-clamping, systemic vascular resistance (SVR) increases and cardiac output decreases.

Renal effects: Cross-clamping of both the suprarenal and infrarenal aorta results in an increase in renin and angiotensin. The increase in angiotensin is thought to contribute to the hypertension observed during cross-clamping. Cross-clamping of the thoracic aorta is associated with severe decreases in renal blood flow, glomerular filtration rate, and urine output. Ischemia-reperfusion injury to the kidneys plays a central role in renal dysfunction after aortic surgery and is also present after infrarenal cross-clamping.

Effects on spinal cord: Cross-clamping of the aorta is associated with a decrease in distal aortic pressure (decreasing ASA pressure, depending on the anatomy and presence of collateral supply), increase in CSF pressure, and a decrease in the compliance of the spinal fluid space. Vasodilators used to decrease proximal aortic pressure should possess minimal cerebral vasodilating properties because these will decrease spinal cord perfusion pressure

by decreasing distal aortic pressure and increasing CSF pressure. In this regard, sodium nitroprusside, which decreases distal aortic pressure and increases CSF pressure, and nitroglycerin, which predominantly decreases distal aortic pressure, both decrease spinal cord perfusion pressure, which can lead to worse neurologic outcome.

Aortic Unclamping

Hemodynamics: Unclamping of the thoracic aorta leads to a decrease in SVR with a resultant decrease in arterial blood pressure. Cardiac output may increase, decrease, or remain the same. Myocardial blood flow increases and LVEDP decreases. Central hypovolemia develops due to pooling of blood into reperfused tissues distal to the aortic occlusion. Hypoxiamediated vasodilation, in addition to accumulation of myocardial-depressant metabolites contributes to the hypotension that is seen after cross-clamp removal.

Acidosis: Metabolic acidosis and an increase in lactate concentration are seen after release of the aortic cross-clamp. The degree of acidosis present depends on the underlying pathology and is greatest in patients undergoing abdominal aortic aneurysm repair. Aortic cross-clamp removal is also associated with a transient increase in carbon dioxide release and oxygen consumption.

Renal effects: Unclamping of the aorta results in a significant increase in renin and angiotensin that lasts for 6 hours but is unrelated to hypertension. A maldistribution of renal blood flow is seen, with a decrease in renal cortical blood flow. Glomerular filtration rate and renal plasma flow are decreased after unclamping and can remain at decreased values for 6 months following surgery.

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C.10. Why does coagulopathy ensue and how is it prevented/treated?

TAA repair is associated with significant hemorrhage from multiple causes, including surgical dissection, hypothermia, CPB, fibrinolysis, dilution or consumption of coagulation factors, anticoagulant therapy, preoperative antithrombotic therapy, and congenital or acquired coagulopathies. Communication with the blood bank should occur early to ensure an adequate supply of blood products for the patient. Five to 10 units of packed red blood cells (pRBCs) should be immediately available in the operating room, with a similar number of units available in the blood bank. Five to 10 units of fresh frozen plasma, typically given in a ratio of one per two to three pRBCs transfused should be readily available. Thrombocytopenia and platelet dysfunction develop secondary to hypothermia and use of extracorporeal mechanical support, and the need for platelet transfusion is common.

Fibrinolysis develops not only from the use of CPB, but supraceliac aortic crossclamping and peripheral ischemia have been shown to cause fibrinolysis and can be attenuated by the use of selective superior mesenteric artery perfusion. Supraceliac cross-clamping and peripheral ischemia promote activity of tissue-type plasminogen activator and decreasing plasminogen activator inhibitor. The use of lysine analogs epsilonaminocaproic acid and tranexamic acid is common in TAA repairs, but its use has been derived from studies in other cardiac surgeries and is not currently supported by the literature in TAA repair.

The use of a blood salvaging device (“cell saver”) is essential to decrease transfusion requirements. Unfortunately, the use of a cell saver is associated with the loss of platelets, plasma proteins, and coagulation factors. In heparinized patients, the use of cardiotomy suction permits the autotransfusion of filtered unwashed whole blood, which preserves platelets and coagulation factors.

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D. Postoperative Anesthetic Management

D.1. What are the postoperative complications after open TAAA repair?

Respiratory Failure

Respiratory failure after TAAA repair remains one of the most commonly reported complications. The large thoracoabdominal incision, diaphragmatic incision, and need for lung isolation all predispose the patient to pulmonary dysfunction. The diaphragmatic incision may lead to hemidiaphragm dysfunction or paralysis. Preoperative pulmonary dysfunction, tobacco use, postoperative cardiac complications, and postoperative renal complications are independent risk factors for postoperative respiratory failure.

Renal Failure

Postoperative renal dysfunction is a common postoperative complication, occurring in as many as 28% of patients and necessitating dialysis in 8% of patients. Risk factors associated with postoperative renal failure include age >50 years, preexisting renal dysfunction, administration of greater than 5 units of either pRBCs or salvaged washed autologous blood, and aortic cross-clamp time of more than 100 minutes. Postoperative renal dysfunction of any degree is associated with an increased perioperative mortality.

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Spinal Cord Injury

Spinal cord injury remains one of the greatest fears after TAAA repair. Spinal cord injury can be immediate or delayed. Spinal cord injury occurs more often with type I and II TAAAs, emergent operations, intercostal sacrifice, and intraoperative hypotension. Spinal cord injury of any severity occurs in 11% of patients undergoing open TAAA repair, with 2% to 6% having total paraplegia. The majority of the deficits are immediate; however, delayed deficits can occur hours to weeks postoperatively. Immediate-onset deficits are irreversible and portend a poor prognosis, whereas delayed-onset deficits typically have a better prognosis with partial and reversible deficits and acceptable functional outcomes. Management of delayed-onset deficits focuses on CSF drainage (to a CSF pressure of 10 mm Hg) and increasing systemic blood pressure (to a MAP of 100) for improved spinal cord perfusion.

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D.2. What are the postoperative complications after endovascular TAAA?

Left Upper Extremity Ischemia

Aneurysms involving the aortic arch can pose a significant risk to cerebral and upper extremity blood flow with endovascular repair. Intentional coverage of the left subclavian artery with the endovascular graft can occur in approximately 50% of thoracic endograft implants. Most patients can tolerate left subclavian artery coverage without left upper extremity ischemia. However, if the right subclavian and vertebral arteries are not patent, ischemia can ensue. Additionally, the patient may experience decreased blood flow to the LIMA, leading to significant ischemia to a prior coronary artery bypass graft. If left upper extremity ischemia occurs, a left subclavian artery bypass should be performed postoperatively.

Stroke

Intravascular wires and endografts that are introduced into the atherosclerotic aorta can come in contact with mobile thrombi in the arch and brachiocephalic vessels, leading to cerebral ischemia. Iatrogenic dissection of the carotid or vertebral arteries and retrograde dissection of the aorta have been described as devastating complications. If the left subclavian artery is covered during endograft deployment, cerebral ischemia may develop due to decreased flow from the left vertebral artery. A left carotid to left subclavian bypass graft should first be placed if the left subclavian will be covered by the graft. The incidence of

stroke after TEVAR ranges from 2% to 8%. Risk factors for perioperative stroke include severe atheromatous aortic disease (grade IV or V aortic disease on TEE), endovascular coverage of aortic arch vessels, history of prior stroke, long extent of aortic coverage, preexisting CAD, longer procedure duration, and female gender.

Spinal Cord Ischemia

Spinal cord ischemia is also a possible complication of endovascular treatment of TAAAs, although with less incidence than after open repair. Intercostal arteries are intentionally covered during endovascular stent placement of a TAAA, possibly compromising spinal cord perfusion by obliterating the collateral circulation. Endovascular coverage of the left subclavian artery may compromise spinal cord perfusion in patients with a left dominant vertebral artery, solitary vertebral artery, carotid artery disease, or an incomplete circle of Willis. Spinal cord injury after TAAA repair is a heterogeneous syndrome manifesting as a spectrum of impairments that varies depending on the severity and extent of ischemia. Additionally, delayed-onset neurologic deficits, similar to that seen after open repair, can also be seen after endovascular treatment. Delayed-onset deficits are thought to be due to postoperative events such as hypotension, thrombosis, hematoma, embolization, and elevated CSF pressure. Injury to the spinal cord is directly related to the extent of the aorta that is involved, and is highest with Crawford type II repairs. Risk factors for spinal cord injury after TEVAR include left subclavian artery coverage without revascularization, concomitant open abdominal aortic surgery, and the use of three or more stent grafts.

Renal Failure

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Similar to open repair of TAAAs, renal insufficiency can develop after endovascular repair with an incidence rate of 14%. Deployment of the endograft in a diseased, atherosclerotic aorta can lead to embolic showers, infarcting mesenteric, splenic, and renal arteries. This phenomenon contributes to the development of renal insufficiency. Risk factors for postoperative renal dysfunction after TEVAR include preoperative chronic renal insufficiency, perioperative blood transfusions, and the thoracoabdominal extent of the aneurysm.

Postimplantation Syndrome

This commonly observed phenomenon consisting of fever, leukocytosis, and an elevation in inflammatory markers normally occurs in the early postoperative period, although it may occasionally have a delayed presentation. It is usually mild and self-limiting, responding to conservative management with nonsteroidal anti-inflammatory drugs.

Endograft Collapse

Endograft collapse is a rare but serious complication after TEVAR, typically presenting in the first 3 months after endovascular repair. Endograft collapse can present asymptomatically or can present with diminished or absent femoral pulses, abdominal pain, or multiorgan failure. Excessive oversizing of the endograft and poor apposition of the proximal endograft to the aortic wall are the primary causes of endograft collapse. Maldeployment of the endograft and progression of the aortic disease are rare causes of endograft collapse.

Endoleaks

An endoleak is a leakage of blood into an aneurysm sac previously excluded during TEVAR. Endoleaks after TEVAR occur in about 5% to 30% of patients. Endoleak is a complication unique to the endovascular approach to aortic repair and there are four types.

Type I endoleak is caused by incomplete seal at the end of the graft, leading to blood flow into the aneurysm sac.

Type II endoleak is caused by leaking of blood into the aneurysm from collateral vessels excluded during repair.

Type III endoleak is caused by inadequate sealing of overlapping graft joints or rupture of graft fabric, leading to blood flow into the aneurysm sac.

Type IV endoleak is caused by the direct leakage of blood through a porous graft.

Management includes aggressive endovascular repair of type I and III endoleaks, with observation of type II endoleaks. Type IV endoleaks are of historical interest because new graft material has virtually eliminated the incidence of this complication. Risk factors for development of endoleaks include larger preoperative aneurysm sac diameter, greater length of stent coverage, and the use of multiple stent grafts.

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Piffarette G, Mariscalco G, Bonardelli S, et al. Predictors and outcomes of acute kidney injury after thoracic aortic endograft repair. *J Vasc Surg*. 2012;56(6):1527-1534.

Ullery BW, Wang GJ, Low D, et al. Neurological complications of thoracic endovascular aortic repair. *Semin Cardiothorac Vasc Anesth*. 2011;15(4):123-140.

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Chapter 10
Abdominal Aortic Aneurysm Repair

Shreysjit R. Kumar
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The patient is a 76-year-old man with a 6-cm infrarenal aortic aneurysm discovered on routine physical examination and confirmed by abdominal computed tomography (CT) scan. He is a former smoker and complains of dyspnea on exertion and claudication. His electrocardiogram (ECG) shows Q waves in leads II, III, and aVF; chest x-ray film displays mild hyperinflation of the lung fields; and his hematocrit is 46%. His baseline serum creatinine is 1.9 mg per dL.

A. Medical Disease and Differential Diagnosis

1. What risk factors are associated with an abdominal aortic aneurysm (AAA)?
2. What other diseases are commonly found in patients with aortic aneurysms?
3. What is the incidence of morbidity and mortality in these patients if they undergo elective open surgical repair? What is the natural history of the disease without surgical repair?
4. What should be done for smaller aortic aneurysms that are found in patients?
5. What is the risk of perioperative myocardial infarction (MI) in patients with ischemic heart disease? What can be done to reduce the risk of ischemic events in these patients?
6. Does the morbidity and mortality of elective repair of an aortic aneurysm differ significantly from that of an emergency repair?

B. Preoperative Evaluation and Preparation

1. Which preoperative laboratory tests would you require for this patient?
2. What is the significance of the preoperative ECG? Would you wish to pursue a preoperative cardiac workup? What tests would you request, and what would they tell you?
3. Is it necessary to evaluate this patient's pulmonary status?
4. Preoperative arterial blood gas (ABG) measurement shows pH, 7.35; $PaCO_2$, 47 mm Hg; and PaO_2, 68 mm Hg on room air. What is the significance of this result?
5. How would you measure creatinine clearance in this patient, and what is its value in this case?
6. Describe the blood flow to the spinal cord. What is its relevance to surgery involving the abdominal aorta?
7. How do you detect spinal cord ischemia?
8. What are the various surgical approaches to repair an AAA?
9. How does the choice of surgical technique affect the anesthetic management?
10. How would you premedicate this patient?

C. Intraoperative Management

1. Would you use an arterial line? What are the complications of arterial line placement?
2. What various monitors are available for myocardial ischemia? Is a pulmonary artery catheter (PAC) helpful in determining the occurrence of ischemia?
3. What additional monitors would you employ?
4. Is there a role for somatosensory evoked potential (SSEP) monitoring during aortic clamping?
5. How would you anesthetize this patient for an open repair of the aorta? What techniques could be used for an endovascular aortic aneurysm repair? Discuss the various anesthetic techniques that can be employed for this surgery.

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6. This patient is to be heparinized intraoperatively, and anticoagulation may be continued postoperatively. Is this a contraindication to the preoperative placement of either an epidural or intraspinal catheter? What if the patient is receiving anticoagulants in the preoperative period?
7. What are your plans for fluid and blood replacement during surgery?
8. What are the hemodynamic changes of aortic cross-clamp placement? What efforts can be made to minimize these changes both before and during cross-clamping? If the patient develops ST-segment depressions with a rising pulmonary capillary wedge pressure (PCWP) during cross-clamp, what maneuvers should be taken?
9. Because this case involves an infrarenal aneurysm, is renal blood flow affected with the placement of the cross-clamp? If an endovascular repair is chosen, what are the risks to the kidneys? Are there any treatment maneuvers that can be taken to minimize these risks in either repair?
10. What are the hemodynamic consequences of aortic cross-clamp removal? What can be done to minimize the effects of removing the aortic cross-clamp? If the systemic blood pressure remains depressed after removal of the cross-clamp, what is the differential diagnosis? How would you diagnose and correct the problem?

D. Postoperative Management

1. What are the parameters used to extubate this patient?
2. What are the anticipated changes in postoperative pulmonary function in these patients? How does the surgical technique affect postoperative pulmonary function? Are there any postoperative maneuvers that can improve respiratory parameters?
3. How would you control postoperative pain? What are the alternatives in the management of this patient's postoperative pain?

A. Medical Disease and Differential Diagnosis

A.1. What risk factors are associated with an abdominal aortic aneurysm (AAA)?

AAA is a full-thickness dilatation of a segment of the abdominal aorta located between the diaphragm and the bifurcation of the aorta to the common iliac arteries. Approximately 200,000 AAAs are diagnosed annually resulting in about 13,000 deaths per year in the United States. Risk factors for AAA include older age, male sex, family history of AAA, smoking, hypertension, hyperlipidemia, atherosclerotic occlusive disease, and obesity. Lifestyle factors reducing risk for AAA include regular exercise, smoking cessation, and favorable diet (includes fruits, vegetables, and nuts). Diabetes mellitus is also associated with decreased risk of AAA. The prevalence of AAA is lower in Blacks, Hispanics, and Asians in comparison to Whites and Native Americans.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1128-1138.

Kent KC. Clinical practice. Abdominal aortic aneurysms. *N Engl J Med*. 2014;371:2101-2108.

Kent KC, Zwolak RM, Egorova NN, et al. Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals. *J Vasc Surg*. 2010;52:539-548.

A.2. What other diseases are commonly found in patients with aortic aneurysms?

The major pathologic cause of aneurysmal disease is atherosclerosis. In addition, hypertension (55%), heart disease (73.5%), peripheral vascular disease (21%), stroke and transient ischemic attacks (22%), diabetes mellitus (7%), and renal insufficiency (10%) are the most common comorbid illnesses. It is worth noting that in some studies, smoking history has been reported in as many as 80% of patients presenting for AAA repair. A recent study demonstrated an association of current smoking with AAA rupture in younger patients. However, hypertension had a greater association than smoking with AAA rupture in older patients. These risk factors, combined with advanced age (greater than 60), are exacerbated by the extreme physiologic changes that occur during aneurysmal surgery.

Cruz CP, Drouilhet JC, Southern FN, et al. Abdominal aortic aneurysm repair. *Vasc Surg*. 2001;35(5):335-344. Ellis JE, Roizen MF, Youngberg JA. Anesthesia for abdominal aortic revascularization. In: Youngberg JA, Lake CL, Roizen MF, et al, eds. *Cardiac, Vascular and Thoracic Anesthesia*. Philadelphia, PA: Churchill Livingstone;

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2000:538-566.

Howard DP, Banerjee A, Fairhead JF, et al. Age-specific incidence, risk factors and outcome of acute abdominal aortic aneurysms in a defined population. *Br J Surg*. 2015;102:907-915.

A.3. What is the incidence of morbidity and mortality in these patients if they undergo elective open surgical repair? What is the natural history of the disease without surgical repair?

Morbidity in this patient group is most commonly due to cardiovascular, pulmonary, and renal complications. Perioperative mortality for elective open AAA repair is 2% to 5%. Increased postoperative mortality was associated with older age, elevated serum creatinine, a lower forced expiratory volume in 1 second (FEV1), and gender. One retrospective study demonstrated higher mortality in women in comparison to men: 7% versus 5% for open repair and 2% versus 1% for endovascular repair. Despite the increasing fraction of patients undergoing endovascular repair, numerous large studies have not shown significant long-term differences in mortality between open and endovascular repair. The major cause of death in the nonsurgically treated patient is rupture with a mortality of up to 80%. Ruptured AAAs account for approximately 9,000 deaths per year in the United States. In one study, resection of AAAs doubled life expectancy. The incidence of rupture within 5 years of diagnosis of an AAA is 80%. The incidence of rupture increases with aneurysmal size: 25% for lesions of 4 to 7 cm in diameter, 45% for lesions 7 to 10 cm, and 60% for lesions larger than 10 cm. Repairing aneurysms smaller than 5.5 cm has not been shown to improve survival. Thus, only patients with aneurysms 5.5 cm or larger should be considered for surgical intervention.

After 10 years, graft patency is worse for patients with disease in distal vessels. Mortality is also increased for patients with diseased distal vessels. Survival rate is 28% in patients with isolated aortoiliac disease and increases to 41% in patients with femoral popliteal or tibial disease.

Brady AR, Fowkes FG, Greenhalgh RM, et al. Risk factors for postoperative death following elective surgical repair of abdominal aortic aneurysm: results from the UK Small Aneurysm Trial. *Br J Surg*. 2000;87(6):742-749.

Ketelsen D, Thomas C, Schmehl J, et al. Endovascular aneurysm repair of abdominal aortic aneurysms: standards, technical options and advanced indications. *Rofo*. 2014;186:337-347.

Reimerink JJ, van der Laan MJ, Koelemay MJ, et al. Systematic review and meta-analysis of population-based mortality from ruptured abdominal aortic aneurysm. *Br J Surg*. 2013;100:1405-1413.

Schermerhorn ML, Bensley RP, Giles KA, et al. Changes in abdominal aortic aneurysm rupture and short-term mortality, 1995-2008: a retrospective observational study. *Ann Surg*. 2012;256:651-658.

A.4. What should be done for smaller aortic aneurysms that are found in patients?

Physical examination and screening, either by abdominal ultrasound or CT scan, uncover many patients with aortic aneurysms less than 5.5 cm in diameter. One study compared patients with smaller aneurysms that were followed until the aneurysm reached 5.5 cm, enlarged by more than 0.7 cm in 6 months, 1.0 cm in 1 year, or were symptomatic from their aneurysm. Mortality was the same in patients randomized to immediate repair or followed closely with no intervention. Aneurysm repair was delayed 4 years in patients who received close monitoring instead of surgical intervention. The U.S. Preventive Services Task Force

(USPSTF) 2015 update on screening recommendations for AAA reinforces that early surgical intervention of smaller AAAs <5.5 cm (open or endovascular) does not reduce mortality. USPSTF recommends repeat ultrasonography every 3 to 12 months for AAAs 3 to 5.4 cm with surgical referral for rapid growth (>1 cm per year) or when the aneurysm reaches 5.5 cm or larger. Therefore, watchful waiting is suggested for aneurysms that are smaller than 5.5 cm.

Lederle FA, Kane RL, MacDonald R, et al. Systematic review: repair of unruptured abdominal aortic aneurysm. *Ann Intern Med*. 2007;146(10):735-741.

LeFevre ML; for U.S. Preventive Services Task Force. Screening for abdominal aortic aneurysm: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014;161:281-290.

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A.5. What is the risk of perioperative myocardial infarction (MI) in patients with ischemic heart disease? What can be done to reduce the risk of ischemic events in these patients?

A retrospective analysis confirmed that cardiac mortality is high for patients who undergo vascular surgery and experience postoperative myocardial ischemia. Key factors that determine perioperative morbidity and mortality rates include the stress of surgery (aortic, peripheral vascular, emergency surgery), increased blood loss, poor preoperative cardiac functional status, history of congestive heart failure (CHF), a low ejection fraction, known coronary artery disease (CAD), and preoperative history of coronary artery bypass grafting.

The occurrence of a recent MI is an important independent predictor of perioperative morbidity and mortality. In a group of patients studied prospectively for perioperative reinfarction by Rao et al., the statistical rate of reinfarction was related to the length of time since the initial MI, decreasing to less than 2% if the infarction occurred more than 6 months earlier. Patients were monitored with PACs and arterial lines and were aggressively treated and monitored in an intensive care unit setting for 3 to 4 days postoperatively. Currently, the acute care for MI has improved and subsequent risk stratification with noninvasive testing allows for a more tailored approach to the timing of surgery in these patients.

Special consideration needs to be given to patients who have recently undergone percutaneous coronary intervention procedures for revascularization of stenotic lesions and are being treated with platelet inhibitors. Depending on the type of intervention undertaken, bare metal stent (BMS) or drug-eluting stent (DES) placement, surgery may need to be delayed for a period of 1 month, 6 months, to 1 year. This is due to the significant risk of acute stent restenosis or thrombosis in these patients if antiplatelet therapy is terminated prematurely. Caring for patients with coronary stents in the perioperative period requires input from a team consisting of anesthesiologists, surgeons, and cardiologists. The management of the dual antiplatelet therapy regimen should be customized to each patient depending on the type and urgency of surgery, type of coronary stent, time since the coronary intervention, and complexity of the coronary intervention. The current recommendations for perioperative management of patients with stents are shown in Figure 10.1. For patients identified at high risk for stent thrombosis, surgery should be planned in a hospital with cardiac catheterization facilities. Postoperatively, these patients require a monitored setting and their antiplatelet agents restarted immediately. Signs and symptoms of stent thrombosis should be promptly recognized and aggressively treated with percutaneous coronary intervention.

In most studies, the morbidity following a perioperative MI approaches 50%. The risk after an MI may be best linked to the ongoing risk of ischemia. Patients who have survived a non-Q-wave infarction are potentially at great risk for further ischemia. Badner et al. reported a 17% post-MI mortality rate after noncardiac surgery. The mortality rate was higher if the ST-segment and T-wave changes occurred during the intraoperative period. These patients should be evaluated by symptom-limited exercise testing and/or cardiac catheterization. The prevention of perioperative myocardial ischemia is the goal of the anesthesiologist regardless of the technique chosen. The basic goal is to reduce myocardial oxygen demand by avoiding tachycardia and hypertension while increasing oxygen supply by preventing hypotension and anemia. Oxygen demand on the left ventricle is dependent on heart rate, contractility, and the ventricular loading conditions. Of the three, the increase in heart rate imposes the greatest demand and should be readily controlled by the anesthesiologist. Left ventricular

preload and afterload also affect oxygen demand by end-diastolic and systolic wall tension. Other factors, such as coronary collateral blood flow, hematocrit, and blood rheology also may influence myocardial ischemia.

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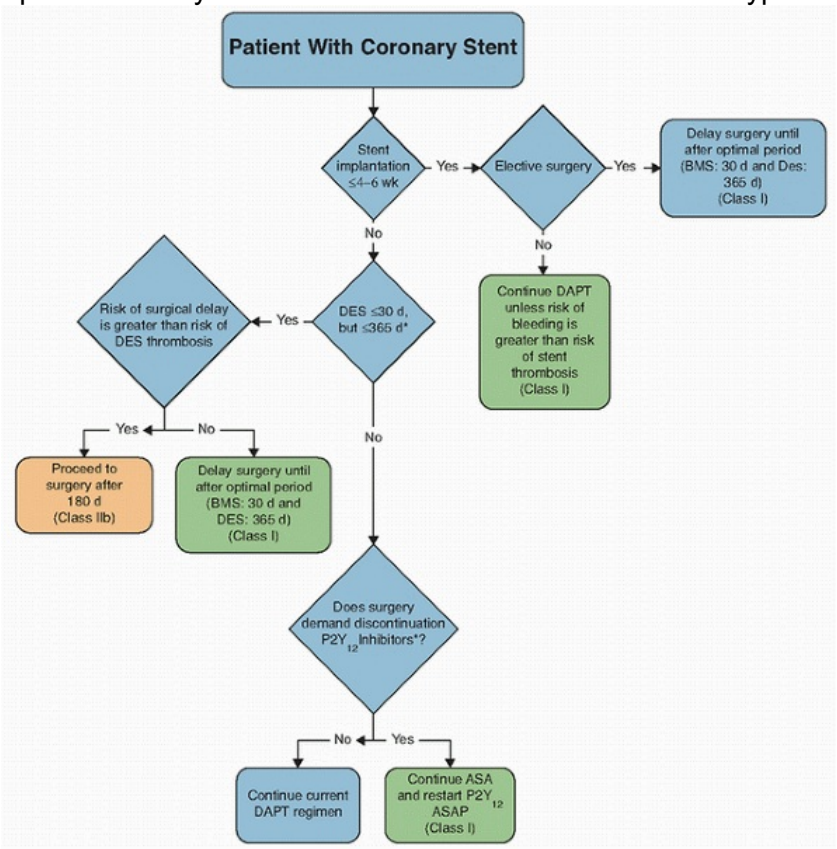


FIGURE 10.1 Algorithm for patients with previous percutaneous coronary interventions (PCI) for non-cardiac surgery. (Reprinted from Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guidelines on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:2215-2245.)

β-Adrenergic antagonists are a well-established class of drugs effective in reducing myocardial oxygen consumption. Some studies suggest that *β*-blockers reduce perioperative ischemia and may reduce the risk of MI and cardiovascular death in patients undergoing high-risk procedures such as vascular surgery. The mechanism of reduction of myocardial oxygen consumption with *β*-antagonism is related to decreases in heart rate and myocardial contractility, counteracting the deleterious effects of sympathetic stimulation. In addition, this class of drugs has antiarrhythmic qualities. However, results of recent trials have not shown efficacy of high-dose, acutely administered, perioperative *β*-blockers to reduce overall mortality in patients undergoing noncardiac surgery. The largest of these trials, the 2008 Perioperative Ischemic Evaluation (POISE) trial, did show better perioperative *cardiac* outcomes with *β*-blocker use; however, *increased mortality* and stroke rate were also noted in the *β*-blocker group. Interestingly, the sub-analysis of vascular surgery patients in the study demonstrated efficacy of perioperative *β*-blockers. Currently, the only class I recommendation for perioperative *β*-blockers use by the American Heart Association (AHA) is to continue their use in the patients who are already on *β*-blockers. Patients undergoing vascular surgery who have multiple risk factors or have reversible ischemia on preoperative testing may benefit from perioperative

β-blockers (class IIa). Although there are some differences between the European Society of Cardiology and the AHA guidelines, they both agree that if *β*-blockers are used for prophylactic purposes, they should be slowly titrated (at least a week prior to elective surgery) and acute administration of high-dose *β*-blockers in high-risk population is not recommended.

Nitrates also can reduce myocardial oxygen demand by decreasing preload and by dilating large epicardial coronary arteries and collateral conduit vessels. However, the benefit of perioperative nitroglycerin prophylaxis has not been proven.

The use of statins in patients with cardiovascular disease is increasingly supported by multiple studies that display a reduction in the risk of MI, stroke, and mortality. Furthermore, accumulating data suggests that continuation of statin therapy in the preoperative period reduces the risk of postoperative death and acute coronary syndromes. The mechanisms by which statin medications attenuate cardiovascular disease extend beyond their lipid-lowering properties. In addition to anti-inflammatory and antioxidant actions, they also improve endothelial function and stabilize plaques. Thus, current American College of Cardiology (ACC)/AHA guidelines recommend continuation of statin therapy in the perioperative period (see also Chapter 14, sections A.7 and A.8).

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Abualsaud AO, Eisenberg MJ. Perioperative management of patients with drug-eluting stents. *J Am Coll Cardiol Intv*. 2010;3:131-142.

Badner NH, Knill RL, Brown JE, et al. Myocardial infarction after noncardiac surgery. *Anesthesiology*. 1998;88:572-578.

Brooke BS. Perioperative beta-blockers for vascular surgery patients. *J Vasc Surg*. 2010;51:515-519.

Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet*. 2008;371:1839-1847.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:2215-2245.

Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2014;35(35):2383-2431.

Le Manach YL, Coriat P, Collard CD, et al. Statin therapy within the perioperative period. *Anesthesiology*. 2008;108:1141-1146.

Lindenauer PK, Pekow P, Wang K, et al. Perioperative beta-blocker therapy and mortality after major noncardiac surgery. *N Engl J Med*. 2005;353(4):349-360.

McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. *N Engl J Med*. 2004;351:2795-2804.

Popescu WM. Perioperative management of the patient with a coronary stent. *Curr Opin Anaesthesiol*. 2010;23:109-115.

Rao TL, Jacobs KH, El-Etr AA. Reinfarction following anesthesia in patients with myocardial infarction. *Anesthesiology*. 1983;59:499-505.

Sprung J, Abdelmalak B, Gottlieb A, et al. Analysis of risk factors for myocardial infarction and cardiac mortality after major vascular surgery. *Anesthesiology*. 2000;93:129-140.

A.6. Does the morbidity and mortality of elective repair of an aortic aneurysm differ significantly from that of an emergency repair?

The overall mortality for a ruptured aortic aneurysm is greater than 50%. One study showed an overall survival rate of 19.8% as compared with an elective surgical survival rate of 95%. The worst prognosis occurred in patients older than 80 years; a systolic blood pressure of less than 80 mm Hg on admission; a prior history of hypertension, angina, or previous MI; and an operating time of greater than 4 hours. Other risk factors include a systolic blood pressure less than 100 mm Hg at the end of surgery and blood loss greater than 11,000 mL. Retroperitoneal rupture was more likely to be associated with a higher rate of survival. Elective surgical intervention should be considered if the size of the aneurysm changes rapidly or if its diameter is greater than 5.5 cm.

Lambert ME, Baguley P, Charlesworth D. Ruptured abdominal aortic aneurysms. *J Cardiovasc Surg (Torino)*. 1986;27:256-261.

Lederle FA, Kane RL, MacDonald R, et al. Systematic review: repair of unruptured abdominal aortic aneurysm. *Ann Intern Med*. 2007;146(10):735-741.

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B. Preoperative Evaluation and Preparation

B.1. Which preoperative laboratory tests would you require for this patient?

The patient should have the following laboratory tests as part of the preoperative evaluation: complete blood count and platelet count, serum electrolytes, BUN, creatinine, and coagulation profile. ABG analysis may be useful, but pulse oximetry can give similar information and $PaCO_2$ may be inaccurate if the patient is hyperventilating or sedated prior to obtaining the test. Chronic hypercarbia may be gleaned from the serum bicarbonate value. A chest radiograph will help ascertain whether signs of heart failure, pulmonary disease, or acute pneumonia are present. Spirometry should be considered in the patient with severe disease and those in whom an adequate medical history is not available. In addition, spirometric data may be useful in assessing the effects of inhaler therapy.

An ECG should be obtained because this patient displays multiple risk factors for ischemic disease. The ECG is a sensitive and simple screening test for active cardiac conditions, such as unstable coronary syndromes and significant arrhythmias, which necessitate further management prior to proceeding to surgery. Additionally, preoperative laboratory tests should be defined by positive findings on history and physical exam.

Roizen MF, Cohn S. Preoperative evaluation for elective surgery: what laboratory tests are needed? In: Stoelting R, ed. *Advances in Anesthesia.* St. Louis, MO: Mosby-Yearbook; 1993:25-48.

B.2. What is the significance of the preoperative ECG? Would you wish to pursue a preoperative cardiac workup? What tests would you request, and what would they tell you?

The patient's preoperative ECG is consistent with a prior inferior wall MI. Patients with a history of a prior MI or angina in conjunction with an abnormal ECG have a fivefold increase in postoperative mortality when compared with those with no clinical indication of CAD. This patient's history of claudication suggests peripheral vascular disease. Peripheral artery disease is associated with a fourfold increase in risk for MI and a twofold to threefold increase in risk of stroke. In selected patients with severe or unstable cardiac ischemia, evaluation may be needed to assess if prior myocardial revascularization is indicated.

When coronary angiography was performed on 1,000 patients undergoing elective peripheral vascular surgery, it was revealed that more than half of the patients had significant CAD (greater than 50% stenosis), and 33% had severe stenosis (greater than 70%). Of the asymptomatic patients with no history or electrocardiographic evidence of ischemic heart disease, 15% had severe CAD, and 22% of these seemingly normal patients had impaired left ventricular function. Hertzer et al. found that only 8% of patients undergoing elective vascular surgery had normal coronary arteries.

A comparison of this patient's current ECG with a prior ECG may aid in assessing the timing of the previous infarction if the history alone is not helpful. The 2014 update to the joint AHA/ACC guidelines concerning perioperative cardiovascular assessment suggest incorporating clinical risk factors, exercise tolerance, and surgical risk when determining whether further testing is necessary. Vascular surgeries, such as AAA repair, are categorized as high-risk procedures. In addition, clinical risk factors include a history of ischemic disease, compensated or prior heart failure, cerebrovascular disease, diabetes mellitus, and renal insufficiency. The algorithm for the cardiac assessment of patients undergoing surgical procedures associated with a high perioperative cardiac risk is shown in Figure 10.2.

Many vascular surgery patients are unable to undergo exercise stress testing because of limitations presented by their cardiac, pulmonary, or peripheral vascular disease. A dipyridamole-thallium stress test or a dobutamine stress echocardiogram is a pharmacologic test to assess ischemic potential. Dipyridamole causes vasodilation of normal coronary arteries. This results in a “steal” of blood flow from the area beyond a coronary stenosis. Blood flow redistributes as the drug dissipates.

Positive results on preoperative stress testing may not always necessitate revascularization. There is evidence to suggest that vascular patients who undergo coronary revascularization have an increased risk of periprocedural and long-term complications. The decision to perform coronary revascularization procedures, rather than employ medical management, should be undertaken in close consultation with a cardiologist and a cardiac surgeon.

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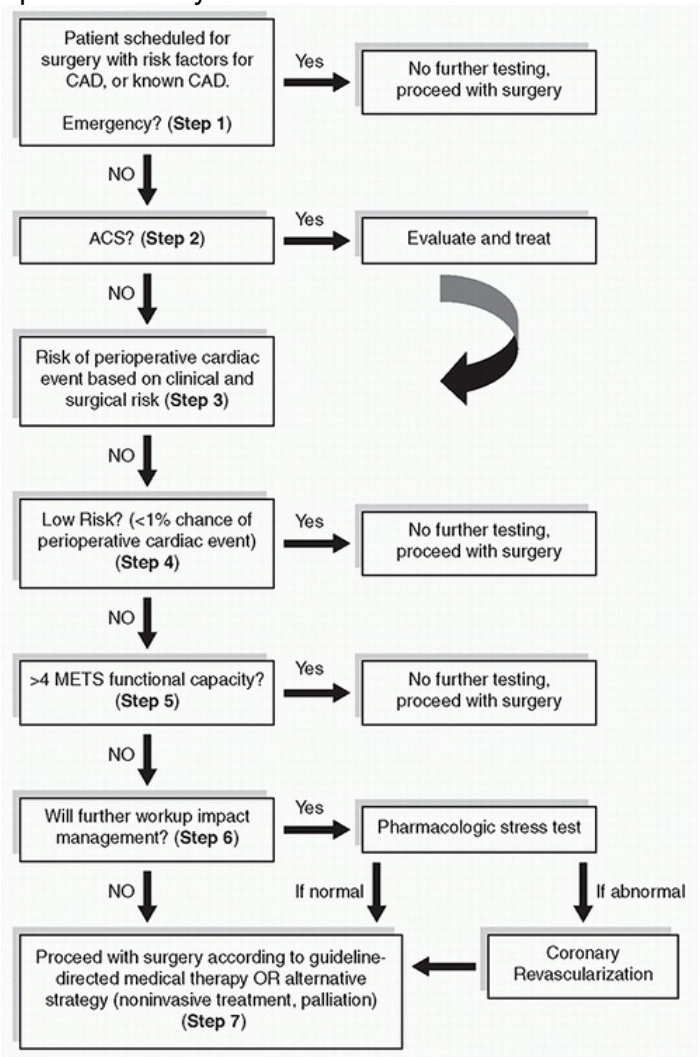


FIGURE 10.2 Stepwise algorithm for preoperative assessment for patients with coronary artery disease (CAD) undergoing noncardiac surgery. ACS, acute coronary syndrome. (Modified from Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guidelines on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:2215-2245.)

Recent evidence also suggests that patients at significant risk for ischemic heart disease may benefit from an endovascular approach, if anatomically feasible.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:2215-2245.

Hertzer NR, Beven EG, Young JR, et al. Coronary artery disease in peripheral vascular patients. A classification of 1000 coronary angiograms and results of surgical management. *Ann Surg.* 1984;199:223-233.

Kertai MD. Preoperative coronary revascularization in high-risk patients undergoing vascular surgery: a core review. *Anesth Analg*. 2008;106:751-758.

Troisi N, Dorigo W, Lo Sapio P, et al. Preoperative cardiac assessment in patients undergoing aortic surgery: analysis of factors affecting the cardiac outcomes. *Ann Vasc Surg*. 2010;24:733-740.

B.3. Is it necessary to evaluate this patient's pulmonary status?

The patient's smoking history and the chronic changes present on his chest radiograph are evidence of chronic obstructive

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pulmonary disease (COPD). Provided the patient is minimally symptomatic and has good functional status, a detailed history and thorough physical exam can provide significant information regarding pulmonary status. A chest radiograph can be particularly useful at detecting underlying lung infection. If the radiograph displays the absence of acute pulmonary processes, as in this patient, further pulmonary testing may not be indicated. In the patient with severe signs and symptoms of COPD, an ABG analysis can be particularly helpful. ABG analysis can evaluate the patient's ability to oxygenate and ventilate. Patients with severe COPD tend may be chronically hypercarbic and hypoxic. A preoperative ABG is particularly helpful at guiding perioperative ventilatory management and predicting the likelihood of postoperative mechanical ventilation in these patients.

In those patients with severe disease, particularly those with poor functional status and significant findings on physical exam and chest radiograph, pulmonary function testing may be indicated. Preoperative pulmonary function testing evaluates baseline forced vital capacity (VC) and FEV1. Maximum midexpiratory flow rate (MMEFR) is an effort-independent value that is a sensitive index of small airway obstruction. Peak expiratory flow rate is related to the FEV1 and MMEFR, although often it is less reproducible. These tests should be performed before and after bronchodilator therapy to assess reversibility of airway obstruction. A 15% improvement is considered a positive response.

This patient is a two pack-per-day smoker with dyspnea on exertion, and the anticipated surgery required an upper abdominal incision. These factors likely affect his baseline pulmonary function and presage postoperative ventilatory problems. A VC less than 50% of predicted, or less than 2 L total, is an indicator of increased risk of pulmonary complications as a VC at least three times the tidal volume is necessary for an effective cough. FEV1 less than 2 L, maximum breathing capacity less than 50% of predicted, and MMEFR less than 50% of predicted are also values associated with increased risk of postoperative mechanical ventilation.

Discontinuation of smoking for 48 hours preoperatively increases oxygen tissue availability and, if stopped 4 to 6 weeks before surgery, may decrease postoperative complications. Pulmonary function tests should be viewed as a management tool to optimize preoperative pulmonary function should not be the sole means of assessing risk. Functional status, severity of illness, and comorbid medical conditions also have significant predictive value.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:181-217.

Niewoehner DE. Clinical practice. Outpatient management of severe COPD. *N Engl J Med*. 2010;362(15): 1407-1416.

Warner DO. Preventing postoperative pulmonary complications. The role of the anesthesiologist. *Anesthesiology*. 2000;92:1467-1472.

B.4. Preoperative arterial blood gas (ABG) measurement shows pH, 7.35; $PaCO_2$, 47 mm Hg; and PaO_2, 68 mm Hg on room air. What is the significance of this result?

The normal value for PaO_2 in young adults ranges from 85 to 100 mm Hg with an average of about 95 mm Hg. This value falls steadily with aging to an average PaO_2 of 80 mm Hg at age 60 years. One formula for estimating PaO_o is PaO_2 = 100 - (age in years / 3). The normal range for $PaCO_2$ is 37 to 43 mm Hg and is unaffected by aging. For every 10 mm Hg increase in $PaCO_2$, pH decreases by 0.05. For every 10 mm Hg decrease in $PaCO_2$, pH increases by 0.1.

The main causes of arterial hypoxemia are hypoventilation, diffusion impairment, shunting, and ventilation/perfusion ([V with dot above]/[Q with dot above]) mismatch. The major causes of hypercarbia or carbon dioxide retention are hypoventilation and [V with dot above]/[Q with dot above] mismatch. Mild [V with dot above]/[Q with dot above] mismatch does not necessarily cause an increase in arterial CO_2. This is due to the fact that CO_2 is a highly diffusible gas and central chemoreceptors compensate for increasing CO_2 tension by causing an increase in ventilation. The same is not true of arterial oxygenation, however, as even mild degrees of [V with dot above]/[Q with dot above] mismatch can lead to hypoxemia.

The assessment of this patient's blood gas analysis reveals moderate hypoxemia with a mildly elevated CO_2 tension. The pH is consistent with a mild respiratory acidosis. The most likely reason for this patient's blood gas abnormality is [V with dot above]/[Q with dot above] mismatch, secondary to COPD, which is likely the result of his extensive smoking history.

West JB. *Respiratory Physiology: The Essentials*. 9th ed. Baltimore: Lippincott Williams & Wilkins; 2012:56-76.

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B.5. How would you measure creatinine clearance in this patient, and what is its value in this case?

Preoperative renal dysfunction indicates potential postoperative impairment. Despite maximal medical management, including hemodialysis, acute renal failure (ARF) after aortic reconstruction carries a mortality of greater than 30% postoperatively. Maintenance of intravascular volume and adequate blood pressure are the best means of avoiding postoperative renal failure. This complication is more likely in patients requiring a suprarenal cross-clamp but also occurs with infrarenal clamping.

Operative mortality is 19% when aortic reconstruction is performed on patients with a creatinine greater than 2 mg per dL, but mortality is only 4.6% if the levels are lower. Therefore, if the creatinine is greater than 2 mg per dL, reversible factors, such as renal stenosis, should be investigated. The most direct measurement of glomerular filtration rate (GFR) is the measurement of creatinine clearance. Although BUN and serum creatinine are related to renal function, they are altered by such nonrenal factors as protein metabolism, diet, liver dysfunction, or skeletal muscle mass. A 24-hour collection of urine is measured, and the following equation is used to calculate GFR: GFR = U × V / P. U, urine concentration of creatinine (mg per dL); V, volume of urine measured (mL per minute); P, plasma concentration of creatinine (mg per dL). A 2-hour sample collected through a Foley catheter has been shown to correlate well with a 24-hour sample collection.

In spite of the widespread use of creatinine clearance to detect renal impairment, it should be noted that as much as 50% of functional nephron mass may be lost before changes in creatinine concentration become apparent. As a result, patients with lower baseline creatinine concentration can have acute kidney injury (AKI) despite normal creatinine clearance. Several novel biomarkers are being studied now that may be able to detect AKI earlier than traditional markers such as urinary output and serum creatinine. Neutrophil gelatinase-associated lipocalin (NGAL) is a protein found in excess in urine and plasma in patients with AKI as many as 48 hours prior to increase in serum concentration. Serum cystatin C, a protease inhibitor that is less affected by sex, age, muscle mass, and diet than creatinine, also allows earlier detection of AKI.

Borthwick E, Ferguson A. Perioperative acute kidney injury: risk factors, recognition, management, and outcomes. *BMJ*. 2010;340:c3365.

Sladen RN. Anesthetic considerations for the patient with renal failure. *Anesthesiol Clin North America*. 2000;18:863-882.

B.6. Describe the blood flow to the spinal cord. What is its relevance to surgery involving the abdominal aorta?

The spinal cord has a system of longitudinal arteries and a system of transverse arteries as shown in Figure 10.3. Anatomic studies have shown that the most important longitudinal arteries are a single anterior spinal artery supplying 75% of the cord and a pair of posterior spinal arteries supplying 25% of the cord. Although in humans the anterior spinal artery is a continuous vessel, modern anatomy has emphasized the importance of the reinforcing transverse arteries rather than the meager longitudinal vessels. The territory supplied by the anterior spinal artery is divided into three functionally distinct levels: cervicodorsal, intermediate or midthoracic, and thoracolumbar. The cervicodorsal region receives its blood supply from the vertebral, subclavian, thyrocervical, and costocervical arteries. The midthoracic region is supplied by a meager left or right intercostal artery arising between the fourth and the ninth thoracic vertebrae. The thoracolumbar region of the anterior spinal artery receives its blood supply mainly from one of the intercostal arteries called the arteria radicularis magna or the

artery of Adamkiewicz. It arises at the level of T5-T8 in 15%, T9-T12 in 60%, L1 in 14%, and L2 in 10% of patients. The arteria radicularis magna often is involved in the surgical repair.

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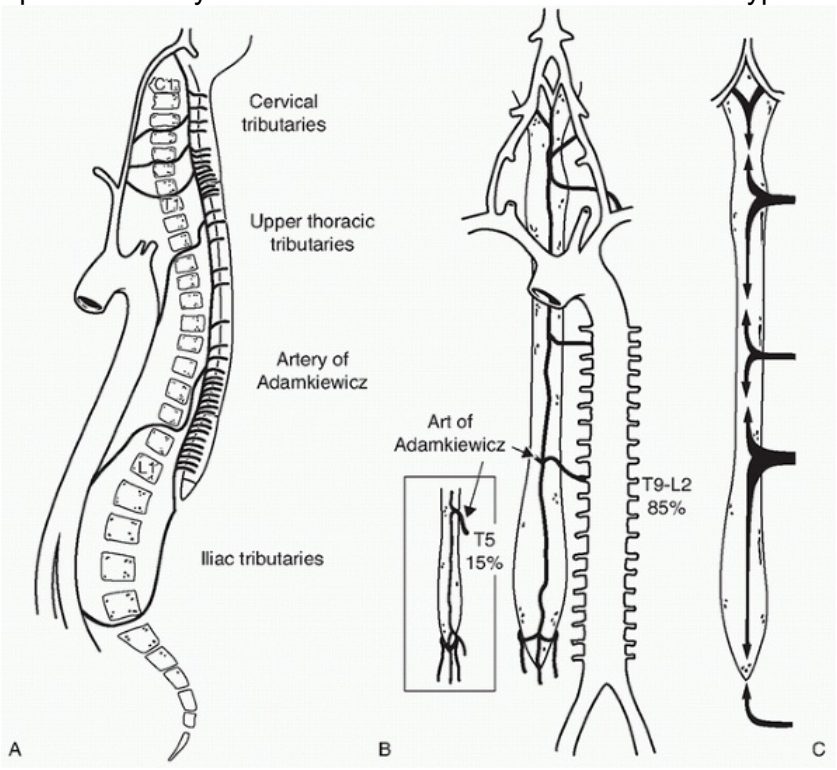
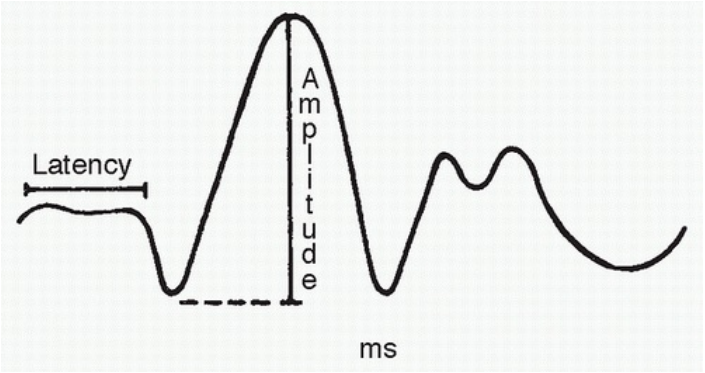


FIGURE 10.3 Diagram to show components of the anterior spinal artery. **A.** Arterial view. **B.** Anteroposterior view showing origins of artery of Adamkiewicz. **C.** Schematic representation of direction and volume of flow from nutrient vessels supplying the anterior spinal artery. Size of arrows is proportional to flow contribution. (Adapted from Bromage PR. *Epidural Anesthesia*. Philadelphia, PA: WB Saunders; 1978:50-54.)

The anterior spinal artery is smaller above than below the entry of the arteria radicularis magna. Resistance to blood flow is 51.7 times greater going up the anterior spinal artery as compared with coming down the artery. Therefore, distal aortic perfusion during thoracic aortic cross-clamping protects the spinal cord below the arteria radicularis magna but not above it. This is why paraplegia still occurs in approximately 2% to 15% of patients having thoracic aortic surgery with distal aortic perfusion. However, reimplantation of intercostal arteries during surgery has been shown to reduce the incidence of neurologic injury.

Spinal cord ischemia can develop during aortic cross-clamping as a result of one of two mechanisms: decreased blood flow through critical intercostal arteries (important in infrarenal cross-clamping) and hypotension in the aorta distal to the cross-clamp, leading to a “steal” phenomenon through the collateral circulation to the distal aorta (important in thoracic cross-clamping). There are many strategies to prevent spinal cord ischemia: moderate hypothermia (local and systemic), cerebrospinal fluid drainage, and femoral-femoral bypass. The only definitive methods of preservation are fast surgery and maintenance of cardiac output.

Ling E, Arellano R. Systematic overview of the evidence supporting the use of cerebrospinal fluid drainage in thoracoabdominal aneurysm surgery for prevention of paraplegia. *Anesthesiology*. 2000;93:1115-1122.



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FIGURE 10.4 Typical somatosensory evoked potential trace. (From Cunningham JN Jr, Laschinger JC, Merkin HA, et al. Measurement of spinal cord ischemia during operations upon the thoracic aorta: initial clinical experience. *Ann Surg*. 1982;196:285-296, with permission.)

B.7. How do you detect spinal cord ischemia?

Evoked potential is used in thoracoabdominal surgery to detect spinal cord ischemia. Two varieties of evoked potential are used in thoracoabdominal aortic aneurysm repair. SSEPs travel through the dorsal root ganglia to the posterior columns of the spinal cord. The potentials continue along the lemniscal pathways on to the thalamus and the cortex. Comparison of the latency and amplitude of the potentials, tested minutes apart, define the degree of change in the SSEP. Temperature, anesthetic depth, and changes in blood flow can alter the evoked potentials. Changes in blood flow through the anterior spinal artery are not reflected in the posterior columns. It is possible, therefore, to have paralysis with normal SSEPs.

Ischemia of the spinal cord is indicated by increases in latency and/or decreases in amplitude of evoked potential tracing. The typical SSEP trace is shown in Figure 10.4, and its response to aortic cross-clamping is shown in Figure 10.5. The latency increases as early as 4 minutes following aortic cross-clamping, with progress to cessation of spinal cord conduction within 7 minutes of cross-clamping. Return of spinal cord conduction occurs 47 minutes following distal aortic reperfusion, with return to normal spinal cord conduction within 24 hours after operation. It has been shown that the loss of SSEP signals for longer than 14 to 30 minutes was associated with postoperative neurologic deficit.

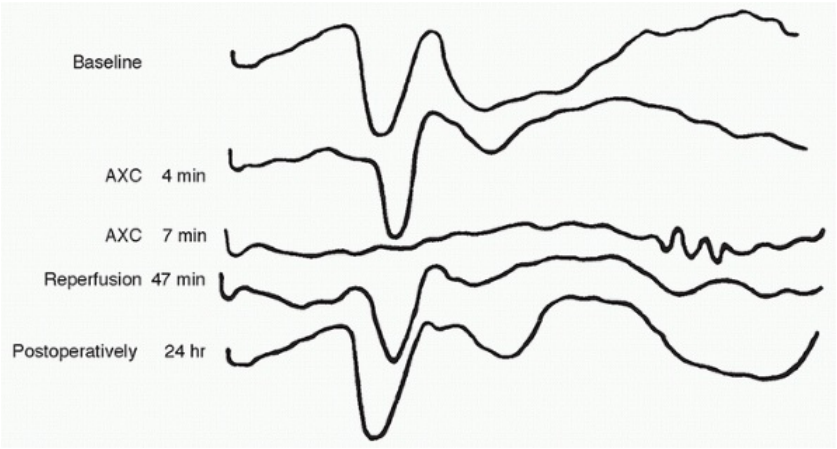


FIGURE 10.5 Somatosensory evoked potential response to aortic cross-clamping (AXC). (From Cunningham JN Jr, Laschinger JC, Merkin HA, et al. Measurement of spinal cord ischemia during operations upon the thoracic aorta: initial clinical experience. *Ann Surg.* 1982;196:285-296, with permission.)

Motor evoked potentials (MEPs) do monitor areas of the cord supplied by the anterior spinal artery. To assess MEP, patients require partial paralysis and light plane of anesthesia. Both of these requirements are suboptimal anesthetic options for a thoracoabdominal aortic aneurysm repair.

Finally, the signal-to-noise ratio of evoked potentials make interpretation of the data in the operating room more difficult and less reliable.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1000-1012.

Meylaerts SA, Jacobs MJ, van Iterson V, et al. Comparison of transcranial motor evoked potentials and somatosensory evoked potentials during thoracoabdominal aortic aneurysm repair. *Ann Surg*. 1999;230:742-749.

B.8. What are the various surgical approaches to repair an AAA?

The classic approach to the abdominal aorta is through a vertical anterior midline incision with a transperitoneal approach to the retroperitoneal space. This gives access to all major arteries in the abdomen and pelvis. A transverse abdominal incision (supraumbilical) is also adequate for a transperitoneal approach. Although the entry is slower, there is less pain and pulmonary impairment postoperatively. The transperitoneal approach, with the necessary exposure of the abdominal

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organs, causes major heat and fluid loss and prolonged postoperative ileus.

The retroperitoneal approach is performed through a left flank incision with the patient in the right lateral decubitus position. In some studies, this approach has been shown to have less respiratory and wound complications, less postoperative ileus, less blood loss, lower fluid requirements, and earlier discharge from the hospital. Monitoring and line placement must take the lateral position into consideration.

A less invasive approach to aortic aneurysm repair is endovascular aortic repair (EVAR) surgery. As stent graft technology improves, this technique is being employed in an increasing number of patients. The EVAR technique has the advantage of a shorter length of stay relative to open repair and a shortened recovery period. Due to the cost of the stents and imaging equipment, this does not necessarily translate to overall cost reduction. Anatomic issues can significantly complicate stent placement. A common problem is iliac and common femoral arteries that are of insufficient caliber. Successful aneurysm exclusion has been achieved in 50% to 90% of selected cases. Problems of the procedure include vessel perforation, inability to seal the aneurysm (endoleaks), and inability to advance the device past the iliac artery, ultimately necessitating the conversion to an open repair.

In the Endovascular Aneurysm Repair (EVAR) and Dutch Randomized Endovascular Aneurysm Management (DREAM) randomized clinical trials, reinterventions were required in two to three times as many patients in the endovascular group as in those who had open repair. Endovascular leaks are one of the leading causes of postoperative complications necessitating reintervention in up to 15% of patients. The various types of endovascular leaks are shown in Figure 10.6. In the EVAR-1 trial, postoperative complications were five times more frequent with endovascular repair when compared to the open repair group. This highlights the importance of close follow-up in these patients and necessitates periodic reimaging for the remainder of these patients' lives. It is also worthy to note that endovascular repair has not been shown to improve survival in patients who have medical contraindication to open repair.

In contrast, when compared with open abdominal repair in the perioperative period, endovascular surgery is associated with 60% less blood loss, sooner extubation, and fewer days spent in the intensive care unit and the hospital in total. Currently, overall mortality of the procedures appears similar, and when using the Eagle criteria as a predictor of adverse cardiac events for patients undergoing major vascular surgery, it appears that a history of CHF and Q waves on ECG are predictive of cardiac events (6% in the open repair group vs. 4.8% in the endovascular group).

EVAR Trial Participants. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet*. 2004;364:843-848.

EVAR Trial Participants. Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysms (EVAR trial 2): randomised controlled trial. *Lancet*. 2005;365:2187-2192.

Huang Y, Gloviczki P, Oderich GS, et al. Outcome after open and endovascular repairs of abdominal aortic aneurysms in matched cohorts using propensity score modeling. *J Vasc Surg*. 2015;62:304-311.

Prinssen M, Verhoeven EL, Buth J, et al; for Dutch Randomized Endovascular Aneurysm Management (DREAM) Trial Group. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med*. 2004;351:1607-1618.

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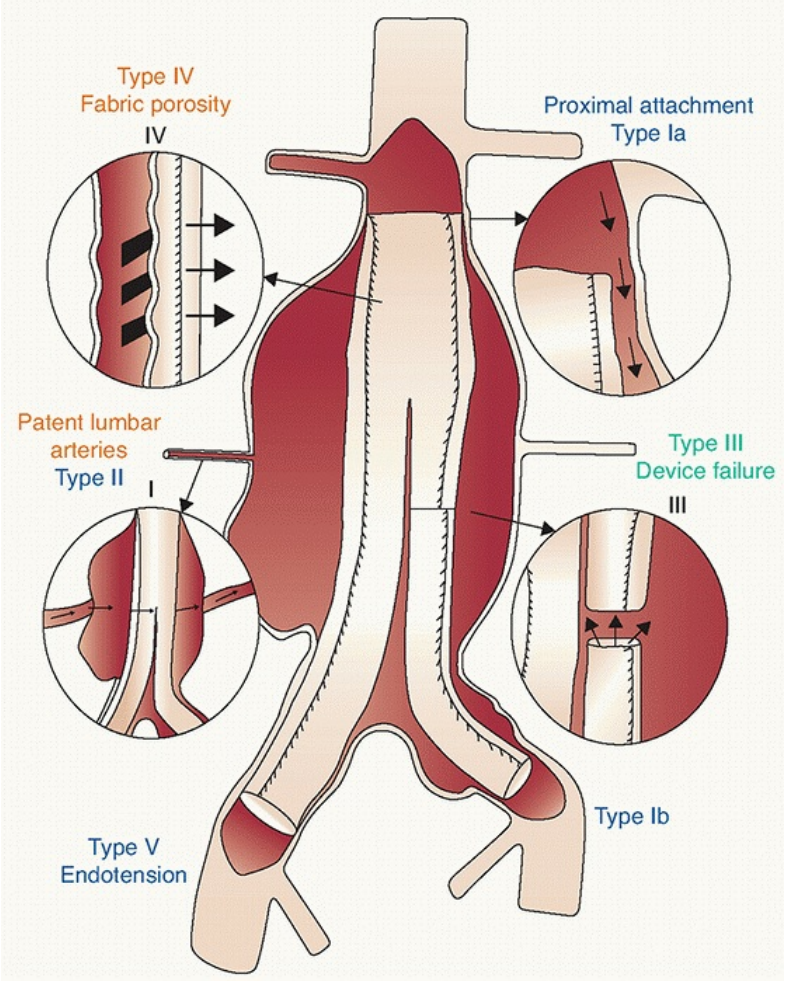


FIGURE 10.6 Types of endovascular leaks. (Adapted from Abdominal aortic aneurysms (AAA). http://www.vascular.co.nz/abdominal_usaortic_usaneurysms .htm. Updated July 13, 2009. Accessed June 2, 2010.)

B.9. How does the choice of surgical technique affect the anesthetic management?

Different anesthetic techniques can be employed for both open and endovascular repairs of AAA (see section C.5). Debate exists over the advantages of general anesthesia compared with regional anesthesia or combined approaches to the management of patients with CAD. Meticulous control of heart rate and blood pressure should be the goals of any method chosen. Regional anesthesia has the potential to decrease coronary perfusion pressure as sympathetic tone is diminished and general anesthesia risks increases in sympathetic stimulation with intubation and emergence. Regional anesthesia may decrease hypercoagulability and thrombotic events in patients undergoing vascular surgery. In addition, the epidural may be used to prevent the sympathetic stimulation caused by postoperative pain.

The goals for the management of patients with CAD should include prevention and control of the effects of sympathetic nervous system stimulation. This can be achieved by using β-antagonists, narcotics, or volatile anesthetics during the perioperative period. Coronary perfusion pressure, defined as aortic diastolic pressure minus left ventricular end

diastolic pressure, should be meticulously maintained. Myocardial contractility and heart rate should not be increased as this will increase oxygen demand.

DeVirgilio C, Romero L, Donayre C, et al. Endovascular aortic aneurysm repair with general versus local anesthesia: a comparison of cardiopulmonary morbidity and mortality rates. *J Vasc Surg*. 2002;36:988-991.

Ellis JE, Roizen MF, Youngberg JA. Anesthesia for abdominal aortic revascularization. In: Youngberg JA, Lake CL, Roizen MF, et al, eds. *Cardiac, Vascular and Thoracic Anesthesia*. Philadelphia, PA: Churchill Livingstone; 2000:336-337.

Warltier DC, Pagel PS, Dersten JR. Approaches to the prevention of perioperative myocardial ischemia. *Anesthesiology*. 2000;92:253-259.

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B.10. How would you premedicate this patient?

The most common problem a patient faces when presenting to the operating room is anxiety. Methods to relieve anxiety need to be individualized for each patient and may vary based on the preference of the anesthesiologist. Any drugs that are given should be titrated to the goals of the induction and surgery and minimize deleterious side effects. Typically, a low-dose anxiolytic is likely to be sufficient premedication for most patients. Any other preoperative medications can be given intravenously upon arrival to the operating room. If oral medications are indicated, they may be taken with a sip of water 1 hour prior to the procedure. In addition, psychological preparation for surgery is an effective technique for reducing preoperative anxiety and should be undertaken by the anesthesiologist.

Additional specific pharmacologic regimens should be tailored to individual patient needs. Various medications and combinations have been used, including narcotics, anticholinergics, barbiturates, and benzodiazepines. No single agent or combination has been demonstrated to be superior to others. Certainly, respiratory depressants should be avoided in patients who are at risk for hypoventilation (e.g., chronic CO_2 retention).

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:846-849.

Clark SK, Rung GW, Hensley FA. Premedication for the vascular surgery patient. In: Kaplan JA, ed. *Vascular Anesthesia*. New York: Churchill Livingstone; 1991:187-204.

C. Intraoperative Management

C.1. Would you use an arterial line? What are the complications of arterial line placement?

Arterial pressure monitoring is exceedingly important in this case, from induction of anesthesia through emergence. In this patient with a history of CAD, an arterial line is particularly important for blood pressure management during induction and should be placed prior to the institution of anesthesia.

Vascular insufficiency and infection are the two major complications of arterial line placement. Catheter size and duration of cannulation are implicated in vascular occlusion. The causes of most vascular injuries are embolic. Radial artery cannulation is a low-risk, high-benefit method that can be used to closely monitor blood pressure in this patient. Open AAA repair is frequently associated with blood pressure lability, particularly on clamping and unclamping, and arterial blood pressure monitoring is particularly helpful in this situation. In addition, frequent sampling of ABGs to assess hematocrit, ventilation, perfusion, electrolyte levels, glucose, and level of anticoagulation may be necessary. If a radial artery catheter cannot be placed, cannulation attempts can be made at the brachial and axillary arteries. Concerns have been raised that brachial artery cannulation might be inadvisable given the lack of adequate collateral supply to the forearm and hand. In practice, however, complications from brachial artery cannulation have been reported rarely and the risk of vascular insufficiency appears to be not different from that of radial cannulation. Axillary artery cannulation, however, may carry an added risk of vascular insufficiency and nerve injury from thrombosis and hematoma formation. This added risk is likely due to the fact that the axillary neurovascular bundle travels in the confined space of the axillary sheath.

Slogoff S, Keats AS, Arlund C. On the safety of radial artery cannulation. *Anesthesiology*. 1983;59:42-47.

C.2. What various monitors are available for myocardial ischemia? Is a pulmonary artery catheter (PAC) helpful in determining the occurrence of ischemia?

Monitoring of the patient undergoing aortic reconstruction surgery should be aimed at preserving myocardial, pulmonary, and renal function as well as maintaining intravascular volume. Therefore, it is mandatory, particularly in the patient with known CAD, to monitor for myocardial ischemia and maintain volume status in the face of fluid shifts. Monitoring of the ST segments of the V_5 and II leads of the ECG is the most common method used to assess for intraoperative myocardial ischemia. However, in some studies, this alone was insufficient to recognize from 40% to 75% of intraoperative ischemic events detected by wall-motion abnormalities seen with a two-dimensional transesophageal echocardiogram.

Monitoring the PA pressure tracing for the appearance of V waves and increasing PCWP with decreasing cardiac output are other methods of detecting intraoperative myocardial ischemia. Unfortunately, the PAC is not a particularly sensitive technique for detecting ischemic events. Wall-motion abnormalities, detected by transesophageal echocardiography (TEE), are highly sensitive markers of myocardial ischemia and appear earlier than either ST segment or PAC waveform

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changes.

A microcomputer-based ECG reader (ST-segment trend monitor) also has been advocated as a monitor of myocardial ischemia. These systems can pick up more subtle changes in ST segments than by simple observation. Multilead ECG systems are most helpful. The most sensitive means for monitoring patients to determine the development of myocardial ischemia at its earliest presentation is, in fact, wall-motion abnormalities demonstrated by two-dimensional TEE. As yet, no improvement in outcome has been demonstrated by the use of any of these monitors.

American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Practice guidelines for perioperative transesophageal echocardiography. An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology*. 2010;112(5):1084-1096.

American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. Practice guidelines for pulmonary artery catheterization: an updated report by the American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. *Anesthesiology*. 2003;99:998-1014.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1137-1138.

C.3. What additional monitors would you employ?

An invasive monitor of volume status is recommended in patients undergoing open AAA repair. The choice of invasive monitoring, central venous pressure (CVP) or PAC can be based on the level of aortic cross-clamping and the severity of the patient's underlying cardiac disease. The CVP is informative at low and high extremes. As the right side of the heart is usually a compliant system, large shifts of intravascular volume may occur without significant CVP alteration. The PCWP, obtained by a PAC, may be more accurate in determining intravascular volume status. In addition, the PAC allows for measurement of cardiac output, helpful during aortic cross-clamp in the patient with left ventricular dysfunction. In this situation, CVP may not accurately represent left-sided pressures reflected by the PCWP. This is also true of the patient with significant pulmonary disease. The decision of PAC placement can also be influenced by the level at which the cross-clamp is applied. Suprarenal and supraceliac cross-clamping are associated with greater hemodynamic lability than infrarenal clamp application. Thus, PAC insertion may be of greater utility during proximal procedures, particularly if cardiac dysfunction is also present.

In spite of all the conceptual benefits attributed to the use of PAC, there is a paucity of evidence demonstrating a reduction of morbidity and mortality. In addition, the risk of pulmonary artery rupture, arrhythmias, and complications associated with introducer placement should be considered prior to placement of a PAC. The ASA practice guidelines support the prudent use of a PAC in select situations. PAC might be used in high-risk procedures (cardiac, aortic reconstruction, anticipated hemodynamic instability, and large-volume fluid shifts), in patients with a minimal risk of complication from catheter placement, and when appropriate staff (familiar with PAC troubleshooting) is available. Further, when such monitoring is employed, it should only be utilized by those who are trained to appropriately interpret and intervene on the data.

TEE is another monitoring modality that is being increasingly utilized in aortic reconstruction procedures. TEE has several potential benefits over other invasive monitors such as the PAC and the CVP. Currently, TEE is the most sensitive modality for detecting myocardial ischemia. It is able to detect regional wall motion abnormalities well before changes appear on other heart monitors such as the ECG or PAC. In addition, TEE allows for detailed analysis of valvular dysfunction which may significantly alter perioperative anesthetic management. The ASA practice guidelines for perioperative TEE make specific recommendations guiding the appropriate use of TEE in noncardiac surgery. According to the guidelines, the use of TEE may be appropriate when the nature of the planned surgery or the patient's cardiovascular pathology might result in severe hemodynamic, pulmonary, or neurologic compromise. In addition, TEE should be used when unexplained life-threatening circulatory instability persists despite corrective therapy.

Another useful measure of intravascular volume status, as well as renal blood flow, is the collection of urine through a Foley catheter. Urine output will diminish with decreasing glomerular filtration caused by decreased renal blood flow. Assessment of urine output, provided kidney function is unimpaired, can be an accurate and cost-effective measure of volume status.

Temperature monitoring should also be employed as with any case under general anesthesia. Body temperature should be closely monitored and aggressively maintained. These patients can undergo tremendous heat and insensible fluid loss as a result of the enormous incisional surface area exposed to room air. If forced hot air thermal blankets are used, they are contraindicated on the lower extremities when an aortic cross-clamp is applied. They may, however, be used on the upper body throughout the procedure, along with fluid warmers, to maintain temperature.

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Finally, pulse oximetry, capnography, and mass spectral analysis of inhaled agents also should be utilized. This data combined with ABG analysis will permit efficient ventilatory management and accurate delivery of anesthetic gases.

American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Practice guidelines for perioperative transesophageal echocardiography. An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology*. 2010;112(5):1084-1096.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1128-1138.

C.4. Is there a role for somatosensory evoked potential (SSEP) monitoring during aortic clamping?

SSEPs can be used during aortic reconstruction surgery to monitor spinal cord function. For thoracic aortic surgery, SSEPs remain stable if the distal aortic pressure is maintained above 60 mm Hg. At lower pressures, SSEPs gradually disappear. In one study, paraplegia occurred in five of six patients whose SSEPs remained absent for more than 30 minutes. Patients should be monitored for SSEP changes if they are at higher risk of spinal cord ischemia. SSEPs are most commonly altered in patients with baseline risk for neurologic complications. Proximal (especially thoracic) or prolonged cross-clamp placement increases risk for neurologic embarrassment. With a conduction block in place, such as epidural or spinal anesthesia, SSEPs will be ablated.

Ellis JE, Roizen MF, Youngberg JA. Anesthesia for abdominal aortic revascularization. In: Youngberg JA, Lake CL, Roizen MF, et al, eds. *Cardiac, Vascular and Thoracic Anesthesia*. Philadelphia, PA: Churchill Livingstone; 2000:336-337.

C.5. How would you anesthetize this patient for an open repair of the aorta? What techniques could be used for an endovascular aortic aneurysm repair? Discuss the various anesthetic techniques that can be employed for this surgery.

All anesthetic techniques have been used and advocated for abdominal aortic surgery. General anesthesia, regional blockade, or combined general and regional techniques have all have been described. Outcome studies are equivocal among the various techniques, affording flexibility in the anesthetic approach to these patients. Tailoring this plan to each patient's medical condition is the most effective strategy. The primary goals in the anesthetic management of patients undergoing aortic reconstruction include protection of myocardial, neurologic, and renal function.

When combined regional (epidural) and general anesthesia techniques are employed, fluid requirements may be increased in order to maintain hemodynamic stability. Typically, this additional fluid requirement can be up to 2 L per case. In addition, neuraxial sympathectomy can predispose to hypotension upon clamp removal. The use of α-agonist vasoconstriction will counteract the vasodilatory effects of epidural anesthesia and may reduce fluid requirements. In addition, the placement of an epidural catheter will afford optimal postoperative pain management of the patient.

Anesthesia for endoluminal repair has ranged from general, general combined with epidural anesthesia, lumbar epidural with sedation, or sedation with local anesthesia. Considerations for choice of anesthesia include the need for patient immobility, the need for systemic anticoagulation (heparin), the possibility of exsanguination, and prevention of heat loss. Blood pressure stability is imperative during aortic balloon occlusion to prevent distal migration of the stent. If neuraxial techniques are used, coagulation status must be carefully monitored in the perioperative period.

Norris EJ, Beattie C, Perler BA, et al. Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. *Anesthesiology*. 2001;95:1054-1067.

Ruppert V, Leurs LJ, Steckmeier B, et al. Influence of anesthesia type on outcome after endovascular aortic aneurysm repair: an analysis based on EUROSTAR data. *J Vasc Surg*. 2006;44:16-21.

Yaeger MP, Burns AK. Regional versus general anesthesia for major vascular surgery. In: Kaplan JA, Lake CL, Murray MJ, eds. *Vascular Anesthesia*. 2nd ed. New York: Churchill Livingstone; 2004:165-186.

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C.6. This patient is to be heparinized intraoperatively, and anticoagulation may be continued postoperatively. Is this a contraindication to the preoperative placement of either an epidural or intraspinal catheter? What if the patient is receiving anticoagulants in the preoperative period?

Epidural catheter placement in the setting of anticoagulation increases the risk of an epidural hematoma and subsequent neurologic deficit. Procedural risk of spinal cord ischemia will confound the diagnosis of neuraxial hematoma and may preclude the placement of an epidural catheter. However, an epidural catheter can be placed with a relative degree of confidence in patients who are not anticoagulated at the time of the puncture but who will receive anticoagulation later. Current guidelines suggest administration of intravenous heparin at least 1 hour after neuraxial catheter placement. Further, in patients who have undergone systemic heparinization, heparin should be discontinued for at least 2 to 4 hours prior to epidural catheter removal. Coagulation status must be assessed prior to catheter manipulation, and frequent lower extremity neurologic assessment must continue for at least 12 hours after catheter removal.

Low molecular weight heparins (LMWHs), which are increasingly being employed for thromboprophylaxis, pose a significant potential for increased risk of neuraxial hematoma. In patients receiving these drugs, needle placement should occur at least 12 hours after the last dose of LMWH. If higher doses have been used (e.g., enoxaparin 1 mg per kg twice daily), needle placement should be delayed at least 24 hours. It is currently recommended that indwelling catheters be removed prior to initiation of LMWH thromboprophylaxis. In addition, the first dose should be administered at least 2 hours after catheter removal.

In those patients who are on chronic anticoagulation with oral warfarin, several recommendations are applicable with regard to perioperative management of neuraxial anesthesia. Oral warfarin should be discontinued at least 4 to 5 days prior to surgery. International normalized ratio (INR) should be measured at least 24 hours prior to the procedure. Neuraxial manipulation must commence only when INR has normalized. Neurologic testing of sensory and motor function should be performed routinely during epidural analgesia for patients on warfarin therapy. The type of analgesic solution should also be tailored to minimize the degree of sensory and motor blockade so as to allow frequent neurologic monitoring. As thromboprophylaxis with warfarin is reinitiated in the postsurgical period, neuraxial catheters should be removed while the INR is less than 1.5.

Fibrinolytic and thrombolytic drugs predispose to a high risk of hematoma formation in conjunction with neuraxial technique. Recent American Society of Regional Anesthesia and Pain Medicine (ASRA) practice guidelines, addressing regional anesthesia in the

anticoagulated patient, recommend avoidance of all neuraxial manipulation in patients who have received thrombolytic or fibrinolytic therapy. There appears to be no clear data detailing the length of time neuraxial puncture should be avoided after discontinuation of these drugs.

While the use of antiplatelet agents such as aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) does not contraindicate the use of neuraxial techniques, care should be exercised when combinations of anticoagulants and antiplatelet drugs are used. Such combinations increase the risk of hemorrhagic complications in the perioperative period. Neurologic testing of sensory and motor function should be routinely performed on patients with indwelling catheters undergoing simultaneous anticoagulation. Again, analgesic solutions should be tailored to minimize sensory and motor changes to allow for close neurologic monitoring.

Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). *Reg Anesth Pain Med*. 2010;35:64-101.

C.7. What are your plans for fluid and blood replacement during surgery?

Fluid replacement should be aimed at maintaining the patient's intravascular filling pressures. Isotonic crystalloid should be used because there is little evidence to suggest that colloid administration poses any advantage over crystalloid administration.

There has been much controversy in recent literature regarding the use of “liberal” versus “restrictive” fluid protocols during open abdominal procedures. Most of this data has been gathered on patients undergoing bowel procedures but applicable to the patient undergoing open AAA repair. There is a lack of consensus regarding the optimal fluid management protocol. What has emerged from this data is the use of fluid therapy to optimize tissue perfusion rather than predefined volume replacement.

Current paradigm suggests a shift away from the classic model of calculation of nothing by mouth (NPO) fluid deficit, intraoperative insensible losses, and third-space losses. Increasingly, most clinicians are employing “demand-related” regimens with the goal of maximizing tissue blood flow while minimizing interstitial edema. Intravascular losses are

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replaced by timely fluid and blood product administration as measured by visual blood loss, vital signs, urinary output, hematocrit, acid-base status, and invasive hemodynamic monitoring (as available). Insensible losses are replaced at 0.5 to 1 mL/kg/hr, a significantly lower rate than what has previously been utilized. The traditional concept of a third-space compartment is increasingly being abandoned. Instead, it is now recognized that fluid shift into the interstitium is a function of crystalloid overload and deterioration of vascular integrity.

The concurrent use of an autotransfuser (e.g., Cell Saver) decreases the need for exogenous blood transfusions. Judicious blood product administration should be avoided due to increased risk of immune suppression, hemolytic transfusion reactions, infectious vector transmission, and lung injury.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1137-1138.

Chappell D, Jacob M, Hofmann-Kiefer K, et al. A rational approach to perioperative fluid management. *Anesthesiology*. 2008;109:723-740.

Grocott MP, Mythen MG, Gan TJ. Perioperative fluid management and clinical outcome in adults. *Anesth Analg*. 2005;100:1093-1106.

Jacob M, Chappell D, Rehm M. Clinical update: perioperative fluid management. *Lancet*. 2007;369:1984-1986.

C.8. What are the hemodynamic changes of aortic cross-clamp placement? What efforts can be made to minimize these changes both before and during cross-clamping? If the patient develops ST-segment depressions with a rising pulmonary capillary wedge pressure (PCWP) during cross-clamp, what maneuvers should be taken?

The systemic hemodynamic response to aortic cross-clamping is shown in Figure 10.7.

Arterial hypertension is the most dramatic and consistent result of the application of an aortic cross-clamp. This is the result of sudden increases in afterload and left ventricular end-diastolic wall stress. Usually, these changes are accompanied by decreased cardiac output. Some of these changes may also be due to redistribution of blood volume from the venous vasculature to

the upper part of the body. All of the previously stated factors are more profound in the case of supraceliac or thoracic cross-clamp placement. Variations in blood volume status or splanchnic vascular tone are affected by the anesthetic depth, anesthesia technique, and intravascular volume status. These factors all determine the pattern of blood volume redistribution.

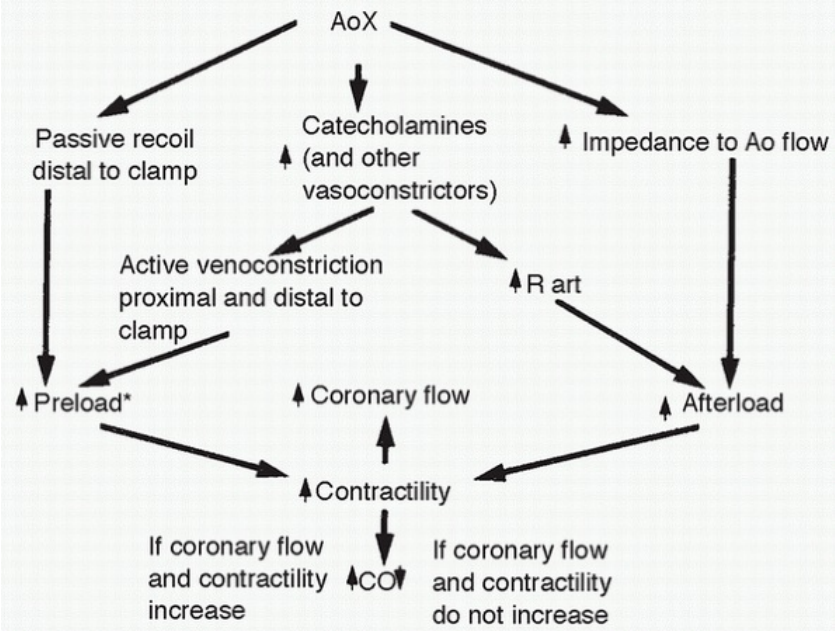


FIGURE 10.7 Systemic hemodynamic response to aortic crossclamping. Ao, aortic; AoX, aortic cross-clamping; R art, arterial resistance; ↑ and ↓, increase and decrease, respectively. [a]Different patterns are possible. (From Gelman

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S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology.* 1995;82:1026-1060, with permission.)

A sudden increase in afterload can lead to left ventricular failure, particularly in the patient with a noncompliant left ventricle. Ideally, the patient should have lower filling pressures for the half hour prior to cross-clamp placement. This mitigates the adverse response to sudden increased afterload. The PAC is helpful in accurately assessing and maintaining preclamp values for the left side of the heart. A potent anesthetic agent and/or a vasodilator such as nicardipine is used to return afterload to near normal. This also helps increase the cardiac output and decrease stress on the left ventricle. If this is insufficient to reverse left ventricular failure, the addition of an inotrope may be necessary.

The increase in afterload, following cross-clamp placement, may also result in myocardial ischemia. Ischemia, reflected as a rising PCWP and ST-segment depressions, can be managed with intravenous nitroglycerin, a potent dilator of the capacitance vessels. This drug is used to decrease left ventricular end-diastolic volume and left ventricular end-diastolic pressure. Decreasing left ventricular end-diastolic pressure also decreases the transluminal pressure across the coronary vasculature. This increases blood flow to the myocardium.

Ellis JE, Roizen MF, Youngberg JA. Anesthesia for abdominal aortic revascularization. In: Youngberg JA, Lake CL, Roizen MF, et al, eds. *Cardiac, Vascular and Thoracic Anesthesia*. Philadelphia, PA: Churchill Livingstone; 2000:538-566.

Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology*. 1995;82:1026-1060.

C.9. Because this case involues an infrarenal aneurysm, is renal blood flow affected with the placement of the cross-clamp? If an endovascular repair is chosen, what are the risks to the kidneys? Are there any treatment maneuvers that can be taken to minimize these risks in either repair?

ARF after aortic aneurysm repair is associated with a mortality of greater than 30%. Decreased renal function is observed in many patients after aortic cross-clamping, even when

the clamp is placed distal to the renal arteries. Although it is clear that a suprarenal crossclamp will decrease renal blood flow up to 80%, an infrarenal cross-clamp also causes a decrease in renal cortical blood flow with an associated decrease in GFR. The degree of decrease in urine output does not correlate with the decrease in GFR nor does it predict postoperative renal failure. The most dangerous complication of alteration in renal blood flow is acute tubular necrosis and ARF.

The maintenance of cardiac output and adequate circulating blood volume is of prime importance in sustaining renal blood flow and in the prevention of renal failure. Low-dose dopamine (2 to 3 μg/kg/min) increases renal blood flow and may improve urine output, although decreased incidence of postoperative renal failure has not been proven. Renal protection may, however, be provided by the administration of mannitol (0.25 g per kg). The use of mannitol attenuates the reduction of renal cortical blood flow—before, during, and after renal ischemia—increases glomerular ultrafiltration flow and is a hydroxyl free radical scavenger. Fenoldopam and furosemide may be utilized during aortic reconstruction procedures to mitigate nephrotoxicity. Unfortunately, strong clinical evidence is currently lacking for any of these measures.

During endovascular repair, radiocontrast material may cause further insult to the kidneys. There is some suggestion that the use of a bicarbonate infusion or pretreatment with *N*-acetyl-cysteine maybe protective. It is prudent to minimize exposure to nonionic contrast or replace with gadolinium dimeglumine.

Ellis JE, Roizen MF, Youngberg JA. Anesthesia for abdominal aortic revascularization. In: Youngberg JA, Lake CL, Roizen MF, et al, eds. *Cardiac, Vascular and Thoracic Anesthesia*. Philadelphia, PA: Churchill Livingstone; 2000:557-559.

Merten GJ, Burgess WP, Gray JV, et al. Prevention of contrast-induced nephropathy with sodium bicarbonate: a randomized clinical trial. *JAMA*. 2004;291(19):2328-2334.

C.10. What are the hemodynamic consequences of aortic cross-clamp removal? What can be done to minimize the effects of removing the aortic cross-clamp? If the systemic blood pressure remains depressed after removal of the cross-clamp, what is the differential diagnosis? How

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would you diagnose and correct the problem?

The hemodynamic response to aortic unclamping is shown in Figure 10.8.

During cross-clamping, blood flow to the lower extremities is grossly decreased. Metabolism switches from aerobic to anaerobic as ischemia develops. This results in maximal vasodilation and lactic acid production. When the cross-clamp is released, systemic vascular resistance and arterial blood pressure decreases dramatically. Reactive hyperemia is a consequence of unclamping. This may be the result of arterial relaxation (myogenic mechanism), an accumulation of vasodilating substances below the occlusion, or anoxic relaxation of smooth muscles. Peripheral vasodilation can result in relative volume depletion and hypotension. Vasodilation may become systemic as the lactic acid is washed out of the extremities into the central circulation. This condition is sometimes known as “declamping shock.”

To minimize the hypotensive response, volume loading in the period prior to cross-clamp release is suggested to raise filling pressures to slightly above normal. Vasodilators such as nitroprusside and/or nitroglycerin during this period allow additional volume loading with maintenance of filling pressures. In addition, gradual release of the clamp allows time for adjustments in volume, pressors, and correction of acidosis.

Sometimes, even in the face of adequate volume loading, the blood pressure remains low following cross-clamp removal. Proximal cross-clamping is associated with a higher incidence of hypotension. In this situation, it is advisable to ask the surgeon to reapply the aortic cross-clamp to varying degree depending on the severity of hypotension. Such maneuvers allow more time for correction of blood volume or acidosis.

Other causes of sustained hypotension in the face of adequate management include a continued site of hemorrhage and myocardial ischemia and/or failure. Measurement of filling pressures or use of TEE can particularly help in the differentiation of the etiology of sustained hypotension. Ischemia or failure can be detected by wall motion abnormalities or

elevated filling pressures accompanying systemic hypotension. In contrast, hemorrhage is diagnosed by low filling pressures and increased systemic vascular resistance (due to reflex vasoconstriction).

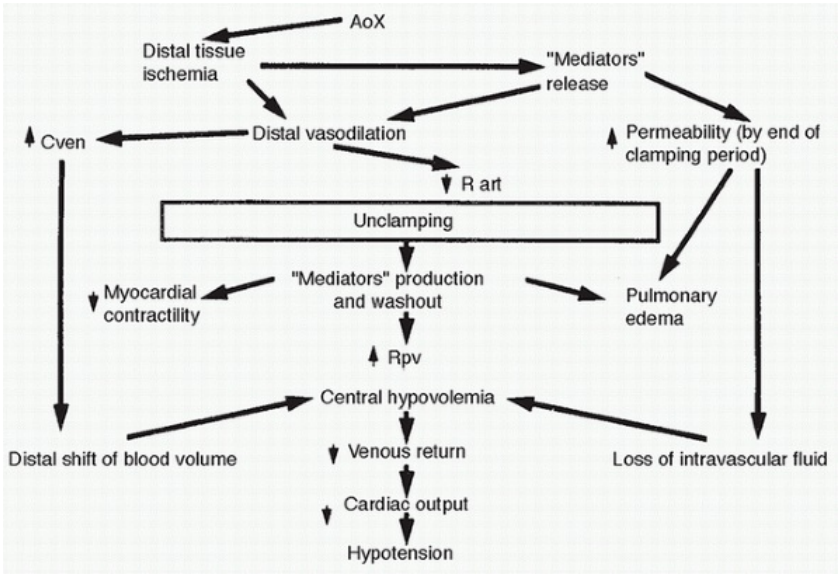


FIGURE 10.8 Systemic hemodynamic response to aortic unclamping. AoX, aortic cross-clamping; Cven, venous capacitance; R art, arterial resistance; Rpv, pulmonary vascular resistance; ↑ and ↓, increase and decrease, respectively. (From Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology.* 1995;82:1026-1060, with permission.)

Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology*. 1995;82:1026-1060.

D. Postoperative Management

D.1. What are the parameters used to extubate this patient?

The following ventilatory criteria can be used to assess suitability for extubation: The patient is awake and alert, has an adequate gag reflex, displays signs of adequate reversal of neuromuscular blockade, and meets minimum respiratory parameters for extubation. The typical respiratory parameters used to assess suitability for extubation are shown in Table 10.1.

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It is important to recognize that such parameters should serve merely as a guide in the clinical assessment of suitability for extubation. The decision to extubate should be ultimately guided by assessment of the patient's overall status and clinical judgment. Extubation may need to be delayed in those patients who display labored breathing on physical exam, inadequate pain control, or hemodynamic instability.

Perioperative fluid management also should be carefully considered when assessing a patient's suitability for extubation. For shorter cases with minimal anticipated fluid shifts, the patient can be extubated in the immediate postoperative period. For longer cases, instances of large volumes of fluid replacement and significant blood product administration, extubation should be delayed until the hemodynamics are stabilized and temperature is normalized. In these cases, airway swelling also can be a significant concern and may lead to ventilatory failure in the postoperative period. A “cuff leak” test may be somewhat indicative of the degree of airway edema. It is performed by occluding the endotracheal tube of a spontaneously breathing patient and auscultating for breath sounds with the cuff deflated.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:209-211.

TABLE 10.1 Typical Respiratory Parameters Used to Determine Suitability for Extubation

Vital capacity greater than 15 mL/kg
pH greater than 7.30
PaO_2 greater than 60 mm Hg at FIO_2 less than 50%
$PaCO_2$ less than 50 mm Hg
Maximal negative inspiratory force greater than -20 cm H_2O
Stable hemodynamic status
Respiratory rate less than 30 breaths per minute

D.2. What are the anticipated changes in postoperative pulmonary function in these patients? How does the surgical technique affect postoperative pulmonary function? Are there any postoperative maneuvers that can improve respiratory parameters?

The transabdominal approach to the aorta involves an upper abdominal incision. Total lung capacity and its subdivisions decrease after upper abdominal surgery. VC decreases 25% to 50% and returns to normal in 1 to 2 weeks, and residual volume increases 13%. Functional residual capacity declines 30% and recovers over 3 to 4 days. Expiratory reserve volume declines 20% after lower abdominal surgery and up to 60% after upper abdominal and thoracic incisions. Tidal volume decreases 20% on the first postoperative day and gradually returns to normal. The retroperitoneal approach to the aorta involves a flank incision, which leads to far less respiratory compromise.

In a series of adult men undergoing abdominal surgery, postoperative pulmonary complications occurred more frequently than cardiac complications (9.6% vs. 5.7%) and were associated with significantly greater length of hospitalization. Many of these complications are related to disruption of the normal activity of the respiratory muscles, from initiation of the anesthetic to the postoperative period. In addition, the effects of surgical trauma are most pronounced after upper abdominal surgery. Lower abdominal and thoracic incisions impact the respiratory muscles to a lesser degree. This occurs through surgical disruption of the respiratory muscles, postoperative pain, and abdominal contents, preventing normal diaphragm excursion. The patient follows a rapid shallow breathing pattern without sighs.

The overall effect of postoperative regional analgesia on the breathing mechanics is complex, but epidural analgesia may decrease the risk for postoperative pulmonary complications. Ambulation and control of postoperative pain diminish splinting and help maximize respiratory parameters. Maneuvers to encourage deep breathing are of proven benefit.

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Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1128-1138.

Warner DO. Preventing postoperative pulmonary complications. The role of the anesthesiologist. *Anesthesiology*. 2000;92:1467-1472.

D.3. How would you control postoperative pain? What are the alternatives in the management of this patient's postoperative pain?

The goal of effective postoperative pain relief is to produce a high quality of pain control with the fewest number of side effects and complications. Neuraxial analgesia in the immediate postoperative period is the preferred method of pain management in this high-risk patient population. The ideal opiate, its concentration, and combination with local anesthetic have yet to be defined. (For suggested protocols, see Table 10.2.)

Complications of the epidural route of analgesia include dural puncture, epidural hematoma, and epidural abscess. The risk of epidural hematoma is small in patients receiving appropriate doses of anticoagulation postoperatively but is prohibitively high in patients

receiving thrombolytic treatment or LMWHs. Careful consideration should be given to the timing of insertion and removal of the catheter. The risk of complications is similar whether the catheter is placed at the thoracic or lumbar level. Other complications include pruritus, nausea, urinary retention, and delayed respiratory depression. The latter is less than 1% when epidural morphine is used, similar to the oral and parenteral route. Difficulty ambulating and orthostatic hypotension are minimized when catheters are placed in the thoracic region with low infusion rates and bupivacaine concentrations used are less than 0.08%.

TABLE 10.2 Epidural Opioid/Bupivacaine Combinations Administered by Continuous Infusion[a]

DRUG COMBINATIONS	SOLUTION[b]	BOLUS DOSE OF BUPIVACAINE	BASAL INFUSION[c]	BREAKTHROUGH DOSES	INCREMENTS IN BREAKTHROUGH[d]
Morphine	0.01%		6-8 mL/hr	1-2 mL every 10-15 min	1 mL of the solution
Bupivacaine[e]	0.05%-0.1%	0.5%-0.25%			
Hydromorphone	0.0025%-0.005%		6-8 mL/hr	1-3 mL every 10-15 min	1 mL of the solution
Bupivacaine[f]	0.05%-0.1%	0.5%-0.25%			
Fentanyl	0.001%		0.1-0.15 mL/kg/hr	1-1.5 mL every 10-15 min	1 mL of the solution
Bupivacaine[g]	0.05%-0.1%	0.5%-0.25%			
Sufentanil	0.0001%		0.1-0.2 mL/kg/hr	1-1.5 mL every 10-15 min	1 mL of the solution
Bupivacaine[h]	0.05%-0.1%	0.5%-0.25%			

[a]Catheter insertion site is the dermatome corresponding to the middle of the surgical incision. Administer a bolus dose of 0.5% bupivacaine or 2% lidocaine to establish surgical anesthesia, or 0.25% bupivacaine to induce postoperative analgesia in 5-mL

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aliquots.

[b] Due to infectious control, a total volume of 150 mL is recommended.

[c] Initial basal infusion rates will depend on the age, general condition, and weight of the patient.

[d] If analgesia is inadequate after 1 hour, increase the breakthrough dose by the recommended amount. If analgesia is inadequate after one additional hour, decrease the lockout interval by 5 minutes.

[e] Prepare this solution by mixing 75-150 mg of bupivacaine with 15 mg of preservative-free morphine in a total volume of 150 mL of preservative-free normal saline.

[f] Prepare this solution by mixing 75-150 mg of bupivacaine with 3.75-7.5 mg of hydromorphone in a total volume of 150 mL of preservative-free normal saline.

[g] Prepare this solution by mixing 75-150 mg of bupivacaine with 1,500 μg of fentanyl in a total volume of 150 mL of preservative-free normal saline.

[h] Prepare this solution by mixing 75-150 mg of bupivacaine with 150-300 μg of sufentanil in a total volume of 150 mL of preservative-free normal saline. From de Leon-Casasola OA, Lema MJ. Postoperative epidural opioid analgesia: what are the choices? *Anesth Analg*. 1996;83:867-875, with permission.

Systemic narcotic analgesia can be used to provide effective postoperative pain control. Intravenous narcotics are commonly administered by a patient-controlled analgesia (PCA) pump after this type of procedure, allowing the patient to titrate the dose of narcotic to achieve adequate pain control. These modified infusion pumps are able to administer infusions of narcotics, small preprogrammed bolus doses on patient demand, and larger bolus doses by prescription. The PCA technique allows the patients to self-titrate narcotic doses to achieve optimal analgesic doses while avoiding the toxic side effects that result from high peak serum levels.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1491-1499.

Mann C, Pouzeratte Y, Boccara G, et al. Comparison of intravenous or epidural patient-controlled analgesia in the elderly after major abdominal surgery. *Anesthesiology*. 2000;92:433-441.

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Chapter 11
Hypertension

Cindy Wang

Fun-Sun F. Yao

A 70-year-old man with cholelithiasis was scheduled for a cholecystectomy. His blood pressure (BP) was 230/120 mm Hg; pulse, 60 beats per minute. Hematocrit was 38%; serum sodium, 140 mEq per L; and serum potassium, 2.7 mEq per L. His medications included metoprolol, aspirin, atorvastatin (Lipitor), and hydrochlorothiazide.

A. Medical Disease and Differential Diagnosis

1. Define hypertension and classify its severity.
2. What is the prevalence of hypertension?
3. What is the general classification of hypertension? Enumerate the causes of each type of hypertension.
4. What are the clinical patterns of hypertension encountered?
5. What is the pathophysiology of essential hypertension?
6. What is the pathophysiology of isolated systolic hypertension (ISH) and of pulse pressure hypertension (PPH)?
7. What are the end-organ damages caused by long-standing hypertension?
8. Are hypertensive patients at an increased risk for perioperative cardiac morbidity?
9. Perioperative cerebral and renal complications are mostly associated with which subtype of hypertension?
10. Would you employ a controlled hypotensive technique for hypertensive patients? How much would you safely lower the BP?
11. What are BP goals for patients with hypertension and when should antihypertensive drugs be initiated?
12. What is the mechanism of action of antihypertensive drugs?
13. Does the choice of antihypertensive therapy influence hemodynamic responses to induction, laryngoscopy, and intubation?
14. Does chronic angiotensin-converting enzyme (ACE) inhibition influence anesthetic induction?

B. Preoperative Evaluation and Preparation

1. How would you evaluate this patient preoperatively?
2. Would you postpone the surgery? Why? What BP would you like the patient to achieve before surgery?
3. Should all or any of the chronic medications be discontinued before the operation?
4. Should hypokalemia be treated before anesthesia? Why?
5. Should hypomagnesemia be treated before anesthesia? Why?
6. Does an asymptomatic carotid bruit increase the risk in these patients?

7. The surgery was postponed for 6 weeks. The patient was on metoprolol, aspirin, atorvastatin, captopril, hydrochlorothiazide, and potassium chloride. His BP was 160/60 mm Hg and potassium 4.0 mEq per L. How would you premedicate this patient?
8. If the patient is an untreated hypertensive patient with BP 170/70 mm Hg, would you treat the patient preoperatively with an antihypertensive agent?

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C. Intraoperative Management

1. How would you monitor this patient?
2. What are the anesthetic goals for hypertensive patients?
3. How would you induce anesthesia for the hypertensive patient?
4. How does tracheal intubation produce hypertension?
5. What happens to the left ventricular ejection fraction during and immediately following intubation?
6. What other measures can prevent hypertension and tachycardia at the time of intubation?
7. After induction and intubation, the BP decreased to 70/40 mm Hg. What would you do?
8. What is your choice of agents for maintenance of anesthesia? Why?
9. How would you manage fluid therapy for hypertensive patients?
10. During the surgery, BP increased to 220/120 mm Hg. How would you treat the hypertension?
11. What could you do to prevent hypertension during extubation and emergence?
12. Would you consider regional anesthesia for this patient?

D. Postoperative Management

1. The patient developed hypertension, BP 210/110 mm Hg in the postanesthesia care unit. What would you do?

A. Medical Disease and Differential Diagnosis

A.1. Define hypertension and classify its severity.

True systemic hypertension can be diagnosed when there is an increase in arterial pressure above accepted normal pressure for age, sex, and race. According to the seventh report on classification and characterization of BP by the Joint National Committee (JNC) on Evaluation, Detection, and Prevention of High Blood Pressure in 2003, a normal BP for adults 18 years or older is less than 120 mm Hg systolic with a diastolic of less than 80 mm Hg. Table 11.1 shows the classification of BP for adults by the JNC 7 report: normal, prehypertension, stage 1 hypertension, and stage 2 hypertension.

TABLE 11.1 Classification of Blood Pressure for Adults

JNC 7 CATEGORY	SBP	DBP
Normal	<120	<80
Prehypertension	120-139	80-89
Hypertension	≥140	≥90
Stage 1	140-159	90-99
Stage 2	≥160	≥100

Adults, 18 years or older; DBP, diastolic blood pressure; JNC, Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; SBP, systolic blood pressure.
From Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the Joint National Committee On Prevention, Detection, Evaluation, And Treatment Of High Blood Pressure: the JNC 7. *JAMA*. 2003;289:2560-2572.

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Hypertension in children and adolescents is defined as BP at the 95th percentile or greater. Prehypertension is defined as BP between the 90th and 95th percentile. The fourth report on high BP in children and adolescents by the National High Blood Pressure Education Program provides BP tables with percentiles based on gender, age, and height.

It is important to note that the classification of hypertension defines and specifies hypertension according to systolic and/or diastolic limits, each representing different pathophysiologic processes. Systolic hypertension is a marker of macrovascular disease and large arterial stiffening (atherosclerosis), and diastolic hypertension is a consequence of microvascular disease involving typically vessels less than 1 mm in size.

Uncontrolled hypertension can escalate to a hypertensive crisis defined as systolic BP greater than 180 mm Hg or diastolic BP greater than 120 mm Hg and categorized as urgent and emergent. According to the JNC 7 Report, hypertensive emergency is defined as elevated BP (usually ≥180/120 mm Hg) complicated by evidence of impending or progressive end-organ damage, whereas hypertensive urgency is severe elevation of BP without progressive end-organ damage.

Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7. *JAMA*. 2003;289(19):2560-2572.

Longo DL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2042-2059.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease*. 10th ed. Philadelphia, PA: Elsevier; 2015:934-952.

National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and

Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics*. 2004;114:555-576.

Rodriguez MA, Kumar SK, De Caro M. Hypertensive crisis. *Cardiol Rev*. 2010;18:102-107.

A.2. What is the prevalence of hypertension?

The prevalence of hypertension depends on both the racial composition of the population and the criteria used to define hypertension. In a white suburban population like that in the Framingham study, nearly one-fifth has a BP greater than 160/95 mm Hg and almost one-half has a BP greater than 140/90 mm Hg. A higher prevalence of hypertension has been found in the non-white population. The frequency increases with the age of the population with nearly two-thirds of hypertensive patients being older than 50 years, and by the age of 75 years, almost 90% will have hypertension. The subtype of hypertension is also influenced by age. Younger individuals suffer from diastolic hypertension and combined systolic and diastolic hypertension, whereas older persons predominantly experience systolic hypertension. The number of hypertensive persons in the United States in 1983 was estimated to be 57.7 million—more than double the estimate made in 1960 to 1962. Currently, approximately 70 million Americans suffer from hypertension.

Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003;289(19):2560-2572.

Franklin SS, Larson MG, Khan SA, et al. Does the relation of blood pressure to coronary heart disease risk change with aging? The Framingham Heart Study. *Circulation*. 2001;103:1245-1249.

Longo DL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2042-2059.

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Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease*. 10th ed. Philadelphia, PA: Elsevier; 2015:934-952.

A.3. What is the general classification of hypertension? Enumerate the causes of each type of hypertension.

Hypertension is classified according to its subtypes: systolic, diastolic, and pulse pressure (Table 11.2). Historically, only diastolic hypertension—essential hypertension—was recognized, but more recently, there has been increasing emphasis and recognition of systolic hypertension, namely, *isolated systolic hypertension* (ISH). ISH is the most common subtype of hypertension affecting predominantly individuals older than 60 years of age. In fact, approximately 70% of hypertensive patients have ISH with approximately half of these individuals having very wide pulse pressure (>65 mm Hg) or *pulse pressure hypertension* (PPH). Isolated diastolic hypertension is most prevalent in individuals younger than 50 years and is an important marker of coronary heart disease and mortality in this age group. Some hypertensive

patients have both systolic and diastolic hypertension categorized as *combined systolic and diastolic hypertension*. The ranges of systolic, diastolic, and pulse pressure that define each subtype of hypertension are presented in Table 11.1.

TABLE 11.2 Classification of Hypertension

Systolic and diastolic hypertension

- Essential
- Renal
- Endocrine
- Neurogenic
- Miscellaneous

Systolic hypertension with wide pulse pressure

- Increased cardiac output
- Rigidity of aorta

Etiology of hypertension

- *Essential hypertension*. Unknown etiology
- *Renal*. Acute and chronic glomerulonephritis, chronic pyelonephritis, polycystic kidney, diabetic nephropathy, hydronephrosis, renovascular stenosis, renin-producing tumors, primary sodium retention
- *Endocrine*. Adrenal—Cushing syndrome, primary aldosteronism, congenital adrenal hyperplasia, pheochromocytoma, acromegaly, hypothyroidism, carcinoid, hyperthyroidism, oral contraceptives, corticosteroids
- *Neurogenic*. Psychogenic, increased intracranial pressure, spinal cord section, familial dysautonomia, lead poisoning, Guillain-Barré syndrome, sleep apnea
- *Miscellaneous*. Coarctation of aorta, increased intravascular volume, pregnancy-induced hypertension, polyarteritis nodosa, acute porphyria, hypercalcemia, alcohol and drug use, acute stress including surgery

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Longo DL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2042-2059.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease*. 10th ed. Philadelphia, PA: Elsevier; 2015:934-952.

Sesso HD, Stampfer MJ, Rosner B, et al. Systolic and diastolic blood pressure, pulse pressure, and mean arterial pressure as predictors of cardiovascular disease risk in men. *Hypertension*. 2000;36:801-807.

A.4. What are the clinical patterns of hypertension encountered?

- "Vasoconstricted" hypertension—in medical patient with chronic renovascular hypertension, characterized by diastolic hypertension and systemic vascular resistant with normal or even decreased cardiac output and heart rate
- "Hyperdynamic" hypertension—in postoperative surgical patient, characterized by acute systolic hypertension; widened pulse pressure; and increased cardiac output, heart rate, and systemic vascular resistant

Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7. *JAMA*. 2003;289(19):2560-2572.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease*. 10th ed. Philadelphia, PA: Elsevier; 2015:934-952.

A.5. What is the pathophysiology of essential hypertension?

The underlying mechanism of essential hypertension is unknown. A variety of abnormalities, including heredity, fetal undernutrition, abnormal sympathetic nervous system activity, cell membrane defects, renal retention of excess salt, microcirculatory alterations, endothelial

cell dysfunction, hyperinsulinemia secondary to insulin resistance, vascular hypertrophy, and altered renin-angiotensin system regulation are implicated. There is increasing evidence that "local renin-angiotensin" paracrine factors may be involved in the development of hypertension. However, characteristic hemodynamic changes are present as follows:

- Increased systemic vascular resistance with normal cardiac output
- Markedly increased sympathetic response to stress such as endotracheal intubation
- A greater increase in BP with vasoconstriction and a greater decrease in BP with vasodilation because of the increased thickening of arterial wall and high ratio of wall thickness to internal diameter

The higher the level of BP, the more likely that various cardiovascular diseases will develop prematurely through acceleration of arteriosclerosis. If untreated, approximately 50% of hypertensive patients die of coronary heart disease or congestive heart failure (CHF), approximately 33% of stroke, and 10% to 15% of renal failure.

Longo DL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2042-2059.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease*. 10th ed. Philadelphia, PA: Elsevier; 2015:934-952.

A.6. What is the pathophysiology of isolated systolic hypertension (ISH) and of pulse pressure hypertension (PPH)?

ISH is a manifestation of atherosclerotic disease involving predominantly the aorta and its major branches. Both ISH and PPH reflect arterial stiffening and represent the pulsatile component of BP, whereas the mean arterial pressure (MAP) represent the static state. Systole, then, is directly influenced by the ventricular contractile state, the ejected volume, heart

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rate, and, importantly, compliance of the aorta and pulse wave velocity. With increasing age and factors such as diabetes, smoking, increased cholesterol as well as some genetic factors, compliance of the aorta diminishes markedly (Fig. 11.1). The net result is stiffening of the arterial

tree and inability to absorb the pulsatile load, causing the systolic pressure to rise sharply. Pulse wave velocity has gained much attention lately because it may be a richer substrate for characterizing the physiology of blood flow and pressure. Under normal physiologic conditions, the ejected blood volume is transmitted peripherally as a propagated wave. After reaching the periphery, in particular, at the bifurcation sites, a reflected wave or a retrograde wave is generated from the encountered impedance. Under normal conditions, wave reflection arrival coincides with the beginning of diastole, thereby augmenting the diastolic pressure. However, with stiffening of the aorta as occurs with aging, both the propagated and the reflected waves travel much more rapidly, and early return of the reflected arterial wave during late systole augments the systolic component, effectively increasing afterload. The ensuing loss of diastolic augmentation results in a disproportionate increase in the systolic BP and lower diastolic BP—a hallmark of ISH and of PPH.

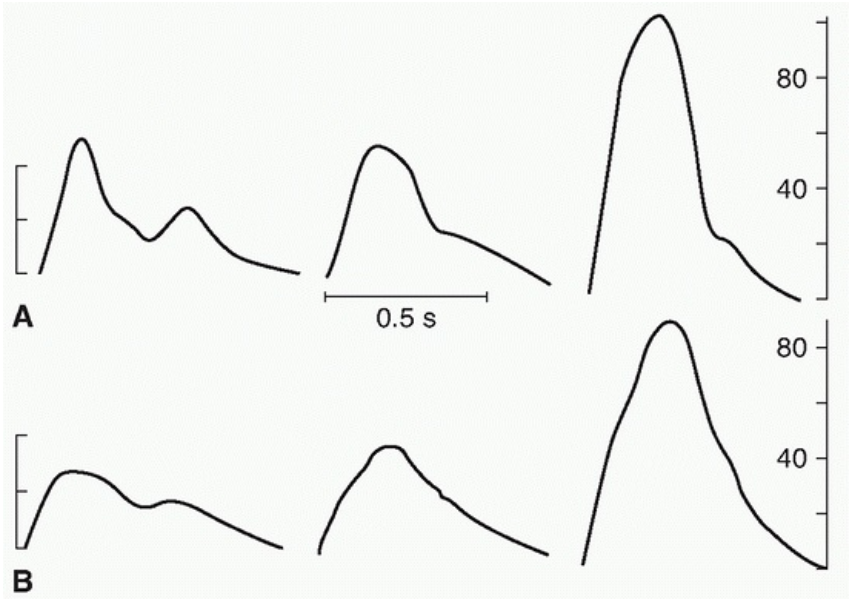


FIGURE 11.1 Change in amplitude and contour of the upper limb **(A)** and ascending aortic **(B)** pressure wave with age, as recorded in three female members of a family: at age 18 **(left)**, at age 48 **(center)**, and at age 97 years **(right)**. Upper limb pulse pressure was just more than twice as high in the old compared with the young subject (102 vs. 46 mm Hg), whereas aortic pulse pressure was more than three times higher (104 vs. 27 mm Hg). (From O'Rourke MF, Nichols WW. Aortic diameter, aortic stiffness, and wave reflection increase with age and isolated systolic hypertension. *Hypertension.* 2005;45[4]:652-658, with permission.)

Mechanistically, pulse pressure is also an index of the stiffness of conduit vessels and the rate of pressure wave propagation and reflection within the arterial tree. Approximately half of patients with ISH also have wide pulse pressure; however, both individuals who are normotensive (systolic, <140 mm Hg) with a low diastolic pressure or persons with combined systolic and diastolic hypertension (systolic >140 mm Hg and diastolic >90 mm Hg) can have wide pulse pressure (normal values being ≤40 mm Hg).

Dart AM, Kingwell BA. Pulse pressure—a review of mechanism and clinical relevance. *J Am Coll Cardiol*. 2001;37:975-984.

O'Rourke MF, Nichols WW. Aortic diameter, aortic stiffness, and wave reflection increase with age and isolated systolic hypertension. *Hypertension*. 2005;45(4):652-658.

Schiffrin EL. Vascular stiffening and arterial compliance. Implications for systolic blood pressure. *Am J Hypertens*. 2004;17:39S-48S.

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A.7. What are the end-organ damages caused by long-standing hypertension?

The end-organ damages caused by long-standing hypertension are as follows:

Cardiac involvement

Left ventricular hypertrophy (LVH)

Angina or myocardial infarction (MI)

Arrhythmias

Congestive failure

Eye involvement

Vascular changes in the fundus reflect hypertensive retinopathy and arteriosclerotic retinopathy

Renal involvement

Nephropathy

Cerebral involvement

Stroke or transient ischemic attack

Complications of hypertension to vascular disease probably involve three interrelated processes: pulsatile flow, endothelial cell dysfunction, and smooth muscle cell hypertrophy. These three interrelated processes are probably responsible for the arteriolar and arterial sclerosis that is the usual consequence of long-standing hypertension. Large vessels such as the aorta may be directly affected and be at risk for aneurysms and dissection. As discussed previously, the consequences of long-standing hypertension need be addressed according to the subtypes of hypertension; for the associated risks for cerebral, cardiac, and renal vascular complications differ according to systolic, diastolic, and PPH. For example, diastolic hypertension being a better predictor of coronary heart disease in younger patients, whereas systolic and pulse pressure hypertension being associated with greater risk of stroke, coronary heart disease, and mortality in persons older than 60 years.

Aronson S, Fontes ML. Hypertension: a new look at an old problem. *Curr Opin Anesthesiol*. 2006;19:59-64.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease*. 10th ed. Philadelphia, PA: Elsevier; 2015:934-952.

A.8. Are hypertensive patients at an increased risk for perioperative cardiac morbidity?

Hypertensive patients are at increased risk for coronary artery disease, silent myocardial ischemia, CHF, and stroke. However, whether preoperative hypertension is predictive of perioperative major cardiac morbidity remains controversial. Some investigators have shown that patients with untreated, poorly controlled, or labile preoperative hypertension are at increased risk for perioperative BP lability, dysrhythmias, myocardial ischemia, and transient neurologic complications. Some suggested that preoperative hypertension predicted perioperative MI. However, Goldman and Caldera demonstrated that mild-to-moderate hypertension did not increase the risk of major morbid events. Instead, preoperative hypertension may predict several intermediates of outcome, such as BP lability and myocardial ischemia. The controversy may be due to the wide variability in the hypertensive population. Hypertension may affect perioperative morbidity through the extent of end-organ damage and not the manifestation of the disease itself. LVH, which signifies long-standing poorly controlled hypertension, can increase the risk of myocardial ischemia from imbalances of myocardial oxygen supply and demand regardless of the presence or absence of coronary artery disease.

ISH (systolic BP >140 mm Hg and diastolic BP <90 mm Hg) has been identified as a risk factor for cardiovascular complications in the general population and treatment reduces the future risk of stroke. Aronson et al. and Fontes et al. found that among the various components of BP, preoperative pulse pressure hypertension was independently and significantly associated with postoperative stroke, renal failure, and mortality in patients undergoing coronary artery

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bypass. Neither ISH nor isolated diastolic hypertension were predictive of vascular complications. This finding is consistent with results of longitudinal studies finding that increase in pulse pressure is a better predictor of major vascular complications than increase in either systolic or diastolic BP. Interestingly, rises in pulse pressure as few as 10 mm Hg in both normotensive and hypertensive individuals is associated with 20% or more increase risk of renal, coronary, and cerebral events.

Aboyans V, Frank M, Nubret K, et al. Heart rate and pulse pressure at rest are major prognostic markers of early postoperative complications after coronary bypass surgery. *Eur J Cardiothorac Surg*. 2008;33:971-976.

Aronson S, Fontes ML, Miao Y, et al; for the Investigators of the Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation. Risk index for perioperative renal dysfunction/failure: critical dependence on pulse pressure hypertension. *Circulation*. 2007;115(6):733-742.

Casadei B, Abuzeid H. Is there a strong rationale for deferring elective surgery in patients with poorly controlled hypertension? *J Hypertens*. 2005;23(1):19-22.

Fontes ML, Aronson S, Mathew JP, et al; for the Multicenter Study of Perioperative Ischemia (McSPI) Research Group and the Ischemia Research and Education Foundation (IREF) Investigators. Pulse pressure and risk of adverse outcome in coronary bypass surgery. *Anesth Analg*. 2008;107:1122-1129.

Goldman L, Caldera DL. Risks of general anesthesia and elective operation in the hypertensive patient. *Anesthesiology*. 1979;50:285-292.

A.9. Perioperative cerebral and renal complications are mostly associated with which subtype of hypertension?

Both systolic hypertension and high pulse pressure are strongly associated with risk for perioperative cerebrovascular accidents and acute renal failure. The brain and the kidneys as well as the heart differ from most organs in that they receive large amount of blood flow and have very low resistance. As such, the pulsatile load (pulse pressure) tends to be very high. Over a period of many years of poorly or untreated hypertension, endothelial injury and vascular remodeling changes can promote both arteriosclerosis and atherosclerosis, which are known risk factors for cerebral and renal vascular complications. The pulsatile stress also can cause dislodgment of plaques from the aorta and its major branches, resulting in embolic stroke.

In hypertensive patients, autoregulation of cerebral blood flow is reset to a higher range than normal, and although it protects the brain against sudden increases in pressure, it makes it more vulnerable to hypotension. Therefore, when BP is lowered acutely, hypertensive patients will show signs of cerebral ischemia at a higher level of BP than normotensive patients.

Hypertension may accelerate cognitive decline with age. Hypertension, particularly systolic, is a major risk factor for initial and recurrent stroke and for transient ischemia attacks caused by extracranial atherosclerosis.

Chronic renal insufficiency is a common sequela of hypertension. Patients with hypertension should have a measurement of baseline serum creatinine. In the original Cardiac Risk Index, an elevated serum creatinine level (gt;3.0 mg per dL [>265.2 mmol per L]) was one of the independent risk factors for perioperative cardiovascular morbidity and mortality. This has been confirmed in the revised Cardiac Risk Index in which a preoperative serum creatinine level greater than 2.0 mg per dL (176.8 mmol per L) was one of six independent factors that predicted increased cardiovascular risk.

Aronson S, Fontes ML, Miao Y, et al; for the Investigators of the Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation. Risk index for perioperative renal dysfunction/failure: critical dependence on pulse pressure hypertension. *Circulation*. 2007;115(6):733-742.

Benjo A, Thompson RE, Fine D, et al. Pulse pressure is an age-independent predictor of stroke development after cardiac surgery. *Hypertension*. 2007;50:630-635.

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Finnerty FA Jr, Witkin L, Fazekas JF. Cerebral hemodynamics during cerebral ischemia induced by acute hypotension. *J Clin Invest*. 1954;33:1227-1232.

A.10. Would you employ a controlled hypotensive technique for hypertensive patients? How much would you safely lower the BP?

Uncontrolled or untreated severe hypertension is a contraindication to controlled hypotension. However, controlled hypotension may be used with caution in treated hypertensive patients. Because cerebral autoregulation is shifted to the right with chronic hypertension, the lower limit of controlled hypotension should be higher for hypertensive patients. However, with long-term treatment, the autoregulation curve shifts leftward to approach that in normals. Strandgaard found that the lower limit of autoregulation was 113 mm Hg in severe untreated or uncontrolled hypertensives; 96 mm Hg in formerly severe, now-treated hypertensives; and 73 mm Hg in normotensive patients. The lowest level of mean BP tolerated without symptoms of hypoperfusion was 65 mm Hg in severe hypertensives, 53 mm Hg in treated hypertensives, and 43 mm Hg in normal patients. However, although the autoregulation may shift toward normal with treatment, in many patients the autoregulation did not shift toward normal even after 12 months of treatment. Because one cannot measure patients' autoregulation, a useful clinical guide is that a 25% decrease in MAP reaches the lower limit of autoregulation and a 55% decrease in MAP reaches symptomatic cerebral hypoperfusion. Another suggested rule is that the systolic pressure of controlled hypotension should not be lower than the diastolic pressure of the patient's usual pressure. It is important to note that peripherally measured blood pressure do not match central aorta blood pressure, which is more reflective of actual cerebral blood pressure.

Recently, noninvasive cerebral oximeter using near-infrared spectroscopy has been used to monitor oxygen saturations of the cerebral cortex. The values of cerebral oxygen saturations correspond with those of a mixture of 85% jugular venous O_2 saturation and 15% of arterial O_2 saturation. It reflects the balance between cerebral O_2 delivery and O_2 demand. In a steady state of anesthesia, the cerebral O_2 demand does not change significantly. Therefore, cerebral O_2 saturations will not decrease until the BP falls below its autoregulation range. Therefore, the cerebral oximeter may be employed to determine the lower limit of autoregulation and to ensure adequate cerebral oxygenation. Unfortunately, there is wide variability in measured cerebral saturations with some individual's baseline oximetric saturation values being near 50% at baseline. Further, the measured value is reflective of regional saturation such that distant areas that may be ischemic are not detected.

It should be mentioned that neither the threshold for upper nor lower limits of systolic and diastolic BP have been established. Frequently, these limits have been chosen arbitrarily and the relation of perioperative hypertension to outcomes has been inconsistent among the studies that have addressed this question. In part, the limitation comes from grouping all types of hypertension together. Moreover, available vasoactive agents are not selective in lowering or raising systolic BP, and diastolic BP without a concomitant increase or fall in the other component. Undermining the broad-based reliance on systolic BP and diastolic BP are a number of studies in humans over the past several decades that clearly show that both morbidity and mortality do not always linearly correlate with rises or fall in BP. In individuals with demonstrable coronary disease, namely, those with previous infarcts, coronary mortality

was significantly related to diastolic pressure in a U-shaped configuration—occurring more frequently in those with very high or very low diastolic BP. Unfortunately, the emphasis on BP management perioperatively has been to control the systolic component with no attention paid to the diastolic component. This is particularly concerning in patients with ISH and with very wide pulse pressure where the diastolic BP is already critically low. By reducing the systolic component, further lowering of the diastolic BP can result in ischemic complications in most sensitive vascular beds such as the brain, the heart, and the kidneys. Lastly, it is critical to recognize that peripheral arterial pressures do not necessarily reflect central pressures with exception of the MAP. In a subset of hypertensive individuals, both the systolic and the pulse pressures are grossly higher peripherally as compared to central aortic pressures, such that lowering of the peripheral BP may result in critical reduction in perfusion pressure.

Fontes ML, Aronson S, Mathew JP, et al; for the Multicenter Study of Perioperative Ischemia (McSPI) Research Group and the Ischemia Research and Education Foundation (IREF) Investigators. Pulse pressure and risk of adverse outcome in coronary bypass surgery. *Anesth Analg*. 2008;107:1122-1129.

Strandgaard S. Autoregulation of cerebral blood flow in hypertensive patients. The modifying influence of prolonged antihypertensive treatment on the tolerance to acute, drug-induced hypotension. *Circulation*. 1976;53(4):720-727.

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Yao FS, Tseng CC, Ho CY, et al. Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth*. 2004;18:552-558.

A.11. What are BP goals for patients with hypertension and when should antihypertensive drugs be initiated?

The latest recommendations from the Eighth Joint National Committee (JNC 8) outline BP treatment goals based on a systematic review of the literature. In comparison to the 2003 JNC 7 recommendations, the thresholds for initiating antihypertensive drugs have been slightly raised. Adults 60 years or older with systolic BP 150 mm Hg or higher or diastolic BP 90 mm Hg or higher should initiate pharmacologic therapy to lower BP. In adults 18 years or older with chronic kidney disease or diabetes, pharmacologic therapy should be initiated when systolic BP is 140 mm Hg or higher or diastolic BP is 90 mm Hg or higher.

James PA, Oparil S, Carter BL, et al. 2014 Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311(5):507-520.

A.12. What is the mechanism of action of antihypertensive drugs?

Antihypertensive drugs are categorized by their mechanism of action as follows.

Diuretics

They include thiazides (e.g., hydrochlorothiazide), loop diuretics (e.g., furosemide, ethacrynic acid), and potassium-sparing agents (e.g., spironolactone, triamterene). All diuretics initially lower the BP by increasing urinary sodium excretion and by reducing plasma volume, extracellular fluid volume, and cardiac output. Within 6 to 8 weeks, the cardiac output returns to normal. The lowered BP is related to a fall in peripheral resistance. Diuretics may cause hypokalemia, hypomagnesemia, hyperuricemia, hyperlipidemia, hypercalcemia, and hyperglycemia. For patients with ST-segment changes and evidence of pulmonary edema and hypertension or with increased intracranial cerebral pressure and hypertension, intravenous furosemide may be appropriate.

Antiadrenergic Agents

- *Centrally acting drugs*. Clonidine, dexmedetomidine, and mivazerol. These drugs and their metabolites are primarily α_2-receptor agonists. Stimulation of α_2 receptors in the vasomotor centers of the brain reduces sympathetic outflow.
- *Peripherally acting drugs*
  - α-Receptor blockers

    α_1 and α_2 Receptors—phenoxybenzamine (Dibenzyline), phentolamine (Regitine)

    α_1 Receptor—prazosin (Minipress), doxazosin (Cardura)

    By blocking α-mediated vasoconstriction, these drugs induce a fall in peripheral resistance with both arteriolar and venous dilation.

    - β-Receptor blockers—atenolol (Tenormin), metoprolol (Lopressor), nadolol (Corgard), pindolol (Visken), propranolol (Inderal), esmolol (Brevibloc). These drugs lower the BP

    by decreasing heart rate, contractility, cardiac output, and renin levels. BP is decreased without reflex tachycardia or widening of the pulse pressure. They also have antiarrhythmic activity and suppress both ventricular and supraventricular ectopic rhythms.
  - α-and β-Receptor blockers—labetalol (Trandate)
  - Endothelin receptor antagonists—act on endothelin A and B receptors to block the effect of endothelin-1, which is the most potent vasoconstrictor that is secreted primarily from vascular smooth muscle and endothelial cells. Bosentan (receptor A and B antagonist) and sitaxsentan (receptor A antagonist) are examples of a few of this class

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of agents used in the management of pulmonary hypertension and less so for hypertension-related heart failure.

Direct Vasodilators

They include hydralazine, nitroprusside, nitroglycerin, and calcium channel blockers. These drugs directly relax the smooth muscle of resistance and capacitance vessels to different degrees.

Dopaminergic Agonists

Dopaminergic agonists (DAs) are classified into DA1 and DA_2 subtypes.

Stimulation of DA1 receptors causes vasodilation, and inhibition of active sodium transport in the proximal tubule, leading to natriuresis.

Stimulation of DA_2 receptors inhibits norepinephrine release and promotes peripheral vasodilation.

Fenoldopam, a dopamine receptor (DA1 selective) agonist and a systemic and renal vasodilator, offers significant advantages as a parenterally administered agent for the management of BP in hypertensive emergencies and in the perioperative setting. Parenteral fenoldopam has a rapid onset and offset of effect, with an elimination half-time of approximately 10 minutes. Prepared in concentration of 10 mg in 250 mL (40 μg per mL), the recommended starting dose is 0.05 μg/kg/min. This should be titrated to effect by 0.025 μg/kg/min every 10 to 15 minutes, to a maximum dose of 0.5 to 0.8 μg/kg/min. The drug should not be administered in boluses; the incidence of reflex tachycardia is related to rapidity of upward titration. Unlike dopamine, it has no β- or α-adrenergic activity, and increasing doses result in increasing vasodilation without tachycardia or tachyarrhythmias.

Calcium Channel Blockers

The cardiovascular effects of calcium antagonists are listed in Table 11.3. These drugs decrease BP mainly by peripheral vasodilation. Renin and aldosterone secretion may be reduced as well.

Angiotensin-Converting Enzyme Inhibitors

They include captopril, enalapril, lisinopril, quinapril, and ramipril. The renin-angiotensin system may be inhibited in four ways as shown in Figure 11.2. These drugs inhibit the conversion of the inactive decapeptide angiotensin I to the active octapeptide angiotensin II. Lower levels of angiotensin II may decrease BP by reducing angiotensin II-induced vasoconstriction and by decreasing aldosterone synthesis. ACE inhibitors also retard the degradation of a potent vasodilator (bradykinin), alter prostaglandin production (most notably with captopril), and can modify the activity of the adrenergic nervous system.

ACE inhibitors provide predominantly arterial vasodilation and have become primary therapy for the treatment of CHF by afterload reduction. Cardiac output is increased without excessive decrease in preload, with a favorable effect on survival.

TABLE 11.3 Cardiovascular Effects of Calcium Channel Blockers

	VERAPAMIL	DILTIAZEM	NIFEDIPINE	NICARDIPINE	CLEVIDIPINE
Heart rate	⇓	⇓	⇓ or -	⇑ or -	-
Nodal conduction	⇓⇓	⇓	⇓ or -	-	-
Myocardial depression	⇑⇑	⇑	-	-	-
Vasodilation	⇑	⇑	⇑⇑	⇑⇑	⇑⇑

↑↑, more increase; ↓↓, more decrease; ↑, increase; ↓ decrease; -, no change.

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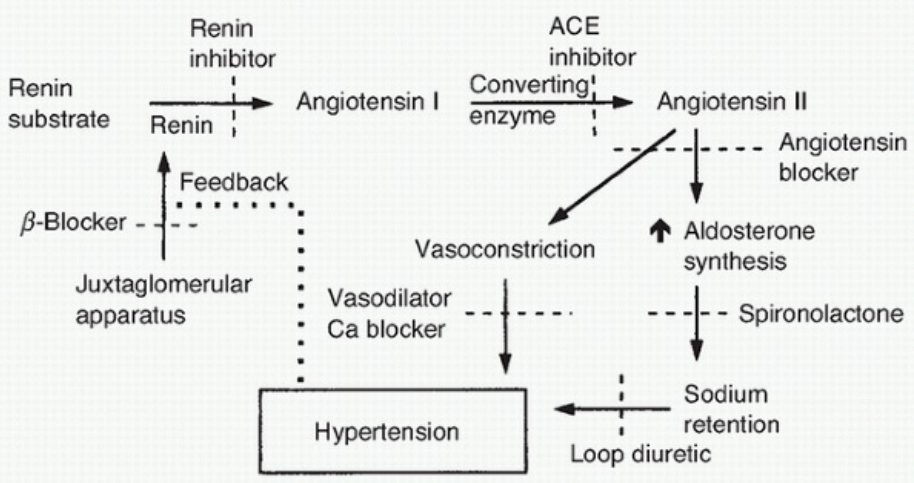


FIGURE 11.2 The renin-angiotensin system and the mechanism of action of antihypertensive drugs. ACE, angiotensin-converting enzyme.

Angiotensin II Receptor Blockers

Angiotensin II receptor antagonists or blockers (ARBs) represent the third class that antagonizes the renin-angiotensin-aldosterone system. Blockade of the action of angiotensin II leads to elevations in plasma levels of renin, angiotensin I, and angiotensin II. However, this build-up of precursors does not overwhelm the receptor blockade, as evidenced by a persistent fall in both BP and plasma aldosterone levels. There are several possible differences between ACE inhibitors and angiotensin II receptor antagonists. These include the following:

- ACE is a kininase. Therefore, inhibiting this enzyme, which normally degrades bradykinin, with an ACE inhibitor leads to increased kinin levels, an effect not seen with an angiotensin II receptor antagonist. High bradykinin levels may also provide additional vasodilation and other benefits not observed with angiotensin II receptor antagonists.
- ACE inhibitors, by decreasing angiotensin II production, reduce the effect of both angiotensin II receptor type 1 (AT1) and type 2 (AT2); only the former are inhibited by the angiotensin II receptor blockers. Chronic stimulation of the AT_2 receptor may be beneficial.
- In the heart, kidney, and perhaps the blood vessels, the production of angiotensin II may be catalyzed by enzymes other than ACE, such as chymase. The effect of the angiotensin II produced by this reaction can be inhibited by the angiotensin II receptor antagonists but not by ACE inhibitors.

There is evidence that ARBs are more effective in treating ISH and PPH particularly in combination with ACE inhibitors and with endothelin receptor blockers.

Other Vasodilators

They include brain natriuretic peptides such as nesiritide that is primarily used in acute exacerbation of heart failure to improve forward flow and reduce symptoms and signs of heart failure. There has been recent controversy about the clinical efficacy of these agents. Importantly, there have been several reports suggesting that the renal outcome is worsened in patients receiving nesiritide.

Doerschug KC, Delsing AS, Schmidt GA, et al. Renin-angiotensin system activation correlates with microvascular dysfunction in a prospective cohort study of clinical sepsis. *Crit Care*. 2010;14:R24.

Ferrari R, Guardigli G, Ceconi C. Secondary prevention of CAD with ACE inhibitors: a struggle between life and death of the endothelium. *Cardiovasc Drugs Ther*. 2010;24:331-339.

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Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease*. 10th ed. Philadelphia, PA: Elsevier; 2015:953-979.

Spinler SA, Cziraky M, Miller A. ACE inhibitors versus ARBs: comparison of practice guidelines and treatment selection considerations. *Formulary*. 2006;41:274-284.

A.13. Does the choice of antihypertensive therapy influence hemodynamic responses to induction, laryngoscopy, and intubation?

The pressor responses to induction, laryngoscopy, and intubation differ little whether patients with mild-to-moderate hypertension receive a *β*-blocker, a calcium channel blocker, an ACE inhibitor, or a diuretic. Even changes of a similar magnitude are also observed in untreated hypertensive patients. On the other hand, hypotensive responses may be magnified in those patients with poorly controlled hypertension following induction—generally due to a reduced intravascular volume in the face of increased vascular sympathetic tone. As mentioned previously, attention should be directed not only to the systolic but also to pulse and diastolic pressures.

Sear JW, Jewkes C, Tellez JC, et al. Does the choice of antihypertensive therapy influence haemodynamic responses to induction, laryngoscopy and intubation? *Br J Anaesth*. 1994;73:303-308.

A.14. Does chronic angiotensin-converting enzyme (ACE) inhibition influence anesthetic induction?

Coriat et al. reported that, in hypertensive patients chronically treated with ACE inhibitors, therapy until the day of surgery is a major factor influencing BP responsiveness to anesthetic induction for vascular surgery. If enalapril (a long-acting ACE inhibitor) treatment is continued, a very low plasma-converting enzyme activity will be observed and an exaggerated hypotensive response may occur at induction. If captopril (a short-acting ACE inhibitor) treatment is continued, the magnitude of the decrease in BP in response to induction, although lower than with enalapril, is enhanced compared with that noted in patients in whom captopril had been stopped. All of the hypotensive episodes in patients who received ACE inhibitors until the day of surgery were easily corrected by administration of an *α* agonist. The temporary withdrawal of these two ACE inhibitors attenuated the hypotensive response to induction but did not lead to an abnormal BP response to induction and intubation. However, Ryckwaert and Colson reported that ACE inhibitor treatment in patients with infarction-induced myocardial dysfunction does not increase the incidence of severe hypotension after induction of anesthesia. Additionally, a retrospective analysis of patients who underwent shoulder surgery in the sitting position by Trentman et al. showed that timing of the last dose of ACE inhibitors or angiotensin receptor antagonists had no impact on intraoperative hypotensive episodes. In all, the overwhelming opinion is to continue all antihypertensive medication including the day of surgery and resumption of such therapy postoperatively. A number of studies have shown an improvement in outcome when therapy is continued versus a worsening in outcome when either ACE inhibitors or *β*-blockers have been withdrawn.

Benedetto U, Sciarretta S, Roscitano A, et al. Preoperative angiotensin-converting enzyme inhibitors and acute kidney injury after coronary artery bypass grafting. *Ann Thorac Surg*. 2008;86:1160-1165.

Coriat P, Richer C, Douraki T, et al. Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. *Anesthesiology*. 1994;81:299-307.

Kwapisz MM, Müller M, Schindler E, et al. The effect of intravenous quinaprilat on plasma cytokines and hemodynamic variables during cardiac surgery. *J Cardiothorac Vasc Anesth*. 2004;18:53-58.

Ryckwaert F, Colson P. Hemodynamic effects of anesthesia in patients with ischemic heart failure chronically treated with angiotensin-converting enzyme inhibitors. *Anesth Analg*. 1997;84:945-949.

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Trentman TL, Fassett SL, Thomas JK, et al. More hypotension in patients taking antihypertensives preoperatively during shoulder surgery in the beach chair position. *Can J Anaesth*. 2011;58(11):993-1000.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate this patient preoperatively?

In addition to the routine systemic preoperative physical and history, special attention should be paid to the following: etiology and severity of hypertension, the subtype of hypertension, current therapy, and the end-organ damage from chronic hypertension.

The underlying cause of hypertension should be clear. Surgical mortality is relatively high in patients with renovascular hypertension. Moreover, failure to diagnose a pheochromocytoma preoperatively, albeit a rare finding, may prove fatal because anesthetic agents are well known to precipitate a crisis in such patients. Meanwhile, the severity of hypertension alters anesthetic risk.

Antihypertensive drugs have different anesthetic implications. Diuretics frequently cause chronic hypokalemia and hypomagnesemia, which may increase the risk of arrhythmia. Therefore, serum electrolytes should be checked preoperatively.

The presence of target-organ damage in the brain, heart, and kidney signifies long-standing, poorly controlled hypertension. Unfortunately, markers of organ damage become demonstrable only after significant end-organ damage has occurred.

For cardiac evaluation, electrocardiogram and chest x-ray film serve as minimal tests. The echocardiogram will be helpful. LVH can increase the risk of perioperative myocardial ischemia from imbalances of myocardial oxygen supply and demand regardless of the presence or absence of coronary artery disease. There is a very high correlation between LVH, ISH, and PPH—it is uncertain which comes first. Some authorities believe that hypertensive patients without evidence of LVH or other risk factors are at a lower perioperative cardiac risk and do not require further evaluation for most operations. Patients with severe hypertension are also at an increased risk for diastolic dysfunction causing CHF.

For renal evaluation, urinalysis, serum creatinine, and blood urea nitrogen should be measured to define the presence and extent of renal parenchymal disease. If chronic renal failure exists, hyperkalemia and elevated plasma volume may be of concern. Normal saline crystalloid intravenous solution is recommended for such cases.

For cerebrovascular evaluation, a history of cerebrovascular accidents and transient ischemic attacks and the presence of hypertensive retinopathy should be looked for.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:583-611.

Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287:2043-2046.

B.2. Would you postpone the surgery? Why? What BP would you like the patient to achieve before surgery?

It is prudent to postpone elective surgery with a BP of 230/120 mm Hg. This patient should be considered to have hypertensive emergency if additional end-organ sequelae are present, in which case he needs to be admitted for intravenous control of BP. Otherwise, for hypertensive urgency, it is recommended that the patient be placed in a quiet environment and managed with rest and oral antihypertensives. The patient should be discharged and instructed to follow-up with his internist for management and control of hypertension. Prior to rescheduling for surgery, if time permits, the BP should be gradually lowered over 6 to 8 weeks to less than 140/90 mm Hg. Acute control within several hours is inadvisable before elective surgery because this practice may put the cerebral or other circulations at risk for ischemia.

In moderate hypertensive patients with severe end-organ involvement, preoperative BP should be normalized as much as possible, although in asymptomatic patients with mild-tomoderate hypertension (diastolic BP <110 mm Hg), elective surgery may proceed without increased cardiovascular risks. Goldman found that patients with mild and moderate

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hypertension were not at increased risk of vascular complications unless they had other risks of coronary heart disease. In all, the thresholds being recommended apply only in part to today's surgical population. Most hypertensive patients presenting for surgery are elderly patients who suffer almost exclusively from ISH and PPH. It is uncertain what acute changes in BP preoperatively will have on outcome giving that the pathologic changes are chronic and unlikely to normalize with treatment. In patients with medically refractory coronary disease requiring coronary artery bypass grafting (CABG) surgery, PPH was associated with an increased risk of major vascular complication.

Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287:2043-2046.

Fontes ML, Aronson S, Mathew JP, et al; for the Multicenter Study of Perioperative Ischemia (McSPI) Research Group and the Ischemia Research and Education Foundation (IREF) Investigators. Pulse pressure and risk of adverse outcome in coronary bypass surgery. *Anesth Analg*. 2008;107:1122-1129.

Goldman L. Cardiac risk in noncardiac surgery: an update. *Anesth Analg*. 1995;80:810-820.

Nikolov NM, Fontes ML, White WD, et al. Pulse pressure and long-term survival after coronary artery bypass graft surgery. *Anesth Analg*. 2010;110:335-340.

B.3. Should all or any of the chronic medications be discontinued before the operation?

Current opinion generally favors continuation of antihypertensive medications, especially *β*-blockers, up to the time of surgery. There is concern that acute withdrawal of these medications may precipitate ischemic myocardial events. Because *β*-blockade does not impair the hemodynamic response to hemorrhage and does not adversely affect responses to hypoxia, the medications should be continued. The withdrawal syndrome is characterized by an enhanced sensitivity to sympathetic stimulation and has been attributed to various factors, including sympathetic overactivity and increased triiodothyronine levels, but most probably it is a result of increased *β*-receptor density.

The safety of *β*-blockers and their benefits (prevention of hypertensive responses, dysrhythmias, and myocardial ischemia) have been long established. Similarly, treatment with calcium channel blockers, ACE inhibitors, statins, and diuretics can be maintained. Indeed, the responses to induction of anesthesia, laryngoscopy, and intubation differ little whether patients receive a *β*-blocker, a calcium channel blocker, an ACE inhibitor, or a diuretic. Withdrawal of clonidine has been associated with rebound hypertension.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:583-611.

Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287:2043-2046.

Sear JW, Jewkes C, Tellez JC, et al. Does the choice of antihypertensive therapy influence haemodynamic responses to induction, laryngoscopy and intubation? *Br J Anaesth*. 1994;73:303-308.

B.4. Should hypokalemia be treated before anesthesia? Why?

Hypokalemia is a frequent finding in hypertensive patients treated with the diuretic thiazides. It is important to maintain normal electrolyte balance in patients with heart or coronary artery disease. A low value of potassium (3.0 to 3.5 mEq per L) in these patients may cause arrhythmias, increase sensitivity to digitalis, and depress neuromuscular function. In patients without risk of cardiac complications of surgery and anesthesia, this modest reduction (3.0 to 3.5 mEq per L) should not prompt postponement of surgery or immediate potassium replacement. Patients with more severe potassium depletion (≤2.9 mEq per L) should be treated and/or undergo workup for such profound hypokalemia. For those patients, at least 1 week before surgery, supplemental potassium should be given if renal function is not impaired. In surgical emergencies, potassium may be given at a rate not to exceed 0.5 mEq per kg of body weight per hour. Administration should be stopped during surgery and restarted postoperatively, depending on serial potassium determinations. Vitez et

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al. concluded that chronic hypokalemia per se is not associated with a higher incidence of intraoperative arrhythmia.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:347-350.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 6th ed. Philadelphia, PA: Saunders; 2012:357-375.

Vitez TS, Soper LE, Wong KC, et al. Chronic hypokalemia and intraoperative dysrhythmias. *Anesthesiology*. 1985;63:130-133.

B.5. Should hypomagnesemia be treated before anesthesia? Why?

The normal level of magnesium is between 1.5 and 2.5 mEq per L. Magnesium ion is essential for the proper function of most enzyme systems. Depletion is characterized by neuromuscular and central nervous system hyperexcitability. These signs are similar to those of calcium deficiency. Cardiovascular abnormalities include coronary artery spasm, cardiac failure, and dysrhythmias. When severe, hypomagnesemia may induce seizures, confusion, and coma. Replacement should be done only in cases of severe depletion. Magnesium should not be given to the oliguric patient and should be given very carefully to patients with renal insufficiency. Small intravenous doses should be used, with careful observation for toxicity (lethargy, weakness, and loss of deep tendon reflexes).

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:356-359.

B.6. Does an asymptomatic carotid bruit increase the risk in these patients?

Yes. The incidence of stroke is increased in such patients, although the stroke may not be thrombotic or related to the carotid artery in which the bruit was heard. Bruits are general predictors of vascular disease and may be predictors of perioperative strokes. It is important to note that in patients who are asymptomatic from their carotid stenosis, endarterectomy is no longer recommended. Nevertheless, there continues to be much debate on this topic.

De Feo M, Renzulli A, Onorati F, et al. The risk of stroke following CABG: one possible strategy to reduce it. *Int J Cardiol*. 2005;98(2):261-266.

Wolf PA, Kannel WB, Sorlie P, et al. Asymptomatic carotid bruit and the risk of stroke. The Framingham study. *JAMA*. 1981;245:1442-1445.

Yatsu FM, Hart RG. Asymptomatic carotid bruit and stenosis: a reappraisal. *Stroke*. 1983;14:301-304.

B.7. The surgery was postponed for 6 weeks. The patient was on metoprolol, aspirin, atorvastatin, captopril, hydrochlorothiazide, and potassium chloride. His BP was 160/60 mm Hg and potassium 4.0 mEq per L. How would you premedicate this patient?

Because half or more of hypertensive patients still have elevated BP despite treatment, the anesthesiologist should determine the anxiety level of the patient. With this knowledge, the premedication with diazepam, lorazepam, or midazolam can be regulated to have the patient arrive in the operating room sedated. However, due to a high occurrence of delirium in the elderly receiving benzodiazepines, premedication with such agents is being discouraged. This will help to prevent a starting BP well above the optimal level. All the antihypertensive medications are continued up to the day of surgery.

Lepousé C, Lautner CA, Liu L, et al. Emergence delirium in adults in the post-anaesthesia care unit. *Br J Anaesth*.

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2006;96(6):747-753.

B.8. If the patient is an untreated hypertensive patient with BP 170/70 mm Hg, would you treat the patient preoperatively with an antihypertensive agent?

Yes. The preoperative administration of clonidine, β-blockers, or angiotensin-converting enzyme (ACE) inhibitors has been advocated to reduce the intraoperative hemodynamic lability and myocardial ischemia in hypertensive patients. Clonidine, a central α_2-agonist, decreases sympathetic outflow and reduces plasma catecholamines, aldosterone levels, and renin activity. A single dose of clonidine, 5 μg per kg orally, 2 hours before surgery significantly decreases anesthetic requirements and hemodynamic lability in patients with mild-tomoderate hypertension. However, preoperative clonidine did not decrease BP lability during aortic operation. Perioperative use of clonidine also has been shown to have short- and longterm benefits related to cardiac morbidity and survival.

The best treatment may be cardioselective β-blocker therapy. A single small oral dose of a β-adrenergic blocking agent such as labetalol, atenolol, or metoprolol given preoperatively to untreated, asymptomatic, mildly hypertensive patients effectively attenuated tachycardia with tracheal intubation and emergence. The incidence of myocardial ischemia was reduced from 28% in the control group to 2% in the β-blocker groups. An oral-dose ACE inhibitor such as enalapril given preoperatively also attenuates the hemodynamic responses to intubation and surgical stimulation.

Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287:2043-2046.

Stone JG, Foëx P, Sear JW, et al. Myocardial ischemia in untreated hypertensive patients: effect of a single small oral dose of a beta-adrenergic blocking agent. *Anesthesiology*. 1988;68:495-500.

Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after noncardiac surgery. *Anesthesiology*. 2004;101(2):284-293.

C. Intraoperative Management

C.1. How would you monitor this patient?

- *Electrocardiogram*. Simultaneous leads V_5 and II, multiple-lead ST-segment analysis, if possible, are essential because hypertensive patients are at increased risk for myocardial ischemia regardless of the presence or absence of coronary disease.

- *BP*. A continuous monitoring of BP is essential because of lability of BP in these patients. Direct intra-arterial measurement of BP permits beat-to-beat observation. However, noninvasive automatic oscillometric techniques usually are sufficient.
- *Pulmonary artery catheter (PAC)* . Only for those hypertensive patients with a history of CHF or a recent MI, a PAC may be helpful in managing fluid replacement and monitoring ventricular function. Of note, there is a strong correlation between hypertension and LVH, which results in poor ventricular compliance reflected by elevated pulmonary artery occlusion pressure in the face of low or normal ventricular volumes and normal contractility. Presence of CHF in hypertensive patients is frequently a marker of diastolic dysfunction and *not* systolic dysfunction.
- *Pulse oximeter*. This should be used to monitor peripheral blood flow and oxygenation.
- *End-tidal CO_2 analyzer*. This monitor will help maintain normocarbia.

C.2. What are the anesthetic goals for hypertensive patients?

The anesthetic goal is to minimize wide lability of BP in response to anesthetic and surgical stimuli to prevent the following:

- Myocardial ischemia from tachycardia or less common from either hypertension or hypotension
- Cerebral hypoperfusion from hypotension

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- Cerebral hemorrhage and hypertensive encephalopathy resulting from hypertension or embolic stroke from rupture of plagues either locally or from the aorta and the neck vessels
- Renal failure from renal hypoperfusion

Particular attention to diastolic BP is strongly recommended while attempting to reduce systolic BP. It is unfortunate that clinical practice perioperatively hinges on manipulation of the systolic BP without attention to the diastolic component. This is particularly troublesome in most elderly patients who suffer from ISH and/or wide pulse pressure. In both subtypes of hypertension, the already lower diastolic pressure can easily be reduced further— predisposing to myocardial hypoperfusion and ischemia.

Lee et al. showed that patients with wide pulse pressure have an increased risk for thrombogenesis marked by elevated levels of D-dimers, von Willebrand factor, and platelet activation. This along with extensive atherosclerotic disease of the aorta, carotid, and renal arteries, which is also common in patients with ISH, provides a pathophysiologic basis for the increase incidence of perioperative stroke, MI, and renal dysfunction observed in hypertensive patients.

Lastly, careful control of the hemodynamic responses to noxious stimuli such as endotracheal intubation, surgical incision and manipulation, and emergence from anesthesia is essential in the hypertensive patient.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 6th ed. Philadelphia, PA: Saunders; 2012:104-119.

Lee KW, Blann AD, Lip GY. High pulse pressure and nondipping circadian blood pressure in patients with coronary artery disease: relationship to thrombogenesis and endothelial damage/dysfunction. *Am J Health*. 2005;18:104-115.

Lovett JK, Howard SC, Rothwell PM. Pulse pressure is independently associated with carotid plaque ulceration. *J Hypertens*. 2003;21:1669-1676.

C.3. How would you induce anesthesia for the hypertensive patient?

While the patient is being preoxygenated, fentanyl, 5 *μ*g per kg, is given slowly to achieve drowsiness. Then, either thiopental in 50-mg increments or propofol in 30- to 50-mg increments is titrated to produce unconsciousness, followed by succinylcholine, 1 mg per kg, or nondepolarizing muscle relaxants to facilitate tracheal intubation.

All anesthetic agents are acceptable with the possible exception of ketamine, which may produce significant hypertension and tachycardia. However, deeper anesthesia with potent inhalation agents to attenuate tachycardia and hypertension should be done with caution because of higher incidence of hypotension arising from both vasodilation and cardiac depression.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 6th ed. Philadelphia, PA: Saunders; 2012:104-119.

Martin DE, Rosenberg H, Aukburg SJ, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesth Analg*. 1982;61:680-684.

C.4. How does tracheal intubation produce hypertension?

Translaryngeal intubation of the trachea stimulates laryngeal and tracheal receptors, resulting in marked increase in the elaboration of sympathomimetic amines. This sympathetic stimulation results in tachycardia and a rise in BP. In normotensive patients, this rise is approximately 20 to 25 mm Hg; it is much greater in hypertensive patients. This increase in BP results from vasoconstriction because of unopposed *α* stimulation in hypertensive patients taking *β*-blocking drugs.

Prys-Roberts C, Greene LT, Meloche R, et al. Studies of anaesthesia in relation to hypertension. II. Haemodynamic consequences of induction and endotracheal intubation. *Br J Anaesth*. 1971;43:531-547.

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C.5. What happens to the left ventricular ejection fraction during and immediately following intubation?

During and immediately following intubation associated with tachycardia and hypertension, there is a decrease in the left ventricular ejection fraction. This is particularly marked in patients with coronary artery disease. Nevertheless, such hemodynamic perturbations can be anticipated and treated accordingly with *β*-blockade, narcotic, and titration of hypnotic and/or inhalation agents.

Giles RW, Berger JH, Barash PG, et al. Continuous monitoring of left ventricular performance with the computerized nuclear probe during laryngoscopy and intubation before coronary artery bypass surgery. *Am J Cardiol*. 1982;50:735-741.

C.6. What other measures can prevent hypertension and tachycardia at the time of intubation?

The rise in BP and heart rate occurs approximately 14 seconds after the start of laryngoscopy and becomes maximal after 30 to 45 seconds of direct laryngoscopy. If possible, laryngoscopy time should be 15 seconds or less to minimize BP elevation. Simultaneous administration of fentanyl, 5 *μ*g per kg with the induction dose of thiopental or propofol, can blunt the cardiovascular response to tracheal intubation. Other measures are described as follows:

- Lidocaine, 1.5 mg per kg, is given 2 minutes before intubation.
- Esmolol, up to 2 mg per kg, appears to be especially effective in providing consistent and reliable protection against hypertension and tachycardia with intubation. It is easy to titrate and does not exacerbate postintubation hypotension because of its short duration of action.
- Labetalol, 0.15 to 0.45 mg per kg, is comparable to esmolol, 1.5 to 4.5 mg per kg, in attenuating hemodynamic effects. However, the half-lives of intravenous esmolol and labetalol are 9 minutes and 5 hours, respectively. Additionally, labetalol has minimal effects on heart rate, and through its action on *α* receptors, it acts similar to a vasodilator, particularly with chronic use.
- Nicardipine, 1 mg intravenously, 2 minutes before tracheal intubation maintained hemodynamic stability during the intraoperative period. Both doses of 0.015 and 0.03 mg per kg attenuated BP but not heart rate responses during emergence and extubation. Greater BP control occurred with the larger nicardipine dose of 0.03 mg per kg.

It is important to remember that all the previously mentioned doses are used with a single agent only. If a combination of different agents or anesthetics is used, doses should be decreased accordingly. Otherwise, severe hypotension may ensue.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:397-402.

Gold MI, Sacks DJ, Grosnoff DB, et al. Use of esmolol during anesthesia to treat tachycardia and hypertension. *Anesth Analg*. 1989;68:101-104.

Helfman SM, Gold MI, Delisser EA, et al. Which drug prevents tachycardia and hypertension associated with tracheal intubation: lidocaine, fentanyl, or esmolol? *Anesth Analg*. 1991;72:482-486.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 6th ed. Philadelphia, PA: Saunders; 2012:104-119.

Kapnoudhis P, Vaghadia H, Jenkins LC, et al. Esmolol versus fentanyl for preventing haemodynamic response to intubation in cardiovascular disease. *Can J Anaesth*. 1990;37:S145.

Kovac AL, McKinley C, Tebbe CJ, et al. Comparison of nicardipine versus placebo to control hemodynamic responses during emergence and extubation. *J Cardiothorac Vasc Anesth*. 2001;15:704-709.

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Martin DE, Rosenberg H, Aukburg SJ, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesth Analg*. 1982;61:680-684.

C.7. After induction and intubation, the BP decreased to 70/40 mm Hg. What would you do?

Hypotension after induction of anesthesia is usually due to combination of vasodilation, hypovolemia, and cardiac depression. Vasodilation can be caused by inducing agents such as thiopental, propofol, or midazolam; moderate-to-high doses of narcotics; and potent inhalation agents. Hypertensive patients are in relative hypovolemia because of chronic vasoconstriction and/or diuretic therapy. Preoperative bowel preparation and nothing by mouth further contribute to hypovolemia. Barbiturates, benzodiazepines, and inhalation agents can cause a mild-to-moderate degree of cardiac depression.

Hypotension after induction of anesthesia usually can be easily corrected by volume replacement and simultaneous titration of vasopressors such as ephedrine 5 to 10 mg or phenylephrine in 0.1-mg increments.

Coriat P, Richer C, Douraki T, et al. Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. *Anesthesiology*. 1994;81:299-307.

C.8. What is your choice of agents for maintenance of anesthesia? Why?

No particular anesthetic technique or specific drug combinations have been demonstrated to be superior to others in hypertensive patients. Potent inhalation anesthetics or narcotics should be titrated to the desired level of central nervous system depression while the BP is monitored continuously.

Narcotics and nitrous oxide provide an anesthetic with less overall lability of BP, but commonly, intraoperative hypertension is difficult to control by moderate doses of narcotics. High doses of narcotics are not suitable for early extubation. Likewise, use of nitrous oxide is debatable in open cholecystectomy given its propensity to increase bowel distention—the severity being related to higher concentration of nitrous oxide and to longer duration of use. This concern is less pertinent for laparoscopic cholecystectomy whereby insufflation of gas to pressurize the abdomen should counteract the distensible property of nitrous oxide (also see Chapter 26, section C.4).

Potent inhalation agents provide greater control of hypertension but seem to produce less stability. Isoflurane, desflurane, and sevoflurane possess the advantage of more peripheral vasodilation and less cardiac depression.

Akca O, Lenhardt R, Fleischmann E, et al. Nitrous oxide increases the incidence of bowel distension in patients undergoing elective colon resection. *Acta Anaesthesiol Scand*. 2004;48(7):894-898.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 6th ed. Philadelphia, PA: Saunders; 2012:104-119.

Taylor E, Feinstein R, White PF, et al. Anesthesia for laparoscopic cholecystectomy. Is nitrous oxide contraindicated? *Anesthesiology*. 1992;76(4):541-543.

C.9. How would you manage fluid therapy for hypertensive patients?

Patients with essential hypertension are usually hypovolemic because of vasoconstriction and diuretic therapy. Hydration of the hypertensive patient should be started before induction of anesthesia to minimize the “roller coaster” often seen with hypertension. However, overhydration should be avoided because it may contribute to postoperative hypertension when the vasodilating effects of anesthetics are gone. Therefore, careful estimation of fluid intake and output is essential. Foley catheter and central venous pressure monitor are indicated for major surgery with extensive fluid exchange.

As discussed previously, presence of LVH in hypertensive patients shifts the left ventricular compliance curve upward and leftward such that for the same ventricular volume, a higher left ventricular diastolic pressure is attained as compared to a

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nonhypertrophied ventricle. When managing these patients with a PAC, higher pulmonary artery occlusion pressure (sometimes >20 mm Hg) is necessary to achieve normovolemia. Cardiac output also must be checked frequently during volume challenges.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 6th ed. Philadelphia, PA: Saunders; 2012:104-119.

C.10. During the surgery, BP increased to 220/120 mm Hg. How would you treat the hypertension?

Intraoperative control of hypertension is outlined in Table 11.4. Severe hypertension that occurs during a surgical procedure is most frequently due to inadequate anesthesia. Inadequate blockade of sensory input from the surgical procedure stimulates the elaboration of sympathomimetic amines, resulting in hypertension and tachycardia. If a potent inhalation anesthetic is being used, the level of anesthesia should be deepened by increasing the inspired concentration of the anesthetic. A narcotic may not control the rise in BP, and it may be necessary to switch to a potent inhalation anesthetic.

Hydralazine, 5-mg increments, may be titrated to decrease BP safely with little chance of excessive reduction. The onset of action is in 10 to 15 minutes with 1 to 2 hours duration.

Labetalol, 5- to 10-mg increments, is very useful in controlling hypertension and tachycardia. It makes the most sense to use β-blockers after a significant rise in BP because these agents act directly to antagonize the effects of the catecholamines. Although other agents may lower the BP, it is highly possible that the excessive availability of both norepinephrine and epinephrine will continue to exert their effects at the receptor site—compromising tissue perfusion from microcirculatory vasoconstriction. This view may explain the broad antiischemic effects of perioperative β-blockers on the brain, the heart, and the kidneys.

Rarely, continuous infusion of nicardipine, nitroglycerin, or nitroprusside, direct arteriolar vasodilators, is needed to control hypertension during anesthesia.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 6th ed. Philadelphia, PA: Saunders; 2012:104-119.

Lindenauer PK, Pekow P, Wang K, et al. Perioperative beta-blocker therapy and mortality after major noncardiac surgery. *N Engl J Med*. 2005;353(4):349-361.

C.11. What could you do to prevent hypertension during extubation and emergence?

It is logical to use antihypertensive agents during extubation and emergence, as the patient is awakened at the end of surgery. Many drugs or combinations are effective, including intravenous lidocaine, esmolol, labetalol, verapamil, or diltiazem 2 minutes before extubation. If BP goes over desired levels after extubation, additional doses may be titrated to control BP.

Mikawa K, Nishina K, Maekawa N, et al. Attenuation of cardiovascular responses to tracheal extubation: verapamil versus diltiazem. *Anesth Analg*. 1996;82:1205-1210.

TABLE 11.4 Intraoperative Control of Hypertension

Anesthetics

Narcotics, inhalation agents, butorphanol, lidocaine

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Antihypertensives

Adrenergic blockers

α-Blocker: phentolamine

β-Blocker: propranolol, metoprolol

α- and *β*-Blocker: labetalol

Calcium channel blockers

Diltiazem, nicardipine, verapamil

ACE inhibitors

Enalapril

Direct vasodilators

Hydralazine, nitroglycerin, nitroprusside

Dopaminergic agonists

Fenoldopam

ACE, angiotensin-converting enzyme.

C.12. Would you consider regional anesthesia for this patient?

Certainly, regional anesthesia can avoid marked increases in sympathetic tone and hemodynamic changes that occur with intubation and extubation. Spinal or epidural anesthesia may be used for lower abdominal surgery. For cholecystectomy, higher levels of regional anesthesia are needed and may compromise respiratory function or unmask hypovolemia. In addition, prolonged surgery in a nonsedated patient can cause anxiety and irritability that may induce hypertension and tachycardia.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 6th ed. Philadelphia, PA: Saunders; 2012:104-119.

D. Postoperative Management

D.1. The patient developed hypertension, BP 210/110 mm Hg in the postanesthesia care unit. What would you do?

The management of postoperative hypertension depends on the etiology of the hypertension, the clinical scenario, and the level of hypertension. First, the cause of hypertension should be determined and treated accordingly. Hypertension per se should also be treated by an antihypertensive agent. The causes of postoperative hypertension include pain, emergence excitement, hypoxemia, hypercarbia, reaction to endotracheal tube, full bladder, hypothermia, relative hypervolemia from intraoperative administration of excess fluid, and chronic medication and withdrawal. The most common cause of

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postoperative hypertension is incisional pain. As the patient awakens, pain triggers an outpouring of catecholamines. The extreme lability of BP in many hypertensive patients makes this rapid increase critical to control. Depending on the cause of hypertension, intravenous analgesics and antihypertensives or diuretics should be titrated to control hypertension. If both tachycardia and hypertension occurred postoperatively, calcium channel blockers such as verapamil, diltiazem, or nicardipine and β-blocking agents such as propranolol, esmolol, labetalol, or metoprolol are preferred agents. Hypertension resulting from pain can be preventable or attenuated by asking the surgeon to inject a long-lasting local anesthetic along the incision or to perform a local nerve block.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1557-1577.

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Chapter 12
Cardiac Tamponade

Nikolaos J. Skubas

James Osorio

A 69-year-old woman presents with shortness of breath, orthopnea, oliguria, and overt weakness 4 days after two-vessel coronary artery bypass graft procedure and mitral valve replacement. On examination, she appears anxious and diaphoretic; her vital signs are as follows: respiratory rate, 38 breaths per minute; heart rate (HR), 120 beats per minute (normal sinus rhythm); and systemic blood pressure, 115/66 mm Hg. A pulmonary artery catheter (PAC) was inserted and revealed: pulmonary artery (PA) pressures, 55/15 mm Hg; pulmonary artery occlusion pressure (PAOP), 14 mm Hg; central venous pressure (CVP), 23 mm Hg; and cardiac output (CO), 2.7 L per minute. Both the prothrombin and the partial thromboplastin times (PTTs) were elevated.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis of low CO postoperatively?
2. What is cardiac tamponade? What are the common etiologies?
3. What is the difference between acute and delayed cardiac tamponade?
4. How is postcardiotomy cardiac tamponade diagnosed?
5. What is regional cardiac tamponade?
6. What is pulsus paradoxus? What is Kussmaul sign?
7. Describe the ventricular interaction in cardiac tamponade.
8. How is coronary blood flow affected in cardiac tamponade?
9. What are the electrocardiographic abnormalities associated with cardiac tamponade?
10. What radiographic and echocardiographic findings are noted in cardiac tamponade?
11. What is in the differential diagnosis of post-cardiopulmonary bypass (post-CPB) bleeding?
12. What is the mechanism of action of low molecular weight heparin (LMWH)?
13. Describe the advantages of LMWH over standard heparin therapy.
14. What is heparin-induced thrombocytopenia (HIT)? How is the diagnosis made?
15. What is the therapy for HIT?
16. Can HIT be caused by LMWH?
17. What is the mechanism of heparin antagonism by protamine?
18. What is “heparin rebound”?
19. How does warfarin affect the coagulation system? What is the therapy for reversing its effect?
20. What do the following measure: prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time, and activated clotting time (ACT)?
21. How is the anticoagulant effect of LMWH monitored?
22. What is point-of-care testing (POCT) and what are the commonly used point-of-care devices?

23. How does desmopressin aid hemostasis?
24. What is fibrinolysis?

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25. What is aminocaproic acid? What is tranexamic acid?

B. Preoperative Evaluation and Preparation

1. Interpret the hemodynamic findings of this patient.
2. How would you treat the low output status of this patient?
3. How would you evaluate this patient's coagulation status?
4. What do fresh frozen plasma (FFP) and cryoprecipitate contain?
5. What are the indications for transfusing FFP, platelet concentrate, and cryoprecipitate?
6. What are the complications associated with blood component transfusions?
7. What is the risk for acquiring HIV from blood exposure?
8. Assuming that the patient has cardiac tamponade, how would you prepare this patient for surgery?

C. Intraoperative Management

1. How would you monitor this patient during transport to the operating room? What emergency drugs would you bring with you?
2. In this patient, what hemodynamic effects would occur from intravenous induction with ketamine, thiopental, fentanyl, propofol, etomidate, or midazolam?
3. Describe the induction process for cardiac tamponade.
4. Following induction and intubation, the systemic blood pressure decreased to 55/30 mm Hg. Describe the clinical events accounting for this perturbation and the management steps required for resuscitation.
5. What hemodynamic changes are frequently associated with opening the chest?
6. What is myocardial stunning? What is myocardial hibernation?

D. Postoperative Management

1. How would you manage hypertension in the intensive care unit (ICU)?
2. When would it be appropriate to extubate this patient?

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis of low CO postoperatively?

CO is the product of stroke volume (SV) and HR: CO = HR × SV. Therefore, a low CO state can occur when SV and/or HR decrease. Fast HRs, of either ventricular or atrial origin (i.e., atrial fibrillation), may also cause a low CO state because the diastolic filling time is decreased or the atrial contribution to the ventricular filling is reduced or abolished. Because SV is the difference between left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV), the etiology of a reduced SV can be more accurately determined by exploring whether there has been a change in the preload (LVEDV), the afterload, and/or the left ventricular contractile state. Therefore, increased (that may cause left ventricular overdistention and systolic dysfunction) or decreased preload can also lower the CO. Myocardial contractility can be compromised by either direct (myocardial ischemia, infarction, stunning, or hibernation) or indirect causes (mechanical factors as in cardiac tamponade, pulmonary embolism; pharmacologic agents; and toxins, such as inflammatory cytokines and bacterial endotoxins). A combination of different hemodynamic disturbances can coexist in the same patient. For example, a patient can have both a decrease in contractility and a reduced preload to account for the low CO state. Therefore, correcting one problem alone may not produce the optimal hemodynamic condition.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:98-131.

Tung A. Critical care of the cardiac patient. *Anesthesiol Clin*. 2013;31:421-432.

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A.2. What is cardiac tamponade? What are the common etiologies?

Cardiac tamponade is defined as significant extrinsic compression of the heart by accumulating intrapericardial blood and clots (postcardiotomy, dissecting aortic aneurysm, trauma, anticoagulant therapy), exudative effusions (malignant states, infective pericarditis, idiopathic pericarditis), nonexudative effusions (uremia, systemic lupus erythematosus, rheumatoid arthritis, idiopathic, radiation), and air. If the intrapericardial pressure is increased enough, globally or regionally, cardiac tamponade may occur irrespective of the actual intrapericardial volume. Cardiac tamponade is a pathophysiologic continuum that on one extreme may be clinically insignificant and on the other extreme present as a life-threatening condition requiring emergent surgical attention. In clinical tamponade, as the pericardial pressure approaches the intra-atrial and intraventricular pressures, the SV progressively declines, thus resulting in systemic hypotension and cardiogenic shock.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:710-713.

Meltser H, Kalaria VG. Cardiac tamponade. *Catheter Cardiovasc Interv*. 2005;64:245-255.

Skubas NI, Fontes ML. Pericardial diseases. In: Mathew J, Swaminathan M, Ayoub C, eds. *Clinical Manual and Reviewof Transesophageal Echocardiography*. 2nd ed. New York: McGraw-Hill; 2010:351-369.

Spodick DH. Pathophysiology of cardiac tamponade. *Chest*. 1998;113:1372-1378.

A.3. What is the difference between acute and delayed cardiac tamponade?

In the setting of cardiac surgery, acute cardiac tamponade can occur over minutes, hours, or after a few days postoperatively, with a reported incidence of 0.5% to 5.8%. In the typical patient, a significant chest tube output (greater than 200 mL per hour) in the immediate postoperative period, with or without hemodynamic signs of inadequate cardiac output, is a sign of an increased amount of blood around the heart. Alternatively, the chest tubes may become clogged by blood clots impeding mediastinal drainage and the clinical picture of cardiac tamponade develops sooner.

Delayed tamponade has been arbitrarily defined as cardiac tamponade occurring 5 to 7 days after pericardiotomy and its incidence is 0.3% to 2.6%. Delayed tamponade is often misdiagnosed because of a low index of suspicion and clinical signs and symptoms that are confused with congestive heart failure, pulmonary embolism, and generalized fatigue (i.e., failure to thrive postoperatively). The most common culprit in delayed cardiac tamponade is anticoagulant therapy with warfarin (Coumadin), heparin, or platelet-inhibiting agents. However, a pericardial effusion after cardiac surgery is common. Using echocardiography, Weitzman et al. evaluated 122 consecutive patients postoperatively and demonstrated that most of them (103 of 122, 84%) had pericardial effusions. Generally, effusions reach their maximum size by the 10th postoperative day and regress spontaneously thereafter.

D'Cruz IA, Overton DH, Pai GM. Pericardial complications of cardiac surgery: emphasis on the diagnostic role of echocardiography. *J Card Surg*. 1992;7:257-268.

Pepi M, Muratori M, Barbier P, et al. Pericardial effusion after cardiac surgery: incidence, site, size, and haemodynamic consequences. *Br Heart J*. 1994;72:327-331.

Weitzman LB, Tinker WP, Kronzon I, et al. The incidence and natural history of pericardial effusions after cardiac surgery—an echocardiographic study. *Circulation*. 1984;69:506-511.

A.4. How is postcardiotomy cardiac tamponade diagnosed?

The diagnosis of cardiac tamponade following cardiac surgery is often difficult to make and requires a high degree of clinical suspicion, physical examination, proficient knowledge of PAC-derived measurements, and diagnostic tools such as echocardiography and chest radiography. Often, the diagnosis is made in the operating room, whereby evacuation of

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clot and blood from the mediastinum is associated with a drastic improvement in hemodynamics (Fig. 12.1). Relying on one modality alone for diagnosis can lead to inaccurate management decisions and increase patient morbidity. For example, the PAC data can be misleading postcardiotomy because the classical teaching of equalization of diastolic blood pressures in cardiac tamponade (CVP = pulmonary artery diastolic pressure [PAD] = PAOP) is infrequently observed because the heart is not surrounded by the transected pericardium. Thus, blood or clot does not distribute homogeneously around the heart for the pericardial diastolic pressures to equalize.

P.296

Generally, the CVP is elevated with significant compression of the right heart, but reduced blood flow to the left heart may result in low left-sided heart pressures that would be inconsistent with “classical” tamponade physiology. The majority of patients with postcardiotomy cardiac tamponade have atypical clinical, hemodynamic, and/or echocardiographic findings, mostly because the compression is localized. Therefore, the diagnosis of postoperative cardiac tamponade should be considered every time hemodynamic deterioration is encountered, particularly when reduction in cardiac output or blood pressure or both are not readily responsive

P.297

to conventional management. Furthermore, in delayed tamponade, the complaints tend to be vague and invasive hemodynamic data (i.e., PAC) is usually not available to allow prompt diagnosis of tamponade. Whenever the patient is not progressing as expected postoperatively and signs of end-organ dysfunction (fall in urine output or increase blood urea nitrogen and creatinine) are present, an echocardiogram should be obtained to rule out cardiac tamponade.

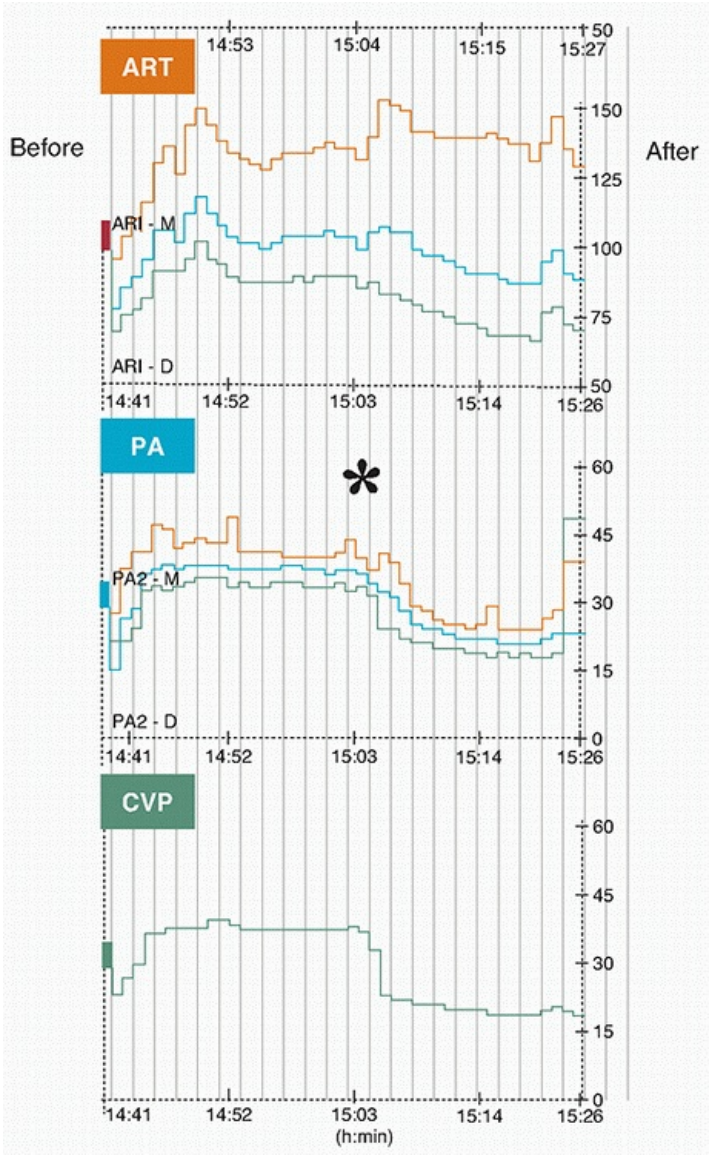


FIGURE 12.1 Intraoperative hemodynamics before and after evacuation of pericardial fluid. Arterial blood pressure (ART), pulmonary artery pressure (PA), and central venous pressure (CVP) are shown during chest exploration for cardiac tamponade. Note the elevated diastolic PA and CVP at the beginning of the anesthetic (left hand of the pressure trends). There is equalization of CVP and diastolic PA pressure, suggesting global pericardial effusion. As

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soon as the chest was opened and the pericardial collection was evacuated *(asterisk)*, the ART increased abruptly and the pulse pressure widened, although both PA and CVP immediately decreased to normal levels. Taking into consideration that ART increased whereas CVP decreased after evacuation of the pericardial collection, one can assume that the cardiac output has increased.

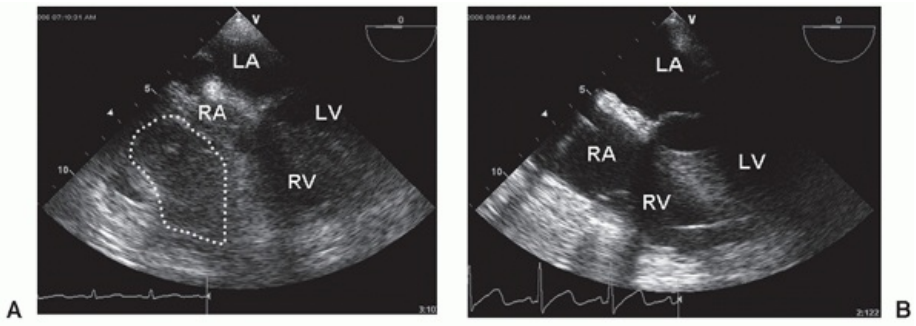


FIGURE 12.2 Regional, acute pericardial effusion. The heart is viewed in the mid-esophageal four-chamber view at 0-degree rotation, before **(A)** and after **(B)** evacuation of a loculated pericardial clot. The pericardial collection *(dotted line)* is around the right atrium (RA), almost obliterating its cavity (compared with the size of RA after evacuation). The collection is partially compressing the cavity of the right ventricle (RV). LA, left atrium; LV, left ventricle.

Chuttani K, Tischler MD, Pandian NG, et al. Diagnosis of cardiac tamponade after cardiac surgery: relative value of clinical, echocardiographic, and hemodynamic signs. *Am Heart J*. 1994;127(4, pt 1):913-918.

Russo AM, O'Connor WH, Waxman HL. Atypical presentations and echocardiographic findings in patients with cardiac tamponade occurring early and late after cardiac surgery. *Chest*. 1993;104:71-78.

Spodick DH. Pathophysiology of cardiac tamponade. *Chest*. 1998;113:1372-1378.

A.5. What is regional cardiac tamponade?

Regional cardiac tamponade occurs when one or more cardiac chambers (and not necessary the entire heart) become compressed by blood or blood clot or both, thereby compromising heart function (Figs. 12.2 and 12.3). Postoperatively, a right atrial hematoma often becomes localized around the anterior and lateral walls. Clots can also be found behind the left atrium at the level of the oblique sinus. Postcardiotomy, the regional collapse of the right atrium or the right ventricle in diastole, is the most common echocardiographic finding in “early” cardiac tamponade. Selective compression of the right heart by hematoma becomes less prominent in “delayed” tamponade, as the right heart becomes adherent or tethered to

the anterior chest wall. The diagnosis of regional tamponade is often misdiagnosed because the classical features of tamponade are often absent and blood and blood clots are unevenly distributed around the heart. The clinical presentation may be mistaken for congestive heart failure, acute left or right ventricular dysfunction, septic shock, or pulmonary embolism.

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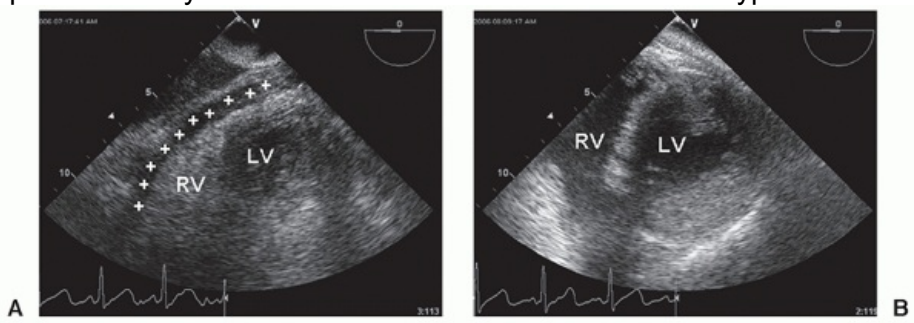


FIGURE 12.3 Pericardial effusion. The heart is viewed in the transgastric mid-papillary, shortaxis view, before **(A)** and after **(B)** the evacuation of a posterior pericardial collection *(asterisks)*. Notice the increase in cavity size of the left ventricle (LV) and reappearance of the cavity of the right ventricle (RV) after evacuation of the pericardial collection.

Jadhav P, Asirvatham S, Craven P, et al. Unusual presentation of late regional cardiac tamponade after aortic surgery. *Am J Card Imaging*. 1996;10:204-206.

Russo AM, O'Connor WH, Waxman HL. Atypical presentations and echocardiographic findings in patients with cardiac tamponade occurring early and late after cardiac surgery. *Chest*. 1993;104:71-78.

Skubas NI, Fontes ML. Pericardial diseases. In: Mathew J, Swaminathan M, Ayoub C, eds. *Clinical Manual and Reviewof Transesophageal Echocardiography*. 2nd ed. New York: McGraw-Hill; 2010:351-369.

A.6. What is pulsus paradoxus? What is Kussmaul sign?

Normally, during spontaneous inspiration, the extrathoracic to intrathoracic pressure gradient is increased and the filling of the right heart is slightly larger than the filling of the left heart. In the latter, the decreased intrapulmonary pressure during inspiration will cause a relative “pooling” of the blood in the lungs and decreases its filling gradient. That is associated with an inspiratory decrease of less than 10 mm Hg in the arterial systolic pressure along with an accompanying inspiratory decrease in the CVP. A paradoxical pulse differs from the normal situation in two aspects: the inspiratory fall of the arterial pressure exceeds 10 mm Hg and the inspiratory venous pressure remains steady or increases (Kussmaul sign), instead of decreasing. Echocardiographic studies of patients with cardiac tamponade by D'Cruz et al. described phasic respiratory changes whereby both left ventricular dimensions and mitral valve excursion decreased during inspiration. In contrast, right ventricular dimensions increased in association with a shifting of the interventricular septum toward the left ventricle. That is, the right heart filling is done at the expense of the left. Of importance, pulsus paradoxes and the phasic respiratory changes in ventricular dimensions and systemic systolic arterial pressure can also be present in respiratory distress, airway obstruction, chronic obstructive pulmonary disease, and pulmonary embolism, but they may be absent when patients cannot generate sufficient negative intrapleural pressure during inspiration, as in chest wall trauma, neuromuscular disease, and pneumothorax. Similarly, patients under positive pressure mechanical ventilation or with severe aortic regurgitation do not exhibit pulsus paradoxus.

D'Cruz IA, Overton DH, Pai GH. Pericardial complications of cardiac surgery: emphasis on the diagnostic role of echocardiography. *J Card Surg*. 1992;7:257-268.

Frey B, Freezer N. Diagnostic value and pathophysiologic basis of pulsus paradoxus in infants and children with respiratory disease. *Pediatr Pulmonol*. 2001;31:138-143.

Skubas NI, Fontes ML. Pericardial diseases. In: Mathew J, Swaminathan M, Ayoub C, eds. *Clinical Manual and Reviewof Transesophageal Echocardiography*. 2nd ed. New York: McGraw-Hill; 2010:351-369.

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A.7. Describe the ventricular interaction in cardiac tamponade.

Under normal conditions, the average SV of the right ventricle equals the SV of the left ventricle; however, cyclical respiratory differences in left and right ventricular SV do occur. During inspiration, the generated negative intrapleural pressure facilitates blood return to the right heart, whereas blood return to the left heart is diminished for the following reasons: (1) lung expansion increases its reservoir for blood and (2) the increase in right ventricular filling causes the interventricular septum to “bulge” leftward, thereby reducing left ventricular dimensions and altering its compliance and filling (ventricular interaction). During exhalation, the reverse process occurs. In the case of cardiac tamponade, the ventricular interaction is augmented and involves not only the interventricular septum but also other chambers depending on the etiology of the tamponade (fluid vs. clot, regional vs. global tamponade). Fundamentally, as intrapericardial content increases, it will reach a point whereby the parietal pericardium cannot stretch to accommodate the rising pressure. Because of the fixed space within the pericardium, the cardiac chamber dimensions become smaller as the pericardial contents increase. First, the thin-walled and more compliant atria progressively get compressed, followed by the right ventricle, and finally by the left ventricle.

Overall, the physiology of ventricular interaction in clinical cardiac tamponade becomes complex as the pressure-volume relation of mediastinal and chest structure is altered with each heartbeat and from respiratory and neuroendocrine influences.

Spodick DH. Pathophysiology of cardiac tamponade. *Chest*. 1998;113:1372-1378.

A.8. How is coronary blood flow affected in cardiac tamponade?

In the absence of coronary artery disease, coronary blood flow is reduced in cardiac tamponade, but this reduction is not sufficient to add an ischemic insult to the heart because there is a proportionate decrease in ventricular preload (underfilled heart) and ventricular afterload. Consequently, both myocardial work and oxygen consumption are reduced. In contrast, patients with coronary artery disease may be at increased risk for myocardial ischemia and infarction.

Reddy PS, Curtiss EL, O'Toole JD, et al. Cardiac tamponade: hemodynamic observations in man. *Circulation*. 1978;58:265-272.

A.9. What are the electrocardiographic abnormalities associated with cardiac tamponade?

Electrocardiographic changes in the setting of cardiac tamponade include nonspecific ST-T wave abnormalities, low-voltage QRS complex, signs of myocardial ischemia and pericarditis, and electrical alternans (Fig. 12.4). The electrocardiographic change of electrical alternans may reflect a hemodynamic pathology rather than an anatomic abnormality and is not very specific (very few patients with tamponade present with electrical alternans).

Fox JJ, McHarg JL, Gilmour RF Jr. Ionic mechanism of electrical alternans. *Am J Physiol Heart Circ Physiol*. 2002;282:H516-H530.

Kosta E, Kronzon I. Electrical alternans in cardiac tamponade. *Echocardiography*. 2000;17(6, pt 1):575-576.

Longo MJ, Jaffe CC. Images in clinical medicine: electrical alternans. *N Engl J Med*. 1999;341:2060.

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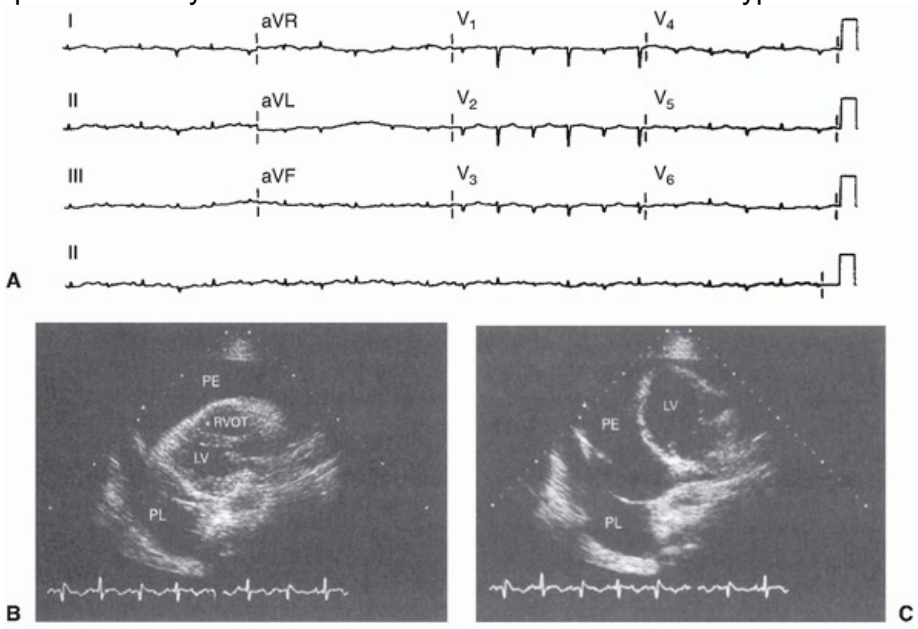


FIGURE 12.4 Depiction of electrical alternans in a patient with cardiac tamponade **(A)**. The images demonstrate significant pericardial effusions (PE) obtained during transthoracic echocardiography. Note the image of the left ventricle (LV) during systole **(B)** and diastole **(C)**. PL, pleural effusion; RVOT, right ventricular outflow tract. (From Longo MJ, Jaffe CC. Images in clinical medicine: electrical alternans. *N Engl J Med*. 1999;341:2060, with permission.)

A.10. What radiographic and echocardiographic findings are noted in cardiac tamponade?

On standard anterior-posterior chest radiography, the cardiac silhouette may appear normal in size or extremely enlarged, depending on the acuity and chronicity of the tamponade process. Normally, the pericardial fluid amounts to 15 to 25 mL. Acute tamponade physiology can arise with as little as 150 mL of effusion, whereas chronic effusions may exceed 1,000 mL before clinical signs and symptoms of cardiac tamponade become evident. In the latter case, on chest radiography film, the cardiac silhouette will appear “widened” with or without features such as obscuring of the pulmonary vessels at the hilum and a globular or “water bottle” configuration of the heart.

Transthoracic or transesophageal echocardiography can differentiate between cardiac dysfunction arising from direct myocardial injury and cardiac dysfunction associated with mechanical processes. Pericardial effusions can be readily seen and semi-quantitated. Likewise, pericardial blood clots can be demonstrated to compress a cardiac chamber. Additional echocardiographic signs observed in tamponade include (1) diminished left ventricular dimension and mitral valve excursion during spontaneous inspiration, (2) shifting of the interventricular septum toward the left ventricle, (3) fluctuation of transvalvular (mitral and aortic) flow seen by Doppler techniques, (4) diastolic expansion of the right ventricular chamber, and (5) in some cases, a systolic notch on the right ventricular epicardium (Figs. 12.2 and 12.3). Although many of the findings of both radiographic film and echocardiogram can be suggestive of cardiac tamponade, not a single sign is 100% sensitive and specific.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:710-713.

Mathew J, Swaminathan M, Ayoub C, eds. *Clinical Manual and Reviewof Transesophageal Echocardiography* . 2nd ed. New York: McGraw-Hill; 2010:351-369.

Singh S, Wann LS, Schuchard GH, et al. Right ventricular and right atrial collapse in patients with cardiac tamponade —a combined echocardiographic and hemodynamic study. *Circulation*. 1984;70:966-971.

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A.11. What is in the differential diagnosis of post-cardiopulmonary bypass (post-CPB) bleeding?

Significant bleeding following cardiac surgery requiring surgical exploration ("bring-back") occurs in approximately 3% of cases. Often, the source of bleeding cannot be ascertained and its etiology is ascribed to a coagulation defect. Procedures that require CPB are known to adversely affect the hemostatic mechanisms, including vascular endothelium, fibrinolytic and coagulation factors, platelet, plasminogen, and inflammatory pathways (Fig. 12.5). Under normal

settings, these systems act in concert and in opposition with one another to prevent bleeding by promoting clot formation at the site of endothelial injury (procoagulant effects) and prevent or destroy clot formation (anticoagulant effects—either directly or indirectly through inhibitory mediators). The procoagulant system becomes activated once blood elements come in contact with a nonendothelialized surface (bypass circuit), resulting in consumption of platelets, coagulation factors, and fibrinogen (tissue factor pathway). The potential for postoperative bleeding will depend on the degree of activation and preexisting levels of the procoagulants as well as other factors such as the duration of CPB, systemic hypothermia, comorbid states (renal and liver insufficiency), type of surgery (reoperation, circulatory arrest, combined procedures), and prior or current treatment with anticoagulant (platelet inhibitors, warfarin process). Of greater importance is the loss of several membrane glycoproteins (IIb-IIIa) that interact with fibrinogen and other cellular elements, allowing for platelet aggregation and propagation of clot formation. Overall, postcardiotomy bleeding is due to (1) a qualitative and a quantitative platelet defect, (2) deficiency, and (3) surgical bleeding. The latter can arise from either venous or arterial sources that were undetected before closure of the chest. Attentive and meticulous effort to surgical hemostasis can significantly reduce the incidence of bring backs.

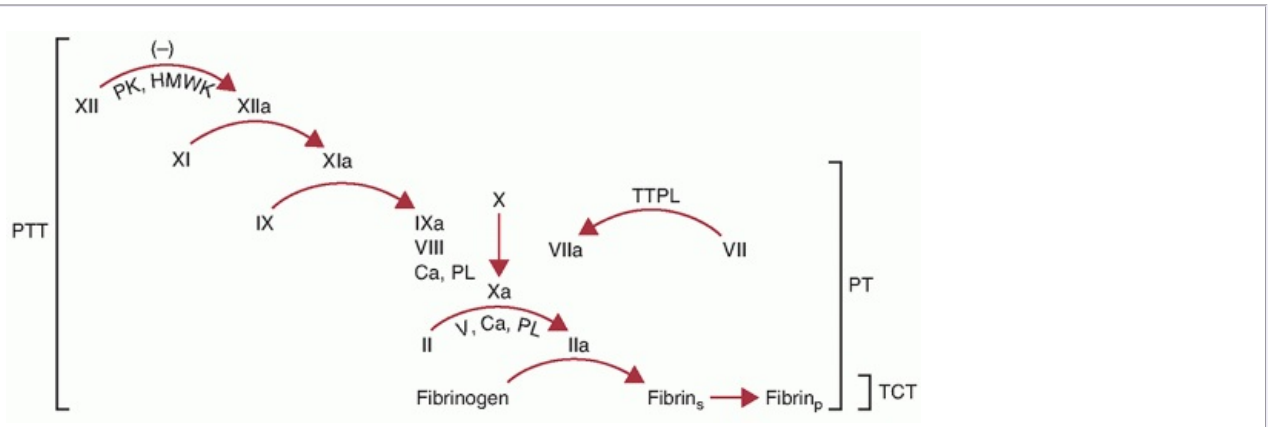


FIGURE 12.5 The coagulation cascade, illustrating the coagulation factors required for various screening tests. HMWK, high molecular weight kininogen; PK, prekallikrein; PL, phospholipid by platelets; PT, prothrombin time; PTT, partial thromboplastin time; TCT, thrombin clotting time; TTPL, tissue thromboplastin; Fibrin$_s$, fibrin single standards; Fibrin$_p$, fibrin polymer. (From Coleman RW, Hirsch J, Marder VJ, et al, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 2nd ed. Philadelphia, PA: JB Lippincott; 1987:1052, with permission.)

Despotis GJ, Avidan MS, Hogue CW Jr. Mechanisms and attenuation of hemostatic activation during extracorporeal circulation. *Ann Thorac Surg*. 2001;72:S1821-S1831.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:949-984.

Karthik S, Grayson AD, McCarron EE, et al. Reexploration for bleeding after coronary artery bypass surgery: risk factors, outcomes, and the effect of time delay. *Ann Thorac Surg*. 2004;78(2):527-534.

Levy JH. Pharmacologic preservation of the hemostatic system during cardiac surgery. *Ann Thorac Surg*. 2001;72:S1814-S1820.

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A.12. What is the mechanism of action of low molecular weight heparin (LMWH)?

Unfractionated heparin exerts its anticoagulant activity through antithrombin III (ATIII). ATIII inhibits factors IIa (thrombin), IXa, Xa, and XIa. Unfractionated heparin accelerates the formation of ATIII-IIa complex by 2,000 folds (and that requires the simultaneous binding of unfractionated heparin of at least 18 saccharide units to both ATIII and IIa) and the formation of ATIII-Xa complex by 1,200 folds. LMWHs are fragments of unfractionated heparin produced by controlled enzymatic or chemical depolymerization processes yielding chains having molecular weight of 6,000 to 7,000 Da. LMWHs consist of 8 to 16 saccharide units and inhibit factor Xa preferentially. This inhibition requires only that LMWH binds to ATIII, and the latter interacts with factor Xa, without the interaction between LMWH and factor Xa being necessary. LMWH has greater inhibitory effect on factor Xa, whereas unfractionated heparin exerts an equipotent effect against both thrombin (IIa) and factor Xa. The aPTT monitors the anti-IIa activity more closely than the anti-Xa activity. Finally, both LMWH and unfractionated heparin cause release of tissue factor pathway inhibitor from vascular endothelium, which then forms a complex with and inhibits factor Xa. This complex in turn inactivates factor VIIa.

Clark SC, Vitale N, Zacharias J, et al. Effect of low molecular weight heparin (Fragmin) on bleeding after cardiac surgery. *Ann Thorac Surg*. 2000;69:762-765.

Gohlke-Bärwolf C. Anticoagulation in valvar heart disease: new aspects and management during non-cardiac surgery. *Heart*. 2000;84:567-572.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:949-984.

A.13. Describe the advantages of LMWH over standard heparin therapy.

There are several clinical and pharmacologic advantages of LMWH over unfractionated heparin. The plasma half-life of LMWH is two to four times longer than unfractionated heparin, which undergoes a dose-dependent elimination by the liver and the kidneys. A significant amount of unfractionated heparin is bound to plasma proteins, vascular endothelium, and macrophages, resulting in less bioavailability and an unpredictable anticoagulant effect. Consequently, careful laboratory monitoring is required. Additional benefits of LMWH over unfractionated heparin include less bleeding (less platelet inhibition and decreased propensity for increased microvascular permeability). Several clinical trials have improved the efficacy

and safety of LMWH over unfractionated heparin. Of note, LMWH is not recommended in the setting of renal failure. The anticoagulant activity of LMWH may be measured by assaying factor Xa levels. Many different types of LMWH are available, each having slightly different pharmacologic effects (bioavailability, anticoagulant effect).

Huse DM, Cummins G, Taylor DC, et al. Outpatient treatment of venous thromboembolism with low-molecular-weight heparin: an economic evaluation. *Am J Manage Care*. 2002;8(suppl 1):S10-S16.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:949-984.

Kleinschmidt K, Charles R. Pharmacology of low molecular weight heparins. *Emerg Med Clin North Am*. 2001;19:1025-1049.

A.14. What is heparin-induced thrombocytopenia (HIT)? How is the diagnosis made?

Heparin normally binds to platelet membranes at glycoprotein Ib (GPIb) and other receptor sites and aggregates normal platelets by releasing adenosine diphosphate. HIT is a serious complication of heparin therapy that is predominantly immune-mediated by a binary complex formed between heparin and platelet factor 4. The reaction is commonly caused by an immunoglobulin G antibody that binds and activates platelets in the presence of heparin. Other immunoglobulins may also potentiate HIT.

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HIT exists in two forms. A benign form of HIT, type I, is observed in approximately 10% to 20% of patients receiving unfractionated heparin. This mild form of thrombocytopenia (rarely less than 100,000 per μL) occurs after 1 to 4 days of therapy with heparin. It is due to proaggregatory effects of heparin on platelets and generally improves despite continuing heparin administration. In contrast, HIT type II is a life-threatening condition that develops 5 to 10 days after initiating heparin therapy and is associated with devastating thromboembolic processes (most commonly arterial thrombosis resulting in limb ischemia, cerebrovascular events, and myocardial infarction) from activated platelets that adhere, aggregate, and form platelet ("white") clots. The platelet count falls to less than 50,000 per μL and in severe cases to less than 5,000 per μL. The incidence of HIT in patients receiving full-dose heparin ranges between 0% and 30%. Although there is no randomized prospective study looking at the true incidence of HIT, the expected incidence is estimated to be less than 5%. Those patients who have had a previous exposure to heparin (recent and in some cases remote history) *may* develop HIT earlier after institution of heparin therapy compared with those with no previous exposure. The frequency of HIT is also higher in patients receiving porcine mucosal heparin compared with bovine lung heparin.

The diagnosis of HIT should be entertained in any patient with a significant fall in platelet count while on heparin therapy (less than 150,000 per μL or a 50% or greater decrease in platelet count after 5 days of heparin therapy). The definitive diagnosis requires the following steps: (1) thrombocytopenia while on heparin, (2) exclusion of other etiology of thrombocytopenia, (3) improvement in platelet count following cessation of heparin therapy, and (4) presence of heparin-dependent platelet antibody by an in vitro test. In most cases, the diagnosis is made on clinical findings.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:949-984.

Warkentin TE, Greinacher A. Heparin-induced thrombocytopenia and cardiac surgery. *Ann Thorac Surg*. 2003;76:2121-2131.

A.15. What is the therapy for HIT?

Because HIT type II is a potentially lethal condition, the most effective therapy is discontinuation of heparin. The thrombocytopenia should improve progressively. Platelet transfusion is discouraged because bleeding occurs infrequently and vascular thrombosis may be potentiated. Several anticoagulants have been recommended as heparin replacement in HIT. These include direct thrombin inhibitors (hirudin, argatroban), LMWH, heparinoid, ancrod, and antiplatelet agents. Hirudin has been extensively used in Europe with demonstrable benefit and safety. LMWH has been shown to have cross reactivity with unfractionated heparin approaching 100% (by C-serotonin release or heparin-induced platelet aggregation assays) and should

not be used in the setting of HIT unless there are demonstrable negative cross reactivity assays with standard heparin. Ancrod is a defibrinogenating agent (not available in the United States) extracted from the Malayan pit viper and is immunologically distinct from heparin. It acts by cleaving fibrinopeptide A from fibrinogen, and its activity can be measured by assaying for plasma fibrinogen concentration. Finally, in the setting of HIT, a synthetic analogue of prostacyclin (iloprost—a potent inhibitor of platelet activation) has been used successfully during cardiac surgery to inactivate platelets and prevent further reduction of platelet count.

Hassell K. Heparin-induced thrombocytopenia: diagnosis and management. *Thromb Res*. 2008;123(suppl 1):S16-S21.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:949-984.

Warkentin TE, Dunn GL, Cybulsky IJ. Off-pump coronary artery bypass grafting for acute heparin-induced thrombocytopenia. *Ann Thorac Surg*. 2001;72:1730-1732.

A.16. Can HIT be caused by LMWH?

Based on confirmed laboratory tests, the prevalence of HIT is 2% for patients receiving unfractionated heparin. Although

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LMWHs can also induce thrombocytopenia, they may be acceptable alternatives for patients who develop HIT from unfractionated heparin, but reactivity of the particular LMWH with the patient's platelets should be confirmed in vitro.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:496-516, 949-984.

Kleinschmidt K, Charles R. Pharmacology of low molecular weight heparins. *Emerg Med Clin North Am*. 2001;19:1025-1049.

A.17. What is the mechanism of heparin antagonism by protamine?

Heparin is a large molecule consisting of chains of alternating residues of D-glucosamine and uronic acid. It is highly negatively charged, whereas protamine is mostly positively charged. The two combine irreversibly to form a heparin-protamine complex that does not have the ability to bind to thrombin or factor Xa. Once neutralized, the complex of heparin and protamine is eliminated.

Carr JA, Silverman N. The heparin-protamine interaction. A review. *J Cardiovasc Surg*. 1999;40:659-666.

Kimmel SE, Sekeres M, Berlin JA, et al. Mortality and adverse events after protamine administration in patients undergoing cardiopulmonary bypass. *Anesth Analg*. 2002;94:1402-1408.

Park KW. Protamine and protamine reactions. *Int Anesthesiol Clin*. 2004;42:135-145.

A.18. What is "heparin rebound"?

The ACT is used to confirm the adequacy of heparin neutralization by protamine. The reappearance of circulating heparin several hours after its neutralization by protamine is called heparin rebound and is usually incriminated for clinical bleeding occurring after cardiac surgery. The concept of heparin rebound following protamine reversal may be explained by sequestration of heparin in tissues that are poorly perfused (i.e., fat), late release of heparin by endothelial cells, and more rapid clearance of protamine in relation to heparin (because heparin is mobilized back into the circulation, it can inhibit thrombin formation and predispose to post-CPB bleeding). Studies in which 1 mg of protamine is given per 100 U of heparin (total dose) found no evidence of heparin rebound.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:949-984.

Subramaniam P, Skillington P, Tatoulis J. Heparin-rebound in the early postoperative phase following cardiopulmonary bypass. *Aust N Z J Surg*. 1995;65:331-333.

A.19. How does warfarin affect the coagulation system? What is the therapy for reversing its effect?

Warfarin (Coumadin) remains the most commonly used anticoagulant agent in the outpatient setting (atrial fibrillation, prosthetic valves, and devices). Its predominant pharmacodynamic

effect is inhibition of synthesis of vitamin K-dependent factors (II, VII, IX, and X) in the liver and its clinical efficacy is monitored by measuring the PT or more specifically the international normalized ratio (INR). The safe or efficacy levels of either INR or PT is variable because of multiple factors, including hepatic, nutritional, drug interaction, age, and presence of other comorbid conditions. On average, it takes several days of therapy to achieve the desired INR (2 to 4); in the interim, administration of LMWH or unfractionated heparin may be necessary for initiating anticoagulation. Complications occur because of inadequate anticoagulation (thrombosis) or because of excessive anticoagulation (bleeding and hemorrhage). To reverse its effect, warfarin should be discontinued for more than 3 days to allow levels of the aforementioned factors to normalize. Acute reversal is achieved with FFP. Administration of vitamin K is often necessary to accelerate the synthetic process.

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Jacobs LG. Warfarin pharmacology, clinical management, and evaluation of hemorrhagic risk for the elderly. *Cardiol Clin*. 2008;26(2):157-167.

A.20. What do the following measure: prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time, and activated clotting time (ACT)?

Prothrombin Time

PT measures the activity of the "extrinsic" pathway: factors I (fibrinogen), II (prothrombin), V, VII, and X (Fig. 12.5). Deficiencies of factors V, VII, and X (decrease to below 50% of normal) significantly prolong the PT. The concentrations of fibrinogen and prothrombin required to prolong the PT are much lower. The activity of three of the four vitamin K-dependent factors (II, VII, IX, and X) are measured by the PT. Normal values are less than 12 seconds.

Activated Partial Thromboplastin Time

aPTT measures the activity of the "intrinsic" pathway: factors XII, XI, IX, VIII, V, X, II (prothrombin), and I (fibrinogen) (Fig. 12.5). The aPTT is prolonged when the concentration of these factors is less than 20% to 30%. Normal values are 25 to 40 seconds.

Thrombin Time

Thrombin time measures the conversion of fibrinogen to fibrin by thrombin—the final step in the coagulation cascade (Fig. 12.5). Heparin prolongs the thrombin time, whereas warfarin has little effect. Normal values are less than 10 seconds. The thrombin time is decreased in the presence of low concentrations of fibrinogen and thrombin.

Activated Clotting Time

ACT measures the overall function of the coagulation system. It is used primarily to measure the adequacy of heparinization during CPB and protamine reversal of heparin following CPB. Prolonged ACTs may be due to heparin, low levels of coagulation factors, or thrombocytopenia. It is not particularly specific for platelet or factor deficiencies. Normal values are 110 to 140 seconds.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:496-516, 949-984.

Owens CD, Belkin M. Thrombosis and coagulation: operative management of the anticoagulated patient. *Surg Clin North Am*. 2005;85:1179-1189.

Sconce EA, Kamali F. Appraisal of current vitamin K dosing algorithms for the reversal of over-anticoagulation with warfarin: the need for a more tailored dosing regimen. *Eur J Haematol*. 2006;77:457-462.

A.21. How is the anticoagulant effect of LMWH monitored?

There is no evidence that monitoring of LMWH dosage improves the clinical efficacy. In contrast, any overdose increases the risk for hemorrhage. Because the kidneys play a significant role in the elimination of LMWH, therapeutic use of these agents should be monitored with an anti-factor Xa assay, especially in patients who have renal insufficiency, are elderly, and have clinical conditions that increase the risk for bleeding.

Boneu B, de Moerloose P. How and when to monitor a patient treated with low molecular weight heparin? *Semin Thromb Hemost*. 2001;27:519-522.

Nutescu EA, Spinler SA, Wittkowsky A, et al. Low-molecular-weight heparins in renal impairment and obesity: available evidence and clinical practice recommendations across medical and surgical settings. *Ann Pharmacother*. 2009;43(6):1064-1083.

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A.22. What is point-of-care testing (POCT) and what are the commonly used point-ofcare devices?

The need for POCT has developed as a result of limitations of central laboratories to timely and completely provide results to clinicians for the diagnosis and management of coagulopathic bleeding associated with cardiac surgery, liver transplantation, and trauma beyond standard coagulation tests (PT/aPTT, platelet count, and fibrinogen level). Specific defects in hemostasis (coagulation, analysis of platelet function, as well as abnormal fibrinolysis) can be identified and guided component transfusion practices accomplished. POCT can be performed on-site, in the operating room, and in the ICU. Decrease in the need for blood and blood components (packed red blood cells, platelets, FFP, cryoprecipitate) has been shown with use of POCT in guiding transfusion practice. Also see Chapter 57, section C.25.

The three devices used in clinical practice are thromboelastography (TEG), rotation thromboelastometry (ROTEM), and Sonoclot analysis.

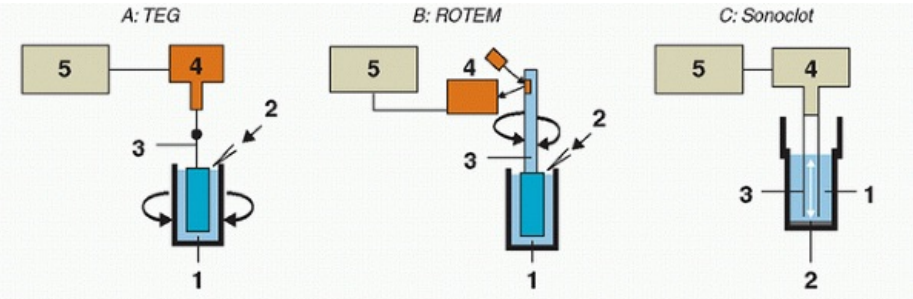
Thromboelastography

The TEG (Haemoscope Corp, Niles, IL) measures physical properties of a clot using a stationary cylindrical cup that holds the blood sample and oscillates at an angle. A pin is suspended in the blood by a torsion wire. Motion of the torsion wire is monitored in different phases of in vitro platelet and clot interaction, fibrin formation, and lysis (Fig. 12.6A). The analysis performed provides a graphic and numerical display (Fig. 12.7A, upper side). The etiology of a coagulopathy may be obtained by analyzing characteristic TEG signatures (Fig. 12.8).

Thromboelastometry

Thromboelastometry also measures viscoelastic properties of a blood sample. ROTEM-rotation thromboelastometry (Pentapharm GmbH, Munich, Germany) is the commercially available device. The principle of the ROTEM is based on the use of a moving pin suspended in a cup of blood sample. The signal is transmitted by an optical detector system from the moving pin (Fig. 12.6B). The ROTEM provides a measure and graphical display of the changes in viscoelasticity recorded at all stages of the developing clot and characteristic tracings of abnormal findings (Fig. 12.7A lower side and Fig. 12.9). Although the basic principles of function as well as the TEG and ROTEM tracings are very similar, the nomenclature and reference ranges are different (Table 12.1).

Abnormal ROTEM tracing's reflective of specific defects of hemostasis are illustrated in Figure 12.9.



A. Thromboelastograph (TEG): Rotating cup with blood sample (1), coagulation activator (2), pin and torsion wire (3), electromechanical transducer (4), data processing (5).

B. Rotation thromboelastography (ROTEM): Cuvette with blood (1), activator added by pipetting (2), pin and rotating axis (3), electromechanical signal detection via light source and mirror mounted on axis (4), data processing (5).

C. Sonoclot: Blood sample in cuvette (1), containing activator (2), disposable plastic probe (3), oscillating in blood sample mounted on electromechanical transducer head (4), data processing (5).

FIGURE 12.6 Working principles of viscoelastic point-of-care coagulation devices.

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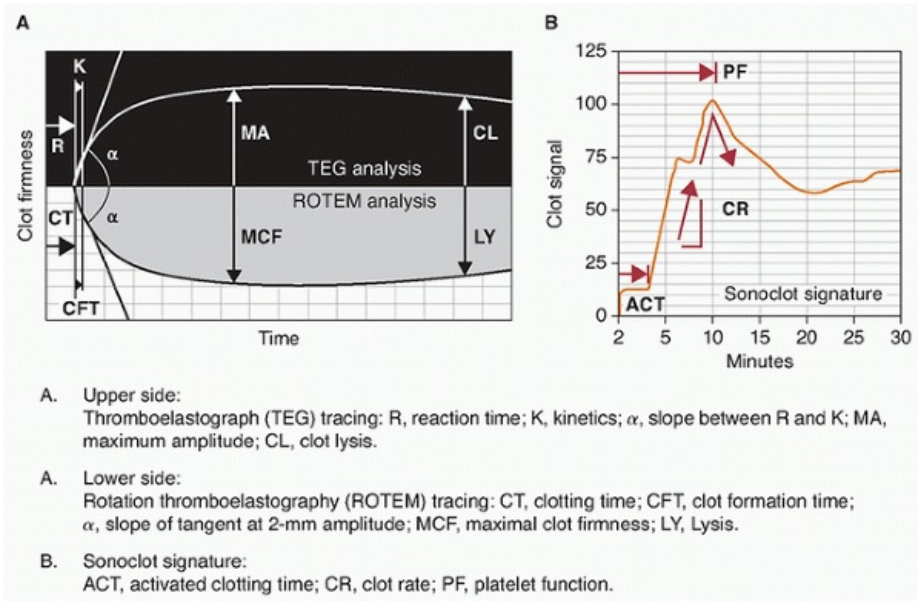


FIGURE 12.7 Typical tracings of viscoelastic point-of-care coagulation devices.

Sonoclot Analyzer

The Sonoclot similarly measures the development of clot viscoelastic strength. The principle of function is based on a vertically moving piston (Fig. 12.6C). The device measures the impedance to vibration at the tip of the probe. Information provided includes function of coagulation, fibrin gel formation, clot retraction (platelet function), and fibrinolysis. The Sonoclot analyzer generates both a qualitative graph (Sonoclot signature)

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and quantitative results on the clot formation time (ACT—onset) and rate of fibrin polymerization (clot rate) (Fig. 12.7B).

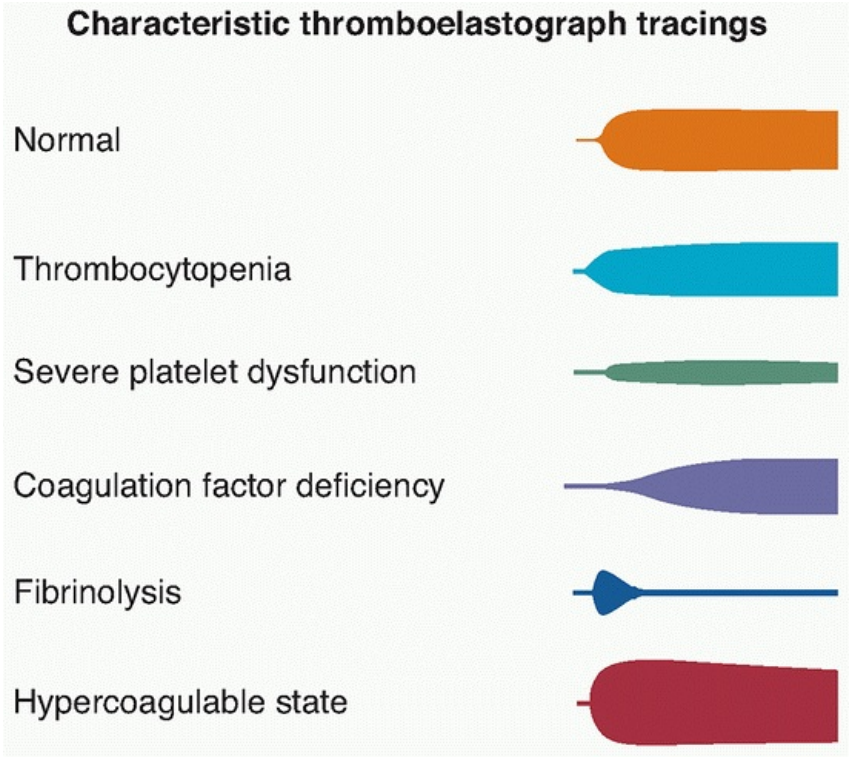


FIGURE 12.8 Qualitative analysis of thromboelastogram.

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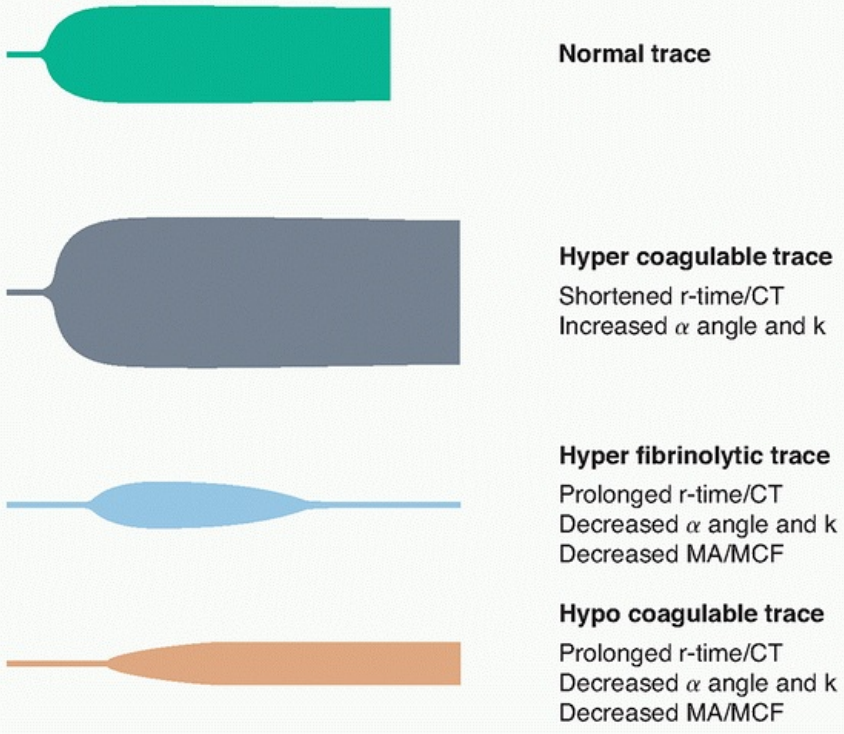


FIGURE 12.9 Examples of abnormal ROTEM traces.

TABLE 12.1 Nomenclature and Reference Values of Thromboelastography (TEG) Thromboelastometry (ROTEM)

	TEG	ROTEM
Clotting time (period to 2 mm amplitude)	*R* (reaction time)	*CT* (clotting time)
	N (WB) 4-8 min	*N* (Cit, in-TEM) 137-246 sec
	N (Cit, kaolin) 3-8 min	*N* (Cit, ex-TEM) 42-74 sec
Clot kinetics (period from 2 to 20 mm amplitude)	*K* (kinetics)	*CFT* (clot formation time)
	N (WB) 1-4 min	*N* (Cit, in-TEM) 40-100 sec
	N (Cit, kaolin) 1-3 min	*N* (Cit, ex-TEM) 46-148 sec
Clot strengthening (*α* angle)	*α* (slope between r and k)	*α* (slope of tangent at 2 mm amplitude)
	N (WB) 47°-74°	*N* (Cit, in-TEM) 71°-82°
	N (Cit, kaolin) 55°-78°	*N* (Cit, ex-TEM) 63°-81°

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Amplitude (at set time)	*A*	*A*
Maximum strength	*MA* (maximum amplitude)	*MCF* (maximum clot firmness)
	N (WB) 55-73 mm	*N* (Cit, in-TEM) 52-72 mm
	N (Cit, kaolin) 51-69 mm	*N* (Cit, ex-TEM) 49-71 mm
		N (Cit, fib-TEM) 9-25 mm
Lysis (at fixed time)	CL30, CL60	LY30, LY60

TEG: *N* = normal values for kaolin activated TEG in native whole blood (WB) or citrated and recalcified blood samples (Cit) (Haemoscope Corp). ROTEM: *N* = normal values for contact (partial thromboplastin phospholipids, in-TEM), tissue factor (ex-TEM), and tissue factor plus platelet inhibitor cytochalasin D (fib-TEM) activated, citrated, and recalcified blood samples. Reference values depend on reference population, blood sampling technique, other preanalytical factors, and coagulation activator. CL, clot lysis; LY, lysis.

Ganter MT, Hofer CK. Coagulation monitoring: current techniques and clinical use of viscoelastic point of care coagulation devices. *Anesth Analg*. 2008:1366-1375.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:496-516.

A.23. How does desmopressin aid hemostasis?

Desmopressin (1-deamino-8-D-arginine vasopressin [DDAVP]) is a vasopressin analog with more potency, longer lasting antidiuretic activity, and much less vasoconstriction than the parent compound. DDAVP increases the activity of von Willebrand factor and factor VII in plasma. von Willebrand factor is found in subendothelial tissue, released from platelets, and is in part responsible for platelet adhesion to damaged blood vessels. DDAVP was initially shown to significantly decrease postoperative bleeding. Although its routine use is not recommended, DDAVP may be beneficial in patients with end-stage renal disease to increase von Willebrand factor that is decreased in those patients. The optimal dose of DDAVP is 0.3 μg per kg.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:949-984.

Kondo NI, Maddi R, Ewenstein BM, et al. Anticoagulation and hemostasis in cardiac surgical patients. *J Card Surg*. 1994;9:443-461.

A.24. What is fibrinolysis?

Fibrinolysis is the fibrin breakdown in thrombi. Plasmin, derived from plasminogen, is the enzyme involved in this process. Physiologic fibrinolysis involves clot remodeling and removal during the healing process. Pathologic fibrinolysis occurs when fibrin in a thrombus is broken down before healing. Although elevated concentrations of plasminogen activators are found during CPB, their half-lives are very short after bypass.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:949-984.

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A.25. What is aminocaproic acid? What is tranexamic acid?

ε-Aminocaproic acid (Amicar) and tranexamic acid are analogues of lysine. Their primary mechanism of action is inhibition of plasminogen and plasmin, resulting in less breakdown of fibrinogen, fibrin (fibrinolysis), and other clotting components. These antifibrinolytic agents have been effective in treating coagulopathy in the setting of heart surgery, portocaval shunts, hematologic disorders such as aplastic anemia, abruptio placentae, hepatic cirrhosis, and neoplastic diseases.

Compared with placebo, use of tranexamic acid or aminocaproic acid in cardiac surgery has been shown to reduce blood loss by 30% to 49% as well as reduce homologous blood transfusion. Considering the low cost associated with aminocaproic acid therapy (less than $12), many cardiac surgical centers use this agent routinely for uncomplicated open-heart procedures.

The standard intravenous preparation and dosage for cardiac surgery include 5 to 10 g of aminocaproic acid diluted and infused over 1 hour, followed by a continuous infusion at a rate of 1 g per hour. Higher infusion rates may be used. There are several adverse events that include thrombosis (early graft closure, myocardial ischemia, and infarction), agranulocytosis, leukopenia, and thrombocytopenia. Although rare, bradycardia and mild reduction in blood pressure have also been reported.

Henry DA, Carless PA, Moxey AJ, et al. Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion. *Cochrane Database Syst Rev*. 2011;(3):CD001886.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:949-984.

B. Preoperative Evaluation and Preparation

B.1. Interpret the hemodynamic findings of this patient.

The patient has an adequate blood pressure; however, this appears to be maintained through compensatory mechanisms, including an increase in both arterial resistance (systemic vascular resistance) and HR. The PA systolic pressure is consistent with pulmonary hypertension arising most likely from either chronic mitral valvular disease (stenosis or insufficiency) or decreased compliance of the left ventricle (as in ischemia). Both the PA diastolic pressure and the PAOP suggest that the left ventricular end-diastolic pressure—a correlate of left ventricular preload—is within the normal limits. Keep in mind that pressure measurements do not correlate with volume status unless the compliance of the chamber (the relation between pressure and volume in diastole) is constant. Therefore, a PAOP of 14 mm Hg could represent hypovolemia, normovolemia, or hypervolemia depending on the compliance of the left ventricle. A CVP of 23 mm Hg is suggestive of right ventricular or biventricular dysfunction, tricuspid stenosis or insufficiency, or obstruction and compression of the right atrium. The CO is inadequate. The derived SV of 22 mL (CO/HR) combined with the other derangements (elevated CVP strongly reflects right heart dysfunction). Taking into consideration the patient's overall presentation (physical examination and laboratory findings), the differential diagnosis includes right ventricular ischemia and/or infarction, pulmonary embolism, atrial or ventricular septal defect causing volume overload of the right ventricle, and cardiac tamponade. An echocardiogram should be performed to assist in the diagnostic process and clinical management.

Kern MJ, Lim MJ, Goldstein JA. *Hemodynamic Rounds: Interpretation of Cardiac Physiology from Pressure Wave Analysis*. 3rd ed. Hoboken, NJ: Wiley-Blackwell; 2009:269.

B.2. How would you treat the low output status of this patient?

Although the HR is increased, it may be unwise to attempt to normalize it before correcting the SV. The SV is a function of the preload, the afterload, and the contractile status of the myocardium. Whereas the preload of the right heart may be excessive (CVP = 23 mm Hg), the preload of the left heart may not be adequate despite a “normal” PAOP of 14 mm Hg. While waiting for the echocardiogram to be performed, a fluid bolus can be attempted. If there is a positive response (i.e.,

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the blood pressure and/or the cardiac output increase), additional fluid bolus can be administered until the limit of the preload reserve has been reached (operating on the flat end portion of the Frank-Starling curve). It is important to note that fluid challenge alone will not improve cardiac performance without addressing the contractility and the afterload that, in this patient, appear to be deranged. Because there is no knowledge of the exact etiology of the low output state, it would be rational to institute inotropic support. With regard to the afterload, both systemic and pulmonary afterload are elevated. On the right side, PA hypertension can be improved with nitroglycerin or nitroprusside, but the associated systemic hypotension would prohibit their use. In fact, most vasodilators with the exception of nitric oxide would compromise the systemic pressures. At the same time, if the compliance of the right ventricle is presumed to be decreased, then the increased CVP does not necessarily correlate with adequate preload of the right ventricle. Alternatively, an inotrope that has vasodilatory properties, such as milrinone or dobutamine, would be a better choice. In summary, a rational management of the hemodynamic findings presented would include administering fluid (crystalloid or blood products as indicated), prescribing inotropic support, obtaining an echocardiogram, and addressing the other systemic complications (pulmonary, renal, and coagulation).

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:1025-1045.

B.3. How would you evaluate this patient's coagulation status?

A complete blood cell count and a complete coagulation panel should be performed. Assuming that both the hematocrit and the platelet function are adequate, attention should be directed

to the elevated PT and the aPTT. The patient has a prosthetic valve and it would be appropriate to surmise that she has been taking anticoagulants. The most common agent to be used 4 days after surgery is warfarin (Coumadin). Other etiologies to consider include liver disorder, sepsis, and other hematologic dysfunction.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:949-984.

B.4. What do fresh frozen plasma (FFP) and cryoprecipitate contain?

FFP contains the labile factors V and VIII as well as the stable coagulation factors (II, VII, IX, X, XI). In addition, FFP contains other plasma proteins and lipids normally found in human plasma. Cryoprecipitate is derived by thawing FFP at 4°C (39.2°F). It contains factors VIII and XIII, von Willebrand factor, and fibrinogen.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:496-516, 949-984.

B.5. What are the indications for transfusing FFP, platelet concentrate, and cryoprecipitate?

Blood usually coagulates appropriately when coagulation factor concentrations are at least 20% to 30% of normal and when fibrinogen levels are greater than 75 mg per dL. Although laboratory values such as PT and PTT may be abnormal, the American Society of Anesthesiologists Task Force on Blood Component Therapy discourages conventional use of FFP for perioperative treatment of bleeding because there are few clinical circumstances whereby coagulopathy arises from factor deficiency. Although massive blood replacement can produce prolongation of PT and/or PTT, the task force states that a true dilutional coagulopathy does not ordinarily occur until more than 100% of the patient's blood volume has been replaced. It supports the use of FFP in patients having vascular bleeding with PT and PTT values greater than 1.5 times the laboratory's normal value. FFP should be administrated in doses calculated to achieve a minimum of 30% of plasma factor concentration (i.e., 10 to 15 mL per kg of FFP).

Recommended indications for fresh frozen plasma

- Replacement of factor deficiencies
- Reversal of warfarin effect

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- Massive blood transfusions
- Treatment of ATIII deficiency in patients who are heparin-resistant requiring systemic anticoagulation with heparin

Platelet transfusions after CPB should be guided by clinical evaluation and POC testing manifesting thrombocytopenia or platelet dysfunction. Transfusion of one platelet concentrate will increase the platelet count by approximately 5,000 to 10,000 per μL in the average adult. The usual therapeutic dose is one platelet concentrate per 10-kg body weight.

Platelet concentrate is indicated in the following:

- Active bleeding associated with thrombocytopenia
- Massive blood transfusions

The American Society of Anesthesiologists Task Force on Blood Component Therapy recommends the administration of cryoprecipitate for the following:

- Prophylaxis in nonbleeding perioperative or peripartum patients with congenital fibrinogen deficiencies or von Willebrand disease unresponsive to DDAVP (whenever possible, these decisions should be made in consultation with the patient's hematologist)
- Bleeding patients with von Willebrand disease
- Correction of microvascular bleeding in massively transfused patients with fibrinogen concentrations less than 80 to 100 mg per dL

One unit of cryoprecipitate per 10-kg body weight raises plasma fibrinogen concentration approximately 50 mg per dL in the absence of continued consumption or massive bleeding.

Bleeding following cardiac surgery without demonstrable abnormalities of coagulation is not considered to be an indication for transfusion of FFP, platelets, or cryoprecipitate. Recent report suggests that postoperative bleeding after CPB may be secondary to excessive fibrinolysis that is responsive to cryoprecipitate. Importantly, the smaller volume of cryoprecipitate compared to FFP makes it a more desirable choice when there is concern of either hemodilution or volume overload.

Ferraris VA, Ferraris SP, Saha SP, et al; for Society of Thoracic Surgeons Blood Conservation Guideline Task Force. Perioperative blood transfusion and blood conservation in cardiac surgery: the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists clinical practice guideline. *Ann Thorac Surg*. 2007;83(5)(suppl):S27-S86.

Napolitano LM. Current status of blood component therapy in surgical critical care. *Curr Opin Crit Care*. 2004;10:311-317.

B.6. What are the complications associated with blood component transfusions?

Complications associated with transfusions of blood elements include transmission of infectious agents (e.g., hepatitis, HIV infection), hemolytic and nonhemolytic transfusion reactions, immunosuppression, anaphylactic or anaphylactoid reactions, and alloimmunization to platelet-specific antigens and the Rh antigen (resulting from erythrocyte contamination because they are stored at room temperature). Platelets in particular may contain proliferating bacteria. Finally, in the immunosuppressed, graft-versus-host effects may occur following platelet transfusion. Also see Chapter 57, sections C.12 and C.14.

Greer JP, Arber DA, Glader B, et al, eds. *Wintrobe's Clinical Hematology*. 13th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2014:547-586.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1830-1867.

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B.7. What is the risk for acquiring HIV from blood exposure?

The risk for HIV infection in the United States is 1 per 1,476,000 per unit transfused. However, with the implementation of donor screening tests for HIV-1 antigen, there is an expectation of preventing up to 25% of the window period cases (the period between viral infection and its detection by tests for the presence of antibodies). Perhaps the immunoviral agent most transmitted by blood transfusion is cytomegalovirus.

Greer JP, Arber DA, Glader B, et al, eds. *Wintrobe's Clinical Hematology*. 13th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2014:547-586.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1830-1867.

B.8. Assuming that the patient has cardiac tamponade, how would you prepare this patient for surgery?

As with any patient undergoing surgery, the following steps should be taken: First, a complete review of the patient's history, physical examination, and laboratory findings is mandated; second, key areas of concern should be identified and appropriate steps taken to address them; third, an anesthetic plan that is tailored to cardiac tamponade is devised; and last, communication with the respective medical (surgeons, nurses, perfusionist, blood bank) and paramedical staff to ensure readiness and teamwork. The patient's presentation suggests that she is in some degree of respiratory distress. Initially, management should consist of supplemental oxygen, review of chest radiograph, and assessment of arterial blood gases. Shortness of breath and the inability to lie supine are frequent symptoms in patients having cardiac tamponade physiology, and every effort should be made to provide comfort and lessen the associated emotional stress. Positive pressure ventilation should be avoided at all cost unless the clinical picture indicates that the patient will have a cardiac arrest. The persistent oliguria most likely reflects prerenal or renal (acute tubular necrosis) process secondary to reduced CO and the associated vasoconstrictive state. As described in the previous answer, optimization of hemodynamics should also improve the renal function. Whereas some may administer diuretics in this setting, such management is strongly discouraged. The most effective management is surgical evacuation of the pericardial

effusion or clot. The hematologic issues include elevated PT and aPTT, blood loss, and the potential for further blood loss perioperatively. The coagulopathy should be corrected appropriately, the patient's hematocrit and platelets should be checked and treated accordingly, and sufficient blood (4 to 6 units) will be required in the operating room before commencing surgery.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:1025-1045.

C. Intraoperative Management

C.1. How would you monitor this patient during transport to the operating room? What emergency drugs would you bring with you?

The patient must be under astute observation, and the vital signs must be continuously assessed, including invasive monitoring of systemic blood pressure, electrocardiogram, and oxygen saturation. In addition, emergency cardioactive and vasoactive drugs should be available during transport:

- Oxygen: Increase the fraction of inspired oxygen (FIO_2) as needed. All necessary equipment for intubation should be present (laryngoscope and several blades, bag-mask units, and adult-size endotracheal tubes).
- Direct current cardioversion unit: in case of tachyarrhythmias
- Phenylephrine: dose: bolus, 0.1 to 0.5 mg; infusion, 25 to 125 μg per minute
- Epinephrine: dose: 0.01 to 0.1 μg/kg/min
- Calcium chloride: dose: 2 to 4 mg per kg
- Lidocaine: 1 to 2 mg per kg

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- Atropine: 0.01 mg per kg

C.2. In this patient, what hemodynamic effects would occur from intravenous induction with ketamine, thiopental, fentanyl, propofol, etomidate, or midazolam?

Ketamine

After intravenous administration, ketamine (1 mg per kg) has a rapid onset of action and achieves a peak plasma concentration in less than 1 minute. It also possesses a short duration of action. After the initial dose, patients may remain unconscious for 10 to 15 minutes, but the analgesic effect (somatic greater than visceral) persists for an additional 30 minutes or longer. Some of the hemodynamic effects of ketamine may include small increases in blood pressure, HR, CO, and myocardial oxygen demand. This response is mediated by a direct central sympathetic stimulation and by inhibition of norepinephrine uptake into the postganglionic sympathetic nerve endings. Ketamine has also been shown to have intrinsic depressant properties on the myocardium. In clinical conditions in which norepinephrine stores are reduced, and in the presence of preexisting cardiac dysfunction (mechanical or myocardial), administration of ketamine can produce hemodynamic depression.

Fentanyl

Fentanyl does not possess any depressant effects on myocardial contractility, but because of its vagotonic effect (decreases in HR) and mild sympatholytic effect (central sympathetic outflow), blood pressure may decrease. This response may be more profound in shock or preshock states and when fentanyl is used concomitantly with other induction agents (benzodiazepines, thiopental, propofol).

Propofol

Propofol produces effects very similar to those of thiopental. It can cause significant reduction in systemic pressures (greater than 30%), and there have been several reports of cardiovascular arrest in both adults and children following inductions with propofol. Propofol also has some antiarrhythmic effect on the atrioventricular node as well as on other conduction pathways. It should be used with caution when other agents that slow down atrioventricular nodal conduction are present (calcium channel blockers, β-blockers, digoxin). As with thiopental, the use of propofol for induction in cardiac tamponade is strongly disfavored.

Etomidate

Etomidate has a very favorable hemodynamic profile and is the preferred agent to be used during induction when cardiovascular collapse is anticipated. With an induction dose (0.2 to 0.3 mg per kg), etomidate may cause a slight decrease in mean arterial pressure, but such changes are not attributable to myocardial depression, as is typical of propofol and sodium thiopental. Pain at the injection site and involuntary muscle movements are the most common adverse events noted with etomidate. It also appears to reduce seizure threshold and enhance its duration when used during electroconvulsion therapy.

Midazolam

Midazolam may cause mild to moderate systemic vasodilation, particularly when used in combination with opioids.

Overall, of the agents discussed, etomidate would be the preferred agent for induction, followed by ketamine, and/or fentanyl; thiopental and propofol would be the least desired.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:1025-1045.

C.3. Describe the induction process for cardiac tamponade.

The patient should have standard monitors placed, as well as invasive monitors, including indwelling arterial access for beat-to-beat monitoring of systemic arterial pressures and for obtaining blood gases. This patient has a PAC in situ; however, its usefulness in this setting remains debatable. The actual induction should proceed *only* in the presence of a surgical team that is ready and gowned and after the patient has been completely prepared and draped. The choice of

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induction agents is limited to opioids, muscle relaxant (depolarizing or nondepolarizing), and either etomidate or ketamine. Regardless of the induction technique, the anesthesiologist should expect, and be prepared to manage, ensuing circulatory collapse.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:1025-1045.

C.4. Following induction and intubation, the systemic blood pressure decreased to 55/30 mm Hg. Describe the clinical events accounting for this perturbation and the management steps required for resuscitation.

Cardiac tamponade is caused by significant pericardial pressure from accumulating pericardial contents (fluid, blood, and blood clots) that impede chamber filing resulting in a low CO state. The precipitous fall in blood pressure observed with induction can be accounted for by the following: First, most induction agents will have negative hemodynamic effects that are either direct or indirect; second, sympatholysis reduces arterial resistance as well as chronotropy and inotropy of the heart; third, the physiologic consequences of switching from negative pressure ventilation to positive pressure ventilation will further reduce cardiac filling by increasing intrathoracic pressure and afterload; and finally, placing the patient in a supine position will also compromise atrial and ventricular preload (i.e., hydrostatic effects, loss of diaphragmatic motion, and mediastinal structures weighing on the heart).

The management of hypotension will require use of vasoactive drugs, cardioactive drugs, and/or fluid challenge. Reducing inspiratory positive pressure (i.e., lowering tidal volume or switching from ventilator-delivered breaths to hand ventilation) may also improve the hemodynamic status by facilitating filling. These would be merely temporizing measures; surgical relief of tamponade would be the definitive treatment of this problem.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:1025-1045.

C.5. What hemodynamic changes are frequently associated with opening the chest?

Chest opening normalizes the pressure relation between the pericardium and the heart chambers, thereby relieving the tamponade and its hemodynamic effects. Unless the myocardium has suffered injury or is stunned, the expected hemodynamic changes include drastic

improvement in both blood pressure and SV. Most of the vasoactive and cardioactive agents being administered can be quickly weaned. In addition, oxygenation, acid-base status, and renal function (urine output) tend to improve significantly.

C.6. What is myocardial stunning? What is myocardial hibernation?

The myocardium can exhibit regional dysfunction or a generalized decrease in function related to injury (i.e., ischemia and infarction). It has also been noted that myocardial function can be coupled or uncoupled with tissue perfusion. For example, following a period of oxygen deprivation and restoration of flow, the affected myocardium can resume normal function or have diminished function or no function (dysfunction). The term *myocardial stunning* represents a state of uncoupling between function and flow in which myocardial flow is normal but function is diminished or absent. In the setting of cardiac surgery, myocardial stunning can be a cause of ventricular dysfunction that generally resolves within the first 6 to 8 hours post-CPB. During this period, inotropic support has been shown to be effective. Myocardial hibernation, on the other hand, is a myocardial process that manifests after weeks or months and denotes a condition in which both myocardial function and flow are reduced (perfusion and function are coupled). Perhaps this is an adaptive process that allows the myocytes to lower their metabolic activity and oxygen consumption to survive during states of oxygen deprivation. The definitive diagnosis of stunning and hibernation may be difficult to make because regional myocardial blood flow is difficult to assess or quantify clinically. Therefore, most cases of stunning and hibernation require a retrospective analysis. First, segmental myocardial dysfunction must be established; second, myocardial blood flow should be restored by revascularization (surgical, pharmacologic, or angioplasty/stenting); and third, improvement of regional function should follow revascularization.

D'Ancona G, Donias HW, Bergsland J, et al. Myocardial stunning after off-pump coronary artery bypass grafting:

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safeguards and pitfalls. *Ann Thorac Surg*. 2001;72:2182-2183.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:838-887.

D. Postoperative Management

D.1. How would you manage hypertension in the intensive care unit (ICU)?

The management of hypertension depends on its etiology. Rather than administering antihypertensive agents indiscriminately, the clinician should exclude the following conditions as causality of hypertension: hypoxemia, hypercarbia, acid-base derangements, and pain. The occurrence of hypertension is a common phenomenon during the first several hours in the ICU. In most cases, the etiology is uncertain and probably represents a state of marked sympathoadrenal activation. Once correctable causes of hypertension have been addressed, antihypertensive therapy can be achieved with a variety of agents. Because the underlying mechanism of the hypertension involves endogenous release of norepinephrine (with minimal epinephrine), the most rational agents to use are the β-blockers. Labetalol antagonizes both α- and β-adrenergic receptors and is an effective antihypertensive agent. Alternatively, metoprolol, atenolol, esmolol, or propranolol can be used, particularly if the hypertension is associated with tachycardia. Unfortunately, these agents are used infrequently because of theoretical concerns of myocardial depression and bradycardia. Current cardiology practice strongly endorses the use of β-blockers in the setting of moderate and severe ventricular dysfunction. In addition, the cardioprotective effects of β-blockers have been shown in several perioperative trials, whereby the incidence of myocardial injury and mortality (up to 2 years postoperatively) are significantly reduced in patients treated perioperatively with β-blockers.

Kotlyar E, Macdonald PS, Keogh AM, et al. Optimization of left ventricular function with carvedilol before high-risk cardiac surgery. *J Heart Lung Transplant*. 2001;20:1129-1131.

Varon J, Marik PE. Perioperative hypertension management. *Vasc Health Risk Manag*. 2008;4:615-627.

D.2. When would it be appropriate to extubate this patient?

The timing of extubation depends on the following:

- Clinical stability (stable hemodynamics without need for significant inotropic or vasoactive support)
- Intact neurologic function (alertness and ability to comprehend and execute simple verbal commands)
- Adequate pulmonary function (acceptable arterial blood gases and acid-base status and adequate weaning parameters—tidal volume, respiratory rate, vital capacity, and inspiratory effort)
- Normal body temperature and neuromuscular function (reverse paralysis if necessary)
- Normal coagulation (bleeding less than 60 mL per hour and normalization of coagulation parameters)

Following relief of tamponade, most patients can be extubated as early as possible assuming that the previously listed criteria have been met.

Kaplan JA, Reich DL, Savino JS, et al, eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia, PA: WB Saunders; 2011:1025-1045.

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Chapter 13
Heart Transplantation and Subsequent Noncardiac Surgery

Jeff T. Granton

Davy C. H. Cheng

A 41-year-old man with a history of idiopathic dilated cardiomyopathy (IDCM) is admitted to the cardiac care unit in a quaternary cardiac center for potential heart transplantation assessment. He has known systolic dysfunction, with an ejection fraction of <20% on transthoracic echocardiogram. Recurrent ventricular arrhythmias necessitated the insertion of an implantable cardioverter-defibrillator (ICD). Right heart catheterization revealed a pulmonary vascular resistance (PVR) of 4 Wood units. Recently, his symptoms have worsened and have progressed to New York Heart Association class IV. He is subsequently placed on the transplant list with high priority. However, due to further deterioration, consideration is being given to the insertion of a left ventricular assist device (LVAD) to maintain adequate end-organ perfusion while waiting for a donor heart to become available.

A. Medical Disease and Differential Diagnosis

1. What are the common diagnoses requiring adult heart transplantation?
2. What are the indications and relative contraindications for recipient selection?
3. What are the criteria for donor heart selection?
4. What are the principles of perioperative donor management?
5. What are the risk factors associated with posttransplant mortality?
6. What is the difference between the biatrial and bicaval surgical techniques of heart transplant?
7. When is a combined heart/lung transplant indicated? What are the important differences?
8. What are the medical and surgical alternatives to cardiac transplantation?
9. What is the role of ventricular assist devices (VADs) in this type of patient?
10. What are the considerations in anesthetizing patients for LVAD insertion?

B. Preoperative Management

Three weeks after insertion of an LVAD, a donor heart becomes available.

1. How would you assess this patient preoperatively?
2. How would you premedicate this patient? Why?

C. Intraoperative Management

1. What anesthetic equipment and monitors would you set up? Why?
2. What is the role of transesophageal echocardiography (TEE)?
3. Describe the induction and maintenance of anesthesia.
4. How would you manage this patient during cardiopulmonary bypass (CPB)?

D. Postoperative Management

1. What are the early postoperative complications?
2. What are the mechanisms of early right ventricular (RV) failure?

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3. How would you treat right ventricular failure following heart transplantation?
4. How does inhaled nitric oxide (NO) work as a selective pulmonary vasodilator?
5. What is the pathophysiology of the denervated heart?
6. What are the common cardiac dysrhythmias following heart transplant?
7. What are the causes of posttransplant bleeding?
8. How would you treat posttransplant bleeding?
9. What are the causes of early graft failure?
10. How would you manage this patient in the intensive care unit?

E. Subsequent Noncardiac Surgery

The patient recovers successfully following heart transplant. However, 2 years postoperatively, he fractures his left radius after a fall. He then presents for open reduction and internal fixation of the fracture.

1. How would you monitor this patient?
2. What type of anesthetic is best for the heart-transplanted patient?
3. Which anesthetic technique would you give this patient?
4. Do you need to use a muscarinic antagonist with cholinesterase inhibitors to reverse the muscle relaxant in heart-transplanted patients?
5. What are the anesthetic implications for heart-transplanted patients?
6. What is the significant implication of the denervated heart?
7. What is the significance of allograft rejection?
8. What is the significance of infection in these patients?
9. What are the significant implications of drug interactions?
10. What is cardiac allograft vasculopathy (CAV)? Why is this important?
11. What is the significant implication of posttransplant hypertension?
12. What is the significant implication of renal dysfunction?
13. What types of malignancy are found in recipients?
14. Is ambulatory surgery appropriate for heart transplant recipients?

A. Medical Disease and Differential Diagnosis

A.1. What are the common diagnoses requiring adult heart transplantation?

Heart transplantation is now considered to be a viable treatment option for selected patients with end-stage heart disease. At present, more than 4,000 heart transplants are done annually worldwide. The indications for adult heart transplantation, as reported to the Registry of the International Society for Heart and Lung Transplantation in 2013, are shown in Figure 13.1. Ischemic coronary artery disease (28.1%) and nonischemic cardiomyopathy (54.2%) represent the most frequent causes for transplantation.

International Society for Heart and Lung Transplantation: Quarterly Data Report. Characteristics for Transplants performed between January 1, 2013 and January 1, 2014.

A.2. What are the indications and relative contraindications for recipient selection?

It should be noted that indications/contraindications can be flexible and can vary from center to center.

Criteria for selection can include the following:

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- End-stage heart disease with poor quality of life or poor survivability
- Refractory arrhythmias or angina despite optimal medical and surgical care
- Physiologic age younger than 70 years. However, in 2013, greater than 15.2% of heart transplant recipients were 65 years of age or older. There are cases of patients older than 70 years receiving a heart transplant.

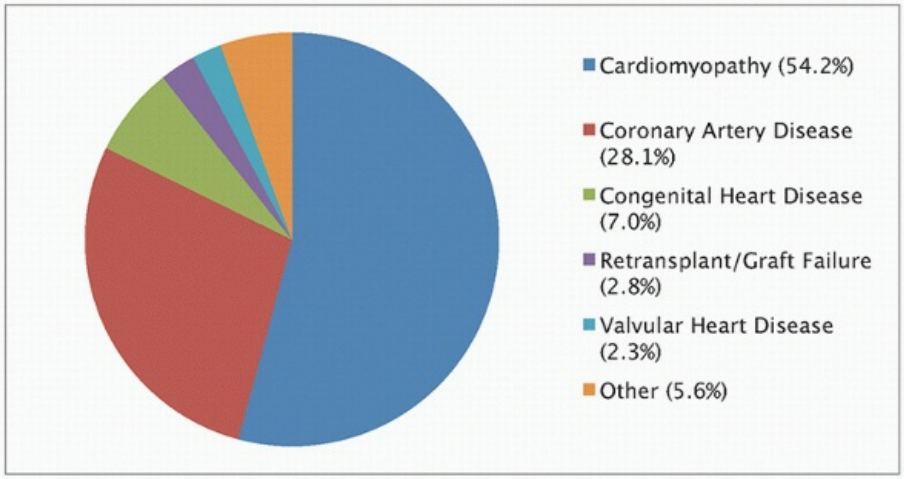


FIGURE 13.1 Indications for adult heart transplant (%). (From International Society for Heart and Lung Transplantation: Quarterly Data Report. Characteristics for Transplants performed between January 1, 2013 and January 1, 2014.)

- Maximal oxygen uptake ([V with dot above]O_{2max}) during cardiopulmonary exercise testing is considered. Although the cut-offs are highly variable and have many caveats, generally, patients with a peak [V with dot above]O_{2max} <10 mL/kg/min have an indication for transplantation.
- A Heart Failure Prediction Scoring system can also be used.

Contraindications (not necessarily absolute)

- Neoplasm with significant chance of recurrence
- Obesity (body mass index [BMI] <30 kg per m^2)
- Fixed (nonresponsive) pulmonary hypertension: PVR greater than 6 Wood units or pulmonary artery transpulmonary gradient greater than 15 mm Hg
- Nonreversible renal dysfunction
- Age older than 70 years
- Peripheral vascular disease, carotid stenosis (depending on severity)
- Diabetes with end-organ damage neuropathy, nephropathy, or retinopathy
- Psychosocial impairments
- Drug or alcohol addiction, smoking, mental defect that will limit compliance with postoperative care or history of noncompliance
- Other diseases that may limit survival (HIV, pulmonary disease, hepatitis, etc.)

Chan WX, Ross H. Who needs a transplant and when? *Curr Opin Organ Transplant*. 2012;17:531-539.

Haddad H, Isaac D, Legare JF, et al. Canadian Cardiovascular Society Consensus Conference update on cardiac transplantation 2008: executive summary. *Can J Cardiol*. 2009;25(4):197-205.

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International Society for Heart and Lung Transplantation: Quarterly Data Report. Characteristics for Transplants performed between January 1, 2012 and December 31, 2013.

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A.3. What are the criteria for donor heart selection?

The limiting factor in heart transplantation is the shortage of donor organs. In Canada, there were 146 adult and 21 pediatric heart transplants performed in 2013, with 167 people on the waiting list at the end of that year. In the United States, 2,655 heart transplants were

performed in 2014, with over 4,000 patients on the waiting list. Following the diagnosis of brain death, organ procurement may be considered for the purpose of donation. Preferably, the donor should not have sustained prolonged cardiac arrest, severe chest trauma, intracardiac injections, septicemia, excessive inotropic support, and be younger than 55 years of age. In all cases, a careful clinical examination of the potential donor is undertaken to rule out coronary artery atherosclerosis and contractile dysfunction; investigations may include angiography and echocardiography. The use of coronary angiography would be dictated by patient age, sex, and risk factors. In general, a contrast left ventriculogram is avoided to reduce the risk of nephrotoxicity.

Poor ejection fraction, despite optimization of physiologic variables, would exclude a potential donation. Transplantation can proceed with mild left ventricular hypertrophy; however, wall thickness >13 mm or electrocardiogram (ECG) criteria for left ventricular hypertrophy would make transplantation unadvisable. In general, severe congenital or valvular abnormalities would preclude donation, with the exception of abnormalities in which “bench” repair can be undertaken before transplant.

Blood group ABO compatibility is important, as mismatch may result in hyperacute rejection. The donor body weight should be within 20% of that of the recipient. However, in the case of a small donor matching, using BMI or height is more accurate than using weight. Preferably, donor heart ischemic time should be less than 4 hours. Prolonged ischemic time may contribute to early allograft failure; however, techniques to allow improved tolerance of ischemia may be on the horizon.

The concept of “extended-donor criteria” is becoming popular, and outcomes are favorable. Donor hearts with one or more of the following: size mismatch, ischemic time longer than 4 hours, ventricular hypertrophy, donor age older than 55 years, malignant brain tumors, long-standing death by poisoning, and significant inotropic requirements, are at times considered for transplant. In fact, looking at a wide variety of traditional reasons not to accept a donor heart, only diabetes mellitus was found to be predictive of 1-year mortality in a recipient, leading to concerns that many viable and “less than perfect” donor hearts are not being used for transplant.

The use of non-heart-beating (donation after cardiac death) donors is now used in multiple jurisdictions for kidney, liver, and lung transplantation. There have been cases of heart transplantation from non-heart-beating donors. However, the ethical and legal issues surrounding the technique for this form of heart donation are controversial.

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Zaroff JG, Rosengard BR, Armstrong WF, et al. Consensus conference report: maximizing use of organs recovered from the cadaver donor: cardiac recommendations, March 28-29, 2001, Crystal City, Va. *Circulation*. 2002;106:836-841.

A.4. What are the principles of perioperative donor management?

The goals of management are to maintain euvolemia, achieve relatively normal afterload, and optimize cardiac output (CO) without excessive use of inotropic medications, in particular *β*-agonists. Unfortunately, the brain-dead patient often can become extraordinarily unstable, and achieving hemodynamic stability can be a challenge. In addition, the treatment modalities to support certain end organs for donation are often at odds with each other. The onset of diabetes insipidus needs to be considered when excessive urine output (greater than 300 mL per hour) is observed and must be treated promptly with desmopressin (1-deamino-8-D-arginine vasopressin [DDAVP]). As a result of dysfunction of the hypothalamic-pituitary system, it is suggested that hormonal replacement therapy be undertaken. This includes the use of intravenous (IV) exogenous thyroid therapy, arginine vasopressin, and methylprednisolone. In addition, adequate glycemic control should be achieved.

Haddad H, Isaac D, Legare JF, et al. Canadian Cardiovascular Society Consensus Conference update on cardiac transplantation 2008: executive summary. *Can J Cardiol*. 2009;25(4):197-205.

Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: recommendations of the forum on medical management to optimize donor organ potential. *CMAJ*. 2006;174(6):S13-S32.

Van Bakel AB, Pitzer S, Drake P, et al. Early hormonal therapy stabilizes hemodynamics during donor procurement. *Transplant Proc*. 2004;36:2573-2578.

Zaroff JG, Rosengard BR, Armstrong WR, et al. Consensus conference report: maximizing use of organs recovered from the cadaver donor: cardiac recommendations, March 28-29, 2001, Crystal City, Va. *Circulation*. 2002;106:836-841.

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A.5. What are the risk factors associated with posttransplant mortality?

Overall survival at 1 year is 84.8% for recipients between 50 and 64 years of age for transplants performed from April 11, 2010 to March 31, 2014. Having congenital heart disease as the indication for transplant is a powerful predictor of postoperative 1-year mortality. In addition, the requirement of extracorporeal circulatory support, dialysis, preoperative mechanical ventilation, female gender, nonidentical ABO matching, previous blood transfusions, coronary artery disease as the indication for transplant, and being hospitalized immediately before transplant all are risk factors for 1-year mortality. Mortality during the first year is greater than the next 4 years combined, so risk factors associated with 1-year mortality are also powerful predictors of 5-year mortality. For those that have survived after 1 year, allograft vasculopathy during the first posttransplant year, diabetes mellitus, treatment for rejection during the first posttransplantation year, recipient age, donor age, recipient weight, and transplant center volume are risk factors for 5-year mortality.

The most common causes of death are the following:

Within 30 days posttransplant

- Graft failure, multiorgan failure, non-cytomegalovirus (CMV) infection

From 31 to 365 days posttransplant

- Non-CMV infection, graft failure, acute rejection

After 5 years

- Allograft vasculopathy, late graft failures, malignancies, non-CMV infections

International Society for Heart and Lung Transplantation: Quarterly Data Report. Survival Rates for Transplants performed between April 1, 2010 and March 31 2014.

Taylor DO, Stehlik J, Edwards LB, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult heart transplant report—2009. *J Heart Lung Transplant*. 2009;28(10):1007-1022.

A.6. What is the difference between the biatrial and bicaval surgical techniques of heart transplant?

The older biatrial technique involves anastomoses of the recipient and donor atrial cuffs. The bicaval technique maintains the above left atrial anastomoses and attempts to maintain cardiac anatomy with separate recipient's bicaval anastomoses to the donor's right atrium.

There may be an advantage of decreased need for pacemakers and improved mortality with the bicaval technique.

Davies RR, Russo MJ, Morgan JA, et al. Standard versus bicaval techniques for orthotopic heart transplantation: an analysis of the United Network for Organ Sharing database. *J Thorac Cardiovasc Surg*. 2010;140:700-708.

Morgan JA, Edwards NM. Orthotopic cardiac transplantation: comparison of outcome using biatrial, bicaval, and total techniques. *J Card Surg*. 2005;20:102-106.

A.7. When is a combined heart/lung transplant indicated? What are the important differences?

Congenital cardiac disease and primary pulmonary hypertension are the most common indications for combined heart/lung transplant. Other indications include cystic fibrosis, α_1-antitrypsin deficiency and other forms of lung disease, such as emphysema and idiopathic pulmonary fibrosis. The procedure is performed through a transverse thoracotomy incision, and the donor heart/lungs are transplanted en bloc. Important postoperative problems include bleeding and reperfusion lung injury, which may require inhaled NO, or occasionally extracorporeal membrane oxygenation (ECMO). Survival following heart/lung transplant is 68% and 51% at 1 and 3 years, respectively.

International Society for Heart and Lung Transplantation: Quarterly Data Report. Survival Rates for Transplants performed between April 1, 2010 and March 31, 2014.

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A.8. What are the medical and surgical alternatives to cardiac transplantation?

An ongoing worldwide shortage of donor hearts has meant ongoing pressure to manage medically patients with end-stage cardiac failure. Patients need to adhere to strict lifestyle modifications and diet; otherwise, any other therapy will have limited usefulness. As heart failure progresses, patients may respond to a variety of medications. Angiotensin-converting enzyme (ACE) inhibitors have been shown to improve symptoms and decrease mortality in patients with heart failure. Angiotensin II receptor blockers can be considered for patients intolerant of ACE inhibitors. Patients with severe forms of heart failure also may benefit from a low-dose aldosterone antagonist (spironolactone), with attention paid to potential hyperkalemia. Tailored doses of diuretic therapy may offer some symptomatic relief. β-Blockade with carvedilol, sustained-release metoprolol, or bisoprolol has been shown to reduce the risk of death. Therapy to maintain sinus rhythm is also recommended. In addition, patients with advanced heart failure may reduce their risk of sudden cardiac death by the insertion of an ICD. Furthermore, ICD implantation can be combined with cardiac resynchronization therapy (this can also be done alone), which has been shown to improve functional class and survival in advanced heart failure, in patients who are under optimal medical management. Intra-aortic balloon pump (IABP) and, increasingly, VAD implantation or semi-implantable paracorporeal devices also are finding a role in the management of patients as a bridge to transplant, particularly for those presenting in acute decompensated heart failure.

Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult—summary article. *Circulation*. 2005;112:1825-1852.

Ramani GV, Uber PA, Mehra MP. Chronic heart failure: contemporary diagnosis and management. *Mayo Clin Proc*. 2010;85:180-195.

Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure. *J Am Coll Cardiol*. 2013;62(16):e147-e239.

A.9. What is the role of ventricular assist devices (VADs) in this type of patient?

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) tracked 1,420 LVAD placements in 2010. Far fewer biventricular assist devices were inserted. The indications for LVAD insertion seem to be changing since 2006, when 40.8% were due to life-threatening cardiogenic shock. In 2010, only 12.3% of the patients had cardiogenic shock, and progressive decline of cardiac function (42%) presented the largest single indication. Of those that received an LVAD, 67.5% were listed or were being considered for heart transplant in 2010. In general, three major categories of patients considered for VAD include (1) temporary insertion while cardiac function recovers from insult (bridge to recovery),

(2) insertion while awaiting transplant or transplant assessment (bridge to transplant), and (3) patients who need long-term support but are not transplant candidates (destination therapy). Interestingly in 2010, the INTERMACS registry found that in 30.6% of patients, LVAD insertion was considered a destination therapy. The vast majority of VADs are continuous flow pumps instead of pulsatile flow.

A variety of composite risk scores have been developed to help guide patient selection for LVAD implantation. LVADs are inserted to improve end-organ function ahead of a heart transplant. Issues such as aortic valve incompetence and the presence of intracardiac shunts need to be investigated, as these may make LVAD insertion unadvisable without repair. RV function needs to be carefully assessed before and after LVAD insertion, as it may preclude the insertion of an LVAD or require a biventricular device.

Kirklin JK, Naftel DC, Kormos RL, et al. The fourth INTERMACS annual report: 4,000 implants and counting. *J Heart Lung Transplant*. 2012;31:117-126.

Miller LW, Guglin M. Patient selection for ventricular assist devices: a moving target. *J Am Coll Cardiol*. 2013;61:1209-1221.

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Wilson SR, Mudge GH Jr, Stewart GC, et al. Evaluation for a ventricular assist device: selecting the appropriate candidate. *Circulation*. 2009;119:2225-2232.

A.10. What are the considerations in anesthetizing patients for LVAD insertion?

Significant cardiac abnormalities (e.g., aortic insufficiency, patent foramen ovale) should be identified preoperatively and, if possible, addressed at the time of surgery. Induction and maintenance of a general anesthetic should be done cautiously (choice and dose of agents) in the context of a patient with severe cardiac dysfunction. These patients may have an ICD in place, and if deactivated, placement of external defibrillator pads is advisable. LVADs can be inserted with a sternotomy or a left thoracotomy. Patients are at high risk for significant perioperative blood loss, large-bore IV access is essential, and antifibrinolytics are often administered. TEE is mandatory for LVAD insertion to assess for the presence of a patent foramen ovale, ensure aortic valve competence, confirm proper position of device and cannulae, assess the amount of air in cardiac chambers, guide fluid management, and monitor the RV function. Inadequate right heart function is a potential complication after LVAD insertion and can be treated with phosphodiesterase inhibitors and inhaled NO. Vasopressin and/or norepinephrine may be required to maintain adequate systemic vascular resistance post-CPB. However, caution needs to be exercised with vasoconstrictors, as excessive afterload can impair the device function.

Broussard D, Donaldson E, Falterman J, et al. Anesthesia for left ventricular assist device insertion: a case series and review. *Ochsner J*. 2011;11(1):70-77.

Feussner M, Mukherjee C, Garbade J, et al. Anaesthesia for patients undergoing ventricular assist-device implantation. *Best Pract Res Clin Anaesthesiol*. 2012;26(2):167-177.

Tan LH, Cokis C. Anesthesia for implantation of the Jarvik 2000 Flowmaker LVAD. *Anaesth Intensive Care*. 2006;34:746-752.

B. Preoperative Management

Three weeks after insertion of an LVAD, a donor heart becomes available.

B.1. How would you assess this patient preoperatively?

Prospective transplant candidates usually have been fully preoperatively evaluated by a multidisciplinary team, including cardiologists, pulmonologists, surgeons, as well as anesthesiologists. The anesthesiologist should review the recipient's current cardiac status, including medications and level of mechanical support, with particular attention to hemodynamic parameters and reversibility of elevated PVR. Pertinent anesthetic history, concomitant diseases, and fasting status also must be ascertained. Baseline electrolytes, urea, creatinine, blood glucose, international normalized ratio (INR)/prothrombin time (PT), and complete blood count should be obtained. In addition, specific preoperative investigations need to be reviewed, such as echocardiogram, pulmonary function tests, ECG, and chest radiograph.

A plan also needs to be devised regarding how to handle an ICD on induction of anesthesia, and preoperative consultation with a cardiologist or electrophysiologist may be appropriate to achieve this.

There are typically two types of patients presenting for heart transplantation. The first type of patient is relatively compensated, possibly requiring IV inotropic support or may even be ambulatory in a nonhospital setting. The second type is moribund and decompensated, requiring mechanical ventilation and/or mechanical circulatory support. It should be noted, however, a third type of patient is emerging (the stable and ambulatory patient with an LVAD in place). At the time of transplant (sampled from 2006 to 2013), 42% of patients are on IV inotropes, 30% have an LVAD, 6.6% have an IABP, and 2.7% are mechanically ventilated. As the use of VADs increases, one would expect more patients to be presenting for transplant with LVADs in place. Recipients who have undergone prior cardiac surgery need to be identified, as this will increase the surgical time to establish CPB due to adhesions and bleeding. Large-bore IV access must be secured and crossmatched blood should be readily available in the operating room before surgery commences. The use of antifibrinolytics is routine for these cases.

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Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report—2014. *J Heart Lung Transplant*. 2014;33(10):996-1008.

B.2. How would you premedicate this patient? Why?

Patients should be transported to the operating room with oxygen supplementation. Caution should be exercised with sedative or narcotic premedication. Sedation may blunt the patient's respiratory and sympathetic drive and can lead to hypoxemia, hypercapnia, and even hypotension. Antibiotic prophylaxis often is achieved with 1 to 2 g of cephazolin or 1 g vancomycin.

Jhaveri R, Tardiff B, Stanley TE III. Anesthesia for heart and lung transplantation. *Anesthesiol Clin North Am*. 1994;12:729-747.

C. Intraoperative Management

C.1. What anesthetic equipment and monitors would you set up? Why?

Anesthetic equipment includes a ventilator/anesthesia machine, airway and intubation setup, fluid/blood warmer, forced air warming blanket, ultrasound for central line insertion, extracorporeal bypass machine (CPB machine), and inhaled NO delivery and monitoring system. Ultrasound may also be useful for arterial line insertion due to the nature of nonpulsatile flow with LVADs. All invasive lines are placed with meticulous attention to sterile technique and under titrated sedation with supplemental oxygen. Monitors include a 5-lead ECG, pulse oximeter, noninvasive blood pressure cuff, capnography, urinary catheter, temperature probe(s), and peripheral nerve stimulator. At least one large-bore peripheral IV may be very useful if bleeding becomes excessive during the case. Routinely, a pulmonary arterial (PA) catheter is inserted via the right internal jugular vein for pre-CPB, post-CPB, and postoperative measurement of PA pressure, PVR, and CO. The PA catheter is withdrawn back to about a 20-cm position in an 80-cm sterile sleeve before cardiectomy. TEE also is very useful in the intraoperative management of the pretransplant and posttransplant periods. A bispectral index monitor may be applied before induction. In some centers, cerebral oximetry also would be used as a monitor of cerebral oxygen delivery.

C.2. What is the role of transesophageal echocardiography (TEE)?

The echocardiographer can provide feedback to the surgeon regarding overall function of the transplanted heart. In particular, wall motion abnormalities, end-diastolic volume, valvular function, and the presence of anomalies (such as a patent foramen ovale) not appreciated prior to transplant can be assessed. Of particular interest is RV function and an assessment of PA pressures. TEE also may be useful in the assessment of surgical anastomosis. Specifically, the main PA anastomosis should be evaluated for stenosis. The long-axis view of

the left atrium is composed of recipient and donor tissue and may appear large. If excessive tissue is present, an acquired cor triatriatum may develop. In addition, the stored images of the baseline function of the transplanted heart may serve as a useful comparison after transplantation.

Bryan AJ, Barzilai B, Kouchoukos NT. Transesophageal echocardiography and adult cardiac operations. *Ann Thorac Surg*. 1995;59:773-779.

Couture R, Carrier M. Heart transplantation. In: Denault AY, Couture P, Buithieu J, et al, eds. *Transesophageal Echocardiography: A Perioperative Transdisciplinary Approach* . New York: Taylor & Francis Group; 2005:471-480.

Romano P, Mangion JM. The role of intraoperative transesophageal echocardiography in heart transplantation. *Echocardiography*. 2002;19(7, pt 1):599-604.

Suriani RJ. Transesophageal echocardiography during organ transplantation. *J Cardiothorac Vasc Anesth*. 1998;12:686-694.

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C.3. Describe the induction and maintenance of anesthesia.

It is important to time the anesthesia induction and surgery carefully to achieve CPB at the time of donor heart arrival in order to minimize ischemia time, particularly for a resternotomy patient. Prompt securing of the airway may be required as the recipient is not always properly fasted for transplantation surgery; however, a rapid induction needs to be balanced against the risk of hemodynamic compromise. The patient can be anesthetized with a variety of agents in combination, such as midazolam and fentanyl or sufentanil, which are titrated based on hemodynamic status and level of consciousness. Muscle relaxation may be achieved with pancuronium, rocuronium, or other nondepolarizing agents. In particular, when an LVAD was not in place, succinylcholine is usually not used because of concern of bradycardia during induction, as blood pressure in pre-heart transplant recipients often is heart rate dependent. Maintenance phase is achieved through the use of a balance anesthetic technique. Volatile agents (sevoflurane or isoflurane) are combined with fentanyl or sufentanil, midazolam, and muscle relaxation as required. NO is avoided due to its effect on PVR.

Previously, many centers would have used aprotinin as an antifibrinolytic therapy. However, Bayer, the manufacturer of aprotinin, removed it from the market after concerns of increased mortality surfaced in clinical trials. Tranexamic acid has taken this role now in many cardiac transplant centers.

At times, a great deal of bleeding can occur during the reopening the sternum after a previous LVAD insertion. Blood should be readily available to deal with what at times is the most challenging part of the case for anesthetic management.

Fergusson DA, Hébert PC, Mazer CD, et al. A comparison of aprotinin and lysine analogues in high-risk cardiac surgery. *N Engl J Med*. 2008;358:2319-2331.

Karkouti K, Beattie SW, Dattilo KM, et al. A propensity score case-control comparison of aprotinin and tranexamic acid in high-transfusion-risk cardiac surgery. *Transfusion*. 2006;46:327-338.

Mangano DT, Tudor IC, Dietzel C. The risk associated with aprotinin in cardiac surgery. *N Engl J Med*. 2006;354:353-365.

C.4. How would you manage this patient during cardiopulmonary bypass (CPB)?

The anesthetic management of CPB in these patients is often not different from that in nontransplant cardiac surgery patients, except that rewarming usually is prolonged because of the profound cooling of the donor heart and the prolonged ischemic time. Early in the perfusion, mixed venous oxygen desaturation and metabolic acidosis must be corrected. The fluid balance, hematocrit, electrolyte composition, and serum glucose must be monitored closely. During CPB, anesthesia maintenance is achieved by narcotic supplementation, an inhalational agent, and/or a benzodiazepine. Once cardiac rhythm has been established and anastomosis of the pulmonary artery is completed, the patient is placed in a head-down position for air evacuation from the left side of the heart. An isoproterenol infusion (1 to 5 μg per minute) may be considered to improve contractility and to increase heart rate to about 90 to 110 beats per minute. The heart may be externally paced via epicardial leads. Milrinone and NO are also often started as the patient is weaned from CPB to augment the RV function. The anesthesia team should be prepared for significant bleeding after separation from CBP. This is particularly true in cases where VADs have been in place.

D. Postoperative Management

D.1. What are the early postoperative complications?

The early postoperative complications include the following:

- Right ventricular failure/Pulmonary hypertension
- Denervated heart
- Bleeding
- Early graft failure

D.2. What are the mechanisms of early right ventricular (RV) failure?

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Right-sided heart failure is an important cause of posttransplant morbidity and mortality. It has a diverse number of causes related to both increases in flow and resistance across the pulmonary vascular bed. One prime cause is long-standing elevation in left ventricular pressure, leading to an increase in pulmonary pressure and vasoconstriction. This pulmonary vasoconstriction may become fixed over time, compromising RV function after transplant. However, a normal preoperative PVR does not rule out the potential for RV failure posttransplant. Poor organ preservation and CPB also can have deleterious effects on graft ventricular function.

Iyer A, Kumarasinghe G, Hicks M, et al. Primary graft failure after heart transplantation. *J Transplant*. 2011;2011:175768.

Stobierska-Dzierzek B, Awad H, Michler RE. The evolving management of acute right-sided heart failure in cardiac transplant recipients. *J Am Coll Cardiol*. 2001;38:923-931.

Wagner F. Monitoring and management of right ventricular function following cardiac transplantation. *Appl Cardiopulm Pathophysiol*. 2011;15:220-229.

D.3. How would you treat right ventricular failure following heart transplantation?

RV failure is associated with dilation, ischemia, and poor contractility. This can result in a shift of the ventricular septum to the left, with a reduction in left ventricular filling, and reduced CO. Basic therapeutic goals are to maintain adequate coronary perfusion, optimize oxygen delivery, prevent further distention of the RV by judicious use of fluids, minimize myocardial oxygen consumption, and reduce PVR to decrease RV afterload.

Phosphodiesterase inhibitors, such as milrinone, which have systemic and pulmonary vasodilatory effects in addition to positive inotropy, are particularly useful. Prostacyclin (PGI_2), isoproterenol (1 to 5 μg per minute), dobutamine, and nitrates also have been used with success to treat RV failure. However, vasodilator use often can be accompanied by arterial hypotension, requiring the administration of vasopressors to maintain adequate coronary perfusion. Inhaled NO also is widely used as a selective pulmonary vasodilator in severe pulmonary hypertension and RV failure. Sildenafil also can be considered when trying to reduce PVR. It should be remembered that the simple management of avoiding hypoxia, hypercarbia, and excessive positive end-expiratory pressure (PEEP) will help avoid elevated PVR.

In severe cases of refractory RV failure, posttransplant mechanical support should be considered, including IABP, right ventricular assist device (RVAD), or ECMO.

Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914-956.

Granton J, Moric J. Pulmonary vasodilators—treating the right ventricle. *Anesthesiol Clin*. 2008;26:337-353.

Stobierska-Dzierzek B, Awad H, Michler RE. The evolving management of acute right-sided heart failure in cardiac transplant recipients. *J Am Coll Cardiol*. 2001;38:923-931.

Wagner F. Monitoring and management of right ventricular function following cardiac transplantation. *Appl Cardiopulm Pathophysiol*. 2011;15:220-229.

D.4. How does inhaled nitric oxide (NO) work as a selective pulmonary vasodilator?

The advantage of inhaled NO as a pulmonary vasodilator lies mainly in the fact that its smooth muscle relaxant effect is limited to the pulmonary vasculature—the in vivo half-life of inhaled NO is only a few seconds. Therefore, it has little effect on the systemic circulation, unlike IV vasodilators, such as nitroprusside, nitroglycerin, prostaglandins, and calcium

channel blockers. Furthermore, inhaled NO selectively causes vasodilation in ventilated lung units, thus decreasing ventilation/perfusion ([V with dot above]/[Q with dot above]) mismatch and shunt. Inhaled NO (1 to 20 ppm) can result in

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significant decreases in PA pressure, PVR, and central venous pressure (CVP) while increasing mean arterial pressure, CO, and arterial oxygenation. In addition, a TEE documented alteration of the ventricular septal shift with a significant reduction in RV chamber and tricuspid valvular annulus size can be seen.

Girard C, Durand PG, Vedrinne C, et al. Inhaled nitric oxide for right ventricular failure after heart transplantation. *J Cardiothorac Vasc Anesth*. 1993;7:481-485.

Haddad H, Isaac D, Legare JF, et al. Canadian Cardiovascular Society Consensus Conference update on cardiac transplantation 2008: executive summary. *Can J Cardiol*. 2009;25(4):197-205.

Konstadt S. Nitric oxide: has it progressed from molecule of the year to wonder drug of the decade? *J Cardiothorac Vasc Anesth*. 1995;9:625-626.

D.5. What is the pathophysiology of the denervated heart?

Following cardiac transplantation, the cardiac plexus is interrupted and the heart is denervated. The recipient atrium remains innervated but hemodynamically unimportant, while the donor atrium is denervated and is responsible for the electrophysiologic responses of the transplanted heart. The ECG often contains two P waves. The denervated heart retains its intrinsic control mechanisms, which include the Frank-Starling mechanism and intact α-and β-adrenoreceptor responses to circulating catecholamines. This denervated heart lacks the ability to respond acutely to hypovolemia or hypotension with reflex tachycardia but responds to stress primarily by an increase in stroke volume. This reflects dependence of the donor heart sinus node on direct stimulation by endogenously released catecholamines and the absence of control via neural mechanisms. This is why heart-transplanted patients are said to be “preload dependent.” Interestingly, however, some studies have demonstrated reinnervation within a year after transplantation. This has led to symptoms of angina pectoris when ischemia develops in the transplanted heart.

Cheng DC, Ong DD. Anaesthesia for non-cardiac surgery in heart-transplanted patients. *Can J Anaesth*. 1993;40:981-986.

Kobashigawa JA. Postoperative management following heart transplantation. *Transplant Proc*. 1999;31:2038-2046.

D.6. What are the common cardiac dysrhythmias following heart transplant?

A wide variety of arrhythmias can occur in the heart transplant recipient. Early on, the course of recovery from heart transplant bradyarrhythmias is common and often self-limited. However, this underscores the utility of epicardial pacemaker placement at the time of surgery. The spectrum of other arrhythmias includes premature ventricular complexes, atrioventricular (AV) blockade, and supraventricular tachycardia. In fact, 5% to 24% of heart transplant recipients suffer from atrial fibrillation. The causes of arrhythmia include surgical disruption of normal conduction pathways and the sinus node, denervation, rejection, and coronary allograft vasculopathy. The presence of persistent arrhythmia, in particular ventricular in origin, is associated with increased long-term morbidity and mortality.

Chang HY, Lo LW, Feng AN, et al. Long-term follow-up of arrhythmia characteristics and clinical outcomes in heart transplant patients. *Transplant Proc*. 2013;45(1):369-375.

Stecker EC, Sterlich KR, Chugh SS, et al. Arrhythmias after orthotopic heart transplantation. *J Card Fail*. 2005;11(6):464-472.

D.7. What are the causes of posttransplant bleeding?

Perioperative bleeding is a significant cause of mortality following heart transplantation. The causes of posttransplant bleeding are anastomosis leaks and coagulopathy. Immediately before weaning from CPB, with the heart filled, the posterior anastomosis is carefully checked again by the surgeon for “water-tightness” because leaks in this area are more difficult and riskier to repair later. Coagulopathy, or what some term “medical bleeding,” often results from a combination of

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mechanisms, including inadequate heparin reversal, dilution of platelets and coagulation factors, hypothermia, and CPB effects on fibrinolysis, platelet function, and factor activation. In addition, those patients with a VAD in place before transplant are at

particular risk for perioperative hemorrhage. Possibly exacerbated due to the development of a von Willebrand syndrome.

Bourge RC, Naftel DC, Costanzo-Nordin MR, et al. Pretransplantation risk factors for death after heart transplantation: a multi-institutional study. *J Heart Lung Transplant*. 1993;12:549-562.

Diaz-Martin A, Escoresca-Ortega AM, Hernandez-Caballero C, et al. Considerations regarding major bleeding after cardiac transplantation. *Transplant Proc*. 2010;42:3204-3205.

Uriel N, Pak SW, Jorde UP, et al. Acquired von Willebrand syndrome after continuous-flow mechanical device support contributes to a high prevalence of bleeding during long-term support and at the time of transplantation. *J Am Coll Cardiol*. 2010;56(15):1207-1213.

Wegner JA, DiNardo JA, Arabia FA, et al. Blood loss and transfusion requirements in patients implanted with a mechanical circulatory support device undergoing cardiac transplantation. *J Heart Lung Transplant*. 2000;19:504-506.

D.8. How would you treat posttransplant bleeding?

Prevention of potential causes of bleeding is key. The use of antifibrinolytics is strongly encouraged, in particular if re-do sternotomy is to be undertaken. Avoidance of excessive crystalloid in the prebypass period may reduce the dilutional component of coagulopathy. Maintaining normothermia with forced air warming devices and fluid warmers also is imperative. When bleeding is evident in the postoperative period, the judicious use of packed red blood cells, fresh frozen plasma, and platelets is a starting point. If hemorrhage is not responsive to conservative measures, disseminated intravascular coagulopathy must be ruled out. If serum fibrinogen is low (less than 0.8 to 1.0 g per L), then the use of cryoprecipitate should be entertained. Although not routine, desmopressin (0.3 μg per kg) also may have a role in refractory cases. Finally, recombinant factor VIIa has been used successfully to treat hemorrhage in cardiac transplant patients. However, the risk of thrombosis needs to be weighed against the risk of ongoing bleeding, and consultation with a hematologist would be advisable before administration. It always should be remembered that bleeding that is excessive and not clearly secondary to coagulopathy warrants surgical re-exploration.

Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914-956.

Kogan A, Berman M, Kassif Y, et al. Use of recombinant factor VII to control bleeding in a patient supported by right ventricular assist device after heart transplantation. *J Heart Lung Transplant*. 2005;24:347-349.

D.9. What are the causes of early graft failure?

Graft failure (primary and nonspecific) is the most common cause of death in the first 30 days after heart transplant. Etiologies include biventricular failure, RV failure (often due to high PVR), flow-limiting coronary stenosis, and hyperacute rejection.

Luckraz H, Goddard M, Charman SC, et al. Early mortality after cardiac transplantation: should we do better? *J Heart Lung Transplant*. 2005;24:401-405.

Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report—2014. *J Heart Lung Transplant*. 2014;33(10):996-1008.

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D.10. How would you manage this patient in the intensive care unit?

Within the first 30 days, posttransplant graft failure (primary and nonspecific), multiorgan failure, and non-CMV infection are the most common causes of death at 39%, 18%, and 12.7%, respectively. Early management goals include prevention of infection and rejection, treatment of bleeding and dysrhythmias, cardiovascular support, and avoidance of elevated PA pressures. If possible, one should aim to wean the patient from the ventilator and extubate within 24 hours. In order to facilitate oxygenation and weaning, strict supervision of fluid balance and body weight is required. Immunosuppression often is achieved with a cocktail of medications, including steroids (methylprednisolone followed by prednisone), calcineurin inhibitor (e.g., tacrolimus), and antiproliferative agent (e.g., mycophenolate mofetil). Some patients may benefit from induction therapy using interleukin-2 (IL-2) antagonists and/or polyclonal antibodies, for example, highly sensitized patients or those with reactive donor-specific antigens, or for tacrolimus-delaying immunosuppression strategies in those with renal dysfunction.

It should be noted that a significant number of centers no longer routinely administer induction immunosuppression with good results. Secondary to immunosuppression, patients sometimes are covered prophylactically with ganciclovir for CMV prophylaxis.

Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109-113.

Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914-956.

Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report—2014. *J Heart Lung Transplant*. 2014;33(10):996-1008.

Taylor DO. Cardiac transplantation: drug regimens for the 21st century. *Ann Thorac Surg*. 2003;75:S72-S78.

E. Subsequent Noncardiac Surgery

The patient recovers successfully following heart transplant. However, 2 years postoperatively, he fractures his left radius after a fall. He then presents for open reduction and internal fixation of the fracture.

E.1. How would you monitor this patient?

This patient should have similar monitoring requirements for nontransplant patients undergoing similar procedures. Smooth and safe anesthesia is contingent upon careful preoperative assessment, which may reduce the need for invasive monitoring with all its attendant risks. Adequate preload must be attained preoperatively and intravascular volume status maintained intraoperatively because these patients are “preload dependent.” Monitors in the given case would include an ECG, noninvasive blood pressure cuff, capnometer, and peripheral oxygen saturation probe, and if general anesthetic was delivered, a temperature probe, agent-specific gas monitor, and a neuromuscular stimulator would be applied. However, for cases with potential for blood loss and fluid shifts, consideration should be given to additional intraoperative monitors, including an arterial line, central venous line, pulmonary artery catheter, and TEE.

Cheng DC, Ong DD. Anaesthesia for non-cardiac surgery in heart-transplanted patients. *Can J Anaesth*. 1993;40:981-986.

E.2. What type of anesthetic is best for the heart-transplanted patient?

In a series of 86 heart-transplanted recipients, 18 returned for 32 noncardiac surgical procedures. The breakdown included 18 neurolept-anesthesia cases, 12 general anesthesia cases with a combination of N_2O/O_2/narcotic/relaxant and low doses of volatile agents, and 2 spinal cases. The patients had normal requirements of IV and inhalational agents, muscle relaxants, and local anesthetics. There was no prolonged action of any anesthetic agents. Generally, the choice of general or regional anesthesia does not affect postoperative outcome in hearttransplanted recipients undergoing subsequent noncardiac surgery.

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Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109-113.

Cheng DC, Ong DD. Anaesthesia for non-cardiac surgery in heart-transplanted patients. *Can J Anaesth*. 1993;40:981-986.

E.3. Which anesthetic technique would you give this patient?

This patient could safely receive general anesthesia or regional blockade of his brachial plexus for the upcoming surgery.

E.4. Do you need to use a muscarinic antagonist with cholinesterase inhibitors to reverse the muscle relaxant in heart-transplanted patients?

Although it does not compromise other hemodynamic parameters, neostigmine has been shown to produce a dose-dependent decrease in heart rate in heart-transplanted patients. In remote transplanted patients (<6 months), a muscarinic antagonist should be administered

simultaneously with cholinesterase inhibitors to block the cardiac and muscarinic side effects, as slow development of cardiac reinnervation may be possible.

Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Dis*. 2002;4:191-198.

Backman SB, Fox GS, Stein RD, et al. Neostigmine decreases heart rate in heart transplant patients. *Can J Anaesth*. 1996;43:373-378.

Wilson RF, Christensen BV, Olivari MT, et al. Evidence for structural sympathetic reinnervation after orthotopic cardiac transplantation in humans. *Circulation*. 1991;83:1210-1221.

E.5. What are the anesthetic implications for heart-transplanted patients?

The anesthetic implications for heart-transplanted patients include the following:

- Denervated heart
- Allograft rejection
- Infection due to immunosuppression
- Drug interaction
- Allograft coronary artery disease
- Hypertension
- Renal dysfunction
- Immunosuppression-related malignancy

Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Dis*. 2002;4:191-198.

Cheng DC, Ong DD. Anaesthesia for non-cardiac surgery in heart-transplanted patients. *Can J Anaesth*. 1993;40:981-986.

E.6. What is the significant implication of the denervated heart?

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The denervated heart retains its intrinsic control mechanisms, which include Frank-Starling mechanism, impulse formation and conductivity, and responsiveness to circulating catecholamines in the form of increased heart rate and contractility. But the normal respiratory variations or response to carotid sinus massage and Valsalva maneuvers are absent. At rest, the heart rate reflects the intrinsic rate of depolarization at the donor sinoatrial node and, in the absence of any vagal tone, is faster than normal at about 90 to 100 beats per minute. The heart rate shows minimal response to drugs, such as muscle relaxants (pancuronium); anticholinergics (atropine, glycopyrrolate, and scopolamine); cholinesterase inhibitors (neostigmine, edrophonium, pyridostigmine, physostigmine); digoxin, nifedipine, phenylephrine, or nitroprusside, but will respond to isoproterenol, ephedrine, dopamine, and epinephrine.

Cardiac dysrhythmias may occur in heart-transplanted patients. Atrial and less frequently ventricular tachyarrhythmias are common. Bradyarrhythmic therapy in these patients should be treated with a direct *β*-adrenergic stimulating agent (epinephrine, isoproterenol). Medications used to treat tachyarrhythmias (calcium channel blockers, *β*-blockers) need to be used with caution due to their negative inotropic effects.

Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Dis*. 2002;4:191-198.

Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109-113.

Chang HY, Lo LW, Feng AN, et al. Long-term follow-up of arrhythmia characteristics and clinical outcomes in heart transplant patients. *Transplant Proc*. 2013;45(1):369-375.

Stein KL, Darby JM, Grenvik A. Intensive care of the cardiac transplant recipient. *J Cardiothorac Anesth*. 1988;2:543-553.

E.7. What is the significance of allograft rejection?

The majority of rejection episodes occur in the first 6 months posttransplant. These patients can present with fever, malaise, arrhythmias, and shortness of breath. Hemodynamic compromise is considered a late sign of rejection. The gold standard for diagnosis is endomyocardial biopsy. Rejection episodes are treated primarily with steroids; however, more severe forms may require more aggressive immunosuppression with antithymocyte antibodies or

plasmapheresis. The type of therapy is guided by symptom severity and the type of rejection (cellular mediated vs. antibody mediated).

Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914-956.

Kobashigawa JA. Postoperative management following heart transplantation. *Transplant Proc*. 1999;31:2038-2046.

E.8. What is the significance of infection in these patients?

Immunosuppressive drugs are continued indefinitely in heart-transplanted patients, and infection remains a major cause of death, with 10% of mortality 5 years posttransplant secondary to non-CMV infections. Early postoperative bacterial infections (e.g., mediastinitis) and opportunistic infections (e.g., CMV, *Pneumocystis carinii*, *Toxoplasma*) are of great concern. Invasive monitoring techniques and all forms of instrumentation should be kept to the minimum consistent with safe anesthesia. Attention to sterile technique should be paramount. Intubation via the orotracheal route is preferable to the nasotracheal route as the latter is associated with infection by diphtheroids and staphylococcal organisms from the nasopharynx and skin.

Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109-113.

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Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report—2014. *J Heart Lung Transplant*. 2014;33(10):996-1008.

Shaw IH, Kirk AJB, Conacher ID. Anaesthesia for patients with transplanted hearts and lungs undergoing noncardiac surgery. *Br J Anaesth*. 1991;67:772-778.

Taylor DO, Stehlik J, Edwards LB, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult heart transplant report—2009. *J Heart Lung Transplant*. 2009;28(10):1007-1022.

E.9. What are the significant implications of drug interactions?

Chronic steroid treatment may result in an abnormal stress response, so patients should receive perioperative steroid coverage. Azathioprine has been reported to antagonize the competitive neuromuscular-blocking drugs by its phosphodiesterase-inhibiting properties; therefore, larger doses of relaxants may be required. In experimental animals, cyclosporine infusions have been shown to potentiate the neuromuscular-blocking effects of atracurium and vecuronium. A single dose of cyclosporine may result in increased duration of action of both barbiturates and narcotics.

Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Dis*. 2002;4:191-198.

Cirella VN, Pantuck CB, Lee YJ, et al. Effects of cyclosporine on anesthetic action. *Anesth Analg*. 1987;66:703-706.

E.10. What is cardiac allograft vasculopathy (CAV)? Why is this important?

The transplanted heart is vulnerable to an accelerated process of coronary atherosclerosis called cardiac allograft vasculopathy (CAV). Between the 1st and 10th year posttransplant, over 40% of patients develop CAV. It is characterized by concentric intimal proliferation and diffuse narrowing along the coronary vessel. Diagnosis is accomplished by coronary angiography or intravascular ultrasound. The etiology is likely multifactorial, with both immunologic and nonimmunologic factors. Traditional risk factors such as pretransplant coronary artery disease, diabetes, and hyperlipidemia put a recipient at risk for CAV. Donor characteristics are also implicated, such as advanced donor age and mechanism of donor death. The type of immunosuppression regime, CMV infections, and episodes of rejection also impacts CAV development.

Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109-113.

Kobashigawa JA. Postoperative management following heart transplantation. *Transplant Proc*. 1999;31:2038-2046.

Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report—2014. *J Heart Lung Transplant*. 2014;33(10):996-1008.

E.11. What is the significant implication of posttransplant hypertension?

After 5 years, 91% of surviving patients have developed hypertension. Calcineurin inhibitors often are cited as a causative factor. Current therapy may consist of a calcium channel blocker such as diltiazem. However, care must be taken, as diltiazem may increase cyclosporine serum levels. Nifedipine has a tendency to cause significant vasodilatation and may be tolerated poorly in these patients. When necessary, an ACE inhibitor may be added. Because cardiac responsiveness during exercise is dependent on circulating catecholamines, *β*-blockers often are avoided after heart transplantation.

Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914-956.

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Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report—2014. *J Heart Lung Transplant*. 2014;33(10):996-1008.

E.12. What is the significant implication of renal dysfunction?

Renal dysfunction is found in 33% of recipients at 5 years. Due to the nephrotoxic effects of calcineurin inhibitors, serum creatinine concentrations often gradually increase after cardiac transplantation, with roughly 6% of recipients requiring dialysis after 10 years. Anesthetic drugs that are excreted mainly by renal clearance should be avoided if renal function is compromised. Also, one needs to be mindful of medications that may compromise further renal function, such as nonsteroidal anti-inflammatory drugs (NSAIDs).

Kobashigawa JA. Postoperative management following heart transplantation. *Transplant Proc*. 1999;31:2038-2046.

Lindenfeld JA, Page RL II, Zolty R, et al. Drug therapy in the heart transplant recipient: part III: common medical problems. *Circulation*. 2005;111:113-117.

Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report—2014. *J Heart Lung Transplant*. 2014;33(10):996-1008.

Miller LW. Long-term complications of cardiac transplantation. *Prog Cardiovasc Dis*. 1991;33:229-282.

Taylor DO, Stehlik J, Edwards LB, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult heart transplant report—2009. *J Heart Lung Transplant*. 2009;28(10):1007-1022.

E.13. What types of malignancy are found in recipients?

Chronic immunosuppression puts patients at risk for the development of cancer. After 10 years, 27% of survivors have some form of malignancy. The vast majority are skin cancers, whereas a much smaller percentage suffer from posttransplant lymphoproliferative disorder. Malignancies account for 23% of deaths 5 years after transplant.

Haddad H, Isaac D, Legare JF, et al. Canadian Cardiovascular Society Consensus Conference update on cardiac transplantation 2008: executive summary. *Can J Cardiol*. 2009;25(4):197-205.

Lund LH, Edwards LB, Kucheryavaya AY, et al. The Registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report—2014. *J Heart Lung Transplant*. 2014;33(10):996-1008.

E.14. Is ambulatory surgery appropriate for heart transplant recipients?

Unfortunately, there is a paucity of evidence supporting either the safety or harm of ambulatory surgery in heart transplant recipients. In addition, the choice of anesthetic technique seems to have no influence on outcome. Regardless, these patients should be seen in preadmission clinics before the day of surgery and have appropriate screening tests done preoperatively, including, but not limited to, an assessment of complete blood count, electrolytes, renal function, ECG, and an accurate blood pressure measurement. They also should be evaluated by the cardiology transplant service and if any concern is raised, further testing should be undertaken, such as echocardiography, coronary angiography, or endomyocardial biopsy. Recommendations also should be obtained from the cardiac transplant service regarding perioperative antibiotic prophylaxis and immunosuppression.

Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109-113.

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Bryson GL, Chung F, Finegan BA, et al. Patient selection in ambulatory anesthesia—an evidence-based review: part I. *Can J Anaesth*. 2004;51:768-781.

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Chapter 14
Ischemic Heart Disease and Noncardiac Surgery

Shamsuddin Akhtar

Paul G. Barash

A 72-year-old man is scheduled for right hemicolectomy for colon cancer. Past history reveals a myocardial infarction (MI) 5 months ago and placement of a right coronary second-generation drug-eluting stent (DES). He also has type 2 diabetes mellitus. He is currently treated with dual antiplatelet therapy (DAPT) (aspirin and clopidogrel), atenolol, diltiazem, metformin, losartan, and an occasional sublingual nitroglycerin (NTG).

A. Medical Disease and Differential Diagnosis

1. What are the preoperative predictors for major adverse cardiac events (MACE) perioperatively?
2. What are the determinants of myocardial oxygen demand? How are they measured clinically?
3. What factors determine myocardial oxygen supply?
4. What is the mechanism of perioperative myocardial ischemia and infarction?
5. What is the incidence of perioperative reinfarction for noncardiac surgery?
6. State the perioperative medical therapy you would employ to reduce the incidence of myocardial ischemia.
7. Based on his MI, would you recommend that the surgery be postponed for a certain period of time? If so, why?
8. Would you recommend that this elective colectomy be postponed, if the patient underwent placement of a right coronary artery, second-generation DES, and is taking aspirin and clopidogrel (Plavix)?

B. Preoperative Evaluation and Preparation

1. How would you evaluate the patient's cardiac condition? What laboratory tests would you like to order?
2. Would you recommend further cardiac testing or coronary revascularization before surgery?
3. How would you classify the cardiac risk according to the type of surgery?
4. What is the role of exercise or pharmacologic stress test for this patient?
5. Would you discontinue any medication before surgery?
6. How would you premedicate this patient?
7. Is there a role for α_2-agonist in premedication?

C. Intraoperative Management

1. What are the intraoperative predictors for perioperative MACE?
2. How would you monitor the patient in the operating room?
3. What electrocardiogram (ECG) leads would you monitor? Why V_5?

4. Would you use a pulmonary artery catheter (PAC)?
5. Would you use transesophageal echocardiography (TEE) as a monitor?
6. Is regional anesthesia better than general anesthesia for patients with cardiac disease?
7. How will you induce general anesthesia?
8. Would you induce anesthesia with etomidate? Why?

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9. What is the best choice of anesthetic agents for maintenance of anesthesia? Why?
10. You notice a new 3-mm ST-segment depression in lead V_5. How would you treat it?
11. Would you give prophylactic intravenous NTG to prevent myocardial ischemia?
12. What is the significance of tight control of the heart rate intraoperatively?
13. When would you extubate the trachea in this patient? What could you do to prevent hypertension and tachycardia during extubation and emergence?

D. Postoperative Management

1. What are the postoperative predictors of perioperative MACE?
2. How would you control postoperative pain?
3. Is postoperative anemia associated with adverse cardiac outcome?
4. Is postoperative hypothermia associated with postoperative myocardial ischemia?
5. How would you make a diagnosis of perioperative myocardial infarction (PMI)?
6. How would you manage the patient with a suspected PMI?

A. Medical Disease and Differential Diagnosis

A.1. What are the preoperative predictors for major adverse cardiac events (MACE) perioperatively?

Perioperative myocardial infarction or injury (PMI) is one of the most important predictors of short- and long-term mortality and morbidity associated with noncardiac surgery. Therefore, the prevention of PMI can improve postoperative outcomes. Numerous risk indices and predictors for perioperative cardiac morbidity (PCM) have been published over the last 40 years.

In 1999, Lee et al. revised the Goldman Cardiac Risk Index, now called the Revised Cardiac Risk Index (RCRI), utilizing six independent predictors of cardiac risk, which are as follows:

- High-risk type of surgery
- History of ischemic heart disease (IHD)
- History of congestive heart failure (CHF)
- History of cerebrovascular disease
- Preoperative treatment of diabetes mellitus with insulin
- Preoperative serum creatinine greater than 2.0 mg per dL

They concluded that the rate of major cardiac complications (MI, pulmonary edema, ventricular fibrillation, and primary cardiac arrest) with 0, 1, 2, and more than or equal to 3 predictors, were 0.5%, 1.3%, 4%, and 9%, respectively.

The 2014 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines categorize the patients into two groups, namely, *lowrisk* and *elevated risk* based on the presence of clinical risk factors and risk of surgical procedures. Patients with less than 1% chance of MACE are categorized as low risk, whereas patients with cumulative risk of MACE more than 1% are categorized as elevated risk. Patients who have two or more RCRIs are considered at elevated risk. The other two indices are the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) Myocardial Infarction and Cardiac Arrest (MICA), and American College of Surgeons NSQIP Surgical Risk Calculator (http://riskcalculator.facs.org). Both are readily available on the web to evaluate patients. The European Society of Cardiology (ESC) guidelines define surgical risk procedures as low-(<1%),

intermediate-(1% to 5%), and high-risk procedures (>5%). By ACC guideline criteria, this patient will be considered elevated risk, scheduled to undergo an intermediate-risk procedure (by ESC guidelines).

Although the new guidelines do not categorize the clinical predictors of MACE into major, intermediate, and minor factors, in addition to the RCRI mentioned earlier, the following clinical factors significantly increase the risk of perioperative MACE.

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- Unstable coronary syndromes: Acute (MI ≤7 days before examination) or recent MI (>7 days but ≤1 month) with evidence of important ischemic risk by clinical symptoms or noninvasive study. A study using discharge summaries demonstrated that the postoperative MI rate decreased substantially as the length of time from MI to operation increased (0 to 30 days = 32.8%; 31 to 60 days = 18.7%; 61 to 90 days = 8.4%; and 91 to 180 days = 5.9%), as did the 30-day mortality rate. However, risk was modified by coronary intervention. It is suggested that more than 60 days should elapse after MI before noncardiac surgery is undertaken in the *absence* of coronary intervention.
- Unstable or severe angina (Canadian class III): marked limitation of ordinary physical activity; walking one to two blocks on the level and climbing one flight of stairs in normal conditions at normal pace; and Canadian class IV: inability to carry on any physical activity without discomfort—anginal syndrome may be present at rest
- Decompensated heart failure (HF): Patients with active HF have significantly higher risk of postoperative death than do patients with coronary artery disease (CAD). Survival after surgery for those with a left ventricular ejection fraction (LVEF) less than 30% is significantly worse than for those with an LVEF ≥30%.
- Severe valvular disease (severe aortic stenosis [AS] with valve area less than 1 cm^2 or symptomatic) have a two to three times higher risk of 30-day mortality than patients without AS. Similar observations have been noted for severe mitral stenosis. Left-sided regurgitant lesions convey increased cardiac risk during noncardiac surgery but are better tolerated than stenotic valvular disease.
- Significant arrhythmias, such as high-grade atrioventricular block, Mobitz type II atrioventricular block, third-degree heart block, or unanticipated symptomatic supraventricular and ventricular arrhythmias, increase operative risk. Risk of other supraventricular and ventricular arrhythmias seems to be lower than reported before.
- Age is considered a risk factor especially when it is associated with frailty. However, its exact role still needs to be defined further.
- Pulmonary hypertension: Patients with pulmonary artery hypertension are at an increased risk of cardiopulmonary complications after noncardiac surgery. Mortality rates of 4% to 26% and cardiorespiratory morbidity rates of 6% to 42% have been reported.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e77-e137.

Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2014;35:2383-2431.

Lee TH, Marcantonio RE, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999;100:1043-1049.

A.2. What are the determinants of myocardial oxygen demand? How are they measured clinically?

The three major determinants of myocardial oxygen demand are (1) myocardial left ventricular (LV) wall tension (LV preload and afterload), (2) cardiac contractility, and (3) heart rate.

A.3. What factors determine myocardial oxygen supply?

The factors determining myocardial oxygen supply include cardiac output, arterial oxygen content, heart rate, aortic diastolic pressure, LV end-diastolic pressure, patency of coronary arteries, and coronary vascular tone.

A.4. What is the mechanism of perioperative myocardial ischemia and infarction?

Myocardial ischemia occurs whenever myocardial oxygen supply does not match myocardial oxygen demand. Intraoperative ischemia can be precipitated by increases in myocardial oxygen demand caused by tachycardia,

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hypertension, anemia, surgical stress, sympathomimetic drugs, or discontinuation of β-blockers. Potential etiologies for decreased supply include hypotension, tachycardia, increased cardiac filling pressures, anemia, hypoxemia, and decreased cardiac output. In one study, ischemia occurred (67%) at the end of anesthesia or immediately after surgery, during a period characterized by high sympathetic output, hypercoagulability, hypertension, and tachycardia. Ischemia in this period is usually silent, with only ST-segment depression as a marker. And in at least one-third of the patients, this ST-segment depression goes unnoticed. Hypotension is strongly correlated with PMI. In addition, internal factors such as acute coronary artery thrombosis and spasm may also play a role.

PMI is one of the most important predictors of short- and long-term morbidity and mortality associated with noncardiac surgery. Unfortunately, the exact nature of PMI remains uncertain and a subject of debate and controversy. The interaction between morphologic and functional factors is unpredictable. Some older pathologic and angiographic studies suggested that the etiology of PMI resembles that in the nonsurgical setting, that is, plaque rupture was the cause of PMI in 50% of the cases. However, newer analysis suggests that myocardial oxygen supply/demand imbalance predominates in the first 3 to 4 postoperative days and patients suffer PMI from demand ischemia. In PMI, the severity of underlying coronary artery stenosis does not necessarily predict the infarct territory. The high incidence of histologically confirmed transmural infarctions seems to be contradictory to the ECG finding of almost exclusively non-Q-wave PMIs. On the other hand, the presence of subendocardial PMIs is consistent with a myocardial oxygen supply/demand mismatch being the main trigger of myocardial injury. However, myocardial oxygen supply/demand mismatch and plaque rupture are not mutually exclusive mechanisms, and PMIs may be developed by different mechanisms at different locations in the same patient.

Most PMIs occur early after surgery (0 to 4 days) and 90% occur within 7 days, are asymptomatic, of the non-Q-wave type (60% to 100%), and are commonly preceded by ST-segment depression rather than ST-segment elevation. Long duration (single duration >20 to 30 minutes or cumulative duration >1 to 2 hours intraoperatively or postoperatively) rather than just the presence of postoperative ST-segment depression seems to be the important factor associated with adverse cardiac outcome.

Biccard BM, Rodseth RN. What evidence is there for intraoperative predictors of perioperative cardiac outcomes? A systematic review. *Perioper Med (Lond)*. 2013;2:14.

Cheung C, Martyn A, Campbell N, et al. Predictors of intraoperative hypotension and bradycardia. *Am J Med*. 2015;128:532-538.

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Galal W, Hoeks SE, Flu WJ, et al. Relation between preoperative and intraoperative new wall motion abnormalities in vascular surgery patients: a transesophageal echocardiographic study. *Anesthesiology*. 2010;112:557-566.

Landesberg G, Beattie WS, Mosseri M, et al. Perioperative myocardial infarction. *Circulation*. 2009;119:2936-2944.

Lonjaret L, Lairez O, Minville V, et al. Optimal perioperative management of arterial blood pressure. *Integr Blood Press Control*. 2014;7:49-59.

Subramaniam B, Subramaniam K. Not all perioperative myocardial infarctions can be prevented with preoperative revascularization. *Anesthesiology*. 2010;112:524-526.

A.5. What is the incidence of perioperative reinfarction for noncardiac surgery?

The risk assessment for noncardiac surgery of patients with CAD is based upon the time interval between the MI and surgery. Using a discharge database of more than half million patients, it was shown that postoperative MI rate for the recent MI cohort decreased substantially as the length of time from MI to operation increased (0 to 30 days = 32.8%; 31 to 60 days = 18.7%; 61 to 90 days = 8.4%; and 91 to 180 days = 5.9%), as did 30-day

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mortality (0 to 30 days = 14.2%; 31 to 60 days = 11.5%; 61 to 90 days = 10.5%; and 91 to 180 days = 9.9%). MI within 30 days of an operation was associated with a highest risk of postoperative MI. However, with improvements in perioperative care, this difference has become blurred. The importance of the timing of the MI in relation to the proposed surgical procedure may no longer be valid in the era of thrombolytics, angioplasty, and risk stratification. Although many patients with a history of an MI may continue to have myocardium at risk, others may not. If a stress test does not indicate residual myocardium at risk, the likelihood of reinfarction is low. The current AHA/ACC guidelines for perioperative cardiovascular evaluation suggests that more than 60 days should elapse after MI, before noncardiac surgery is undertaken in the *absence* of coronary intervention. Landesberg et al. reported that early mortality after PMI ranges from 3.5% to 25% and is higher among patients with marked troponin elevation compared with patients with minor troponin elevation (0% to 7%). This is in contrast to older data that reported a very high incidence of mortality.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e77-e137.

Landesberg G, Beattie WS, Mosseri M, et al. Perioperative myocardial infarction. *Circulation*. 2009;119: 2936-2944.

Li SL, Wang DX, Wu XM, et al. Perioperative acute myocardial infarction increases mortality following noncardiac surgery. *J Cardiothorac Vasc Anesth*. 2013;27:1277-1281.

Livhits M, Ko CY, Leonardi MJ, et al. Risk of surgery following recent myocardial infarction. *Ann Surg*. 2011;253:857-864.

A.6. State the perioperative medical therapy you would employ to reduce the incidence of myocardial ischemia.

β-Adrenergic Antagonists (Esmolol, Atenolol, Metoprolol, Bisoprolol)

These drugs reduce myocardial oxygen consumption, improve coronary blood flow by prolonging diastolic perfusion period, improve supply/demand ratio, stabilize cellular membranes, improve oxygen dissociation from hemoglobin, and inhibit platelet aggregation. *β*-Blockers suppress perioperative tachycardia and appear most efficacious in preventing perioperative myocardial ischemia. In view of their beneficial effects, prophylactic use of *β*-blocker to decrease PMI has been explored in many trials. Mangano et al. reported a beneficial effect of atenolol in a randomized double-blind, placebo-controlled trial on overall survival and cardiovascular morbidity in noncardiac surgery patients with or at risk for CAD. Poldermans et al. reported that the *β*-blocker, bisoprolol, reduced the perioperative incidence of death from cardiac causes and nonfatal MI in vascular surgical patients with known CAD. Bisoprolol, started before noncardiac surgery (30 days), can substantially reduce perioperative cardiac complications in all but the highest risk patients. However, results of subsequent large trials have not shown efficacy of high-dose, acutely administered, perioperative *β*-blockers to reduce overall mortality in patients undergoing noncardiac surgery. The largest of these trials, the PeriOperative ISchemic Evaluation (POISE) study, did show better perioperative *cardiac* outcomes with *β*-blocker use; however, *increased mortality* and stroke rate also was noted in the *β*-blocker group. ACC/AHA has conducted a systematic review on the topic, and the main findings are (1) preoperative use of *β*-blockers was associated with a reduction in cardiac events in the studies examined, but few data support the effectiveness of preoperative administration of *β*-blockers to reduce the risk of surgical death; and (2) a clear association exists between *β*-blocker administration and adverse outcomes, such as bradycardia and stroke. Currently, the only class I recommendation for perioperative *β*-blockers use is to continue their use in the patients who are already on *β*-blockers (class I, level of evidence B). *β*-Blockers can be used in patients with elevated risk, such as ischemia during preoperative stress testing or in patients with three or more RCRI risk factors (class IIb, level of evidence B). Although there are some differences between the ESC and the AHA guidelines, both recommend that if *β*-blockers are used for prophylactic purposes, they should be slowly titrated (2 to 7 days prior to elective surgery) and acute administration of high-dose *β*-blockers in high-risk patients undergoing low-risk surgery is not recommended (class III, level of evidence B).

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α_2-Adrenergic Agonist (Clonidine)

α_2-Agonist (clonidine) decrease sympathetic outflow, blood pressure, and heart rate. Although older studies suggested possible beneficial effect of α_2-agonists, the most recent POISE-2 trial that enrolled 10,010 patients did not show any statistically beneficial effect of clonidine. Clonidine did not reduce the rate of 30-day risk of all-cause death or nonfatal MI in patients with or at risk of atherosclerotic disease who were undergoing noncardiac surgery. Clonidine did increase the rate of nonfatal cardiac arrest and clinically important hypotension. Based on the ACC/AHA guidelines, α_2-agonists for prevention of cardiac events are not recommended in patients who are undergoing noncardiac surgery (class III, level of evidence B).

Nitrovasodilators (Nitroglycerin, Isosorbide Dinitrate)

Nitrates are associated with the following:

- Decreased LV preload (low dose)
  - Systemic venous dilation
  - Pulmonary arterial bed dilation
  - Pulmonary vein dilation
  - Decreased LV filling pressure
  - Decrease in LV diastolic compressive forces
  - Decreased LV diastolic chamber size
- Decreased LV afterload (high dose)
  - Decreased systolic pressure
  - Decreased systemic vascular resistance
  - Decreased aortic impedance
- Coronary circulation
  - Coronary artery and arteriolar dilation (high dose)
  - Spasm reversal or prevention
  - Stenosis dilation
  - Increased collateral flow
  - Improvement of regional subendocardial ischemia

NTG, one of the oldest antianginal therapies, has had very few trials in noncardiac surgery to evaluate its role in perioperative ischemia reduction. However, there are no significant studies within the past 10 years examining the effect of prophylactic NTG on perioperative myocardial ischemia. Prior studies yielded conflicting results, were small (<50 patients), and not blinded. The current guidelines do not recommend the use of prophylactic intravenous NTG to reduce myocardial ischemia undergoing noncardiac surgery.

Calcium Channel Blockers (Verapamil, Diltiazem, Nifedipine, Nicardipine)

Calcium channel blockers reduce myocardial oxygen demand by depression of myocardial contractility and dilation of coronary and collateral vessels, which improves blood flow. However, the most important effect may be the prevention of sympathetically mediated coronary vasoconstriction.

A meta-analysis of perioperative calcium channel blockers in noncardiac surgery (11 studies involving 1,007 patients) showed significantly reduced ischemia and postoperative supraventricular tachycardia. The beneficial effects were mostly due to the use of diltiazem, whereas the use of a 1,4-dihydropyridine (DHP) derivative nifedipine was associated with ischemia. Another study in 1,000 patients having acute or elective aortic aneurysm surgery showed that DHP calcium channel blocker use was independently associated with an increased incidence of perioperative mortality. The use of short-acting DHP, in particular nifedipine capsules, should be avoided. The AHA makes no specific recommendations for the prophylactic use of calcium channels blockers. Routine use of calcium channel blockers to reduce the risk of perioperative cardiovascular complications is not recommended (class III).

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Aspirin

Aspirin (acetylsalicylic acid) inhibits platelet aggregation by blocking the production of thromboxane A_2. Observational data suggest that preoperative withdrawal of aspirin increases thrombotic complications. However, the value of aspirin in nonstented patients in preventing

ischemic complications is uncertain. The Pulmonary Embolism Prevention (PEP) trial, which randomized 13,356 patients undergoing hip surgery to 160 mg aspirin or placebo, did not show benefit of aspirin. The POISE-2 trial randomized 10,010 patients who were undergoing noncardiac surgery to aspirin 200 mg or placebo. Aspirin did not have a protective effect for MACE or death in patients either continuing aspirin or starting aspirin. However, aspirin increased the chance of major bleeding especially in the first 5 days after surgery. This is supported by a previous large meta-analysis, including 41 studies in 49,590 patients, which compared periprocedural withdrawal versus bleeding risks of aspirin, concluded that the risk of bleeding complications was increased by 1.5, but that aspirin did not lead to higher severity levels of bleeding complications. Initiation of aspirin is not beneficial in patients undergoing elective noncardiac, noncarotid surgery who have not had previous coronary stenting, unless the risk of ischemic events outweighs the risk of surgical bleeding.

Statins

Statins are primarily used for their lipid-lowering effects and are widely prescribed in patients with or at risk for IHD. Statins also induce coronary plaque stabilization by decreasing lipid oxidation, inflammation, matrix metalloproteinase, and cell death. These so-called non-lipid or pleiotropic effects may prevent plaque rupture and subsequent MI in the perioperative period. A meta-analysis of 223,010 patients from 12 retrospective and 3 prospective trials showed that statins reduced mortality significantly by 44% in noncardiac surgery and by 59% in vascular surgery. The accumulated evidence to date suggests a protective effect of perioperative statin use on cardiac complications during noncardiac surgery. Most of the data come from observational studies. The time of initiation of statin therapy and the duration of therapy are often unclear in the observational trials. Randomized clinical trials are limited in patient numbers and types of noncardiac surgery. Both the AHA and ESC guidelines recommend continuing statin therapy for patients currently taking statins and scheduled for noncardiac surgery (class I). ESC recommends that preoperative statin therapy should be considered in patients undergoing vascular surgery and initiated at least 2 weeks before surgery.

Devereaux PJ, Mrkobrada M, Sessler DI, et al. Aspirin in patients undergoing noncardiac surgery. *N Engl J Med*. 2014;370(16):1494-1503.

Devereaux PJ, Sessler DI, Leslie K, et al. Clonidine in patients undergoing noncardiac surgery. *N Engl J Med*. 2014;370(16):1504-1513.

Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet*. 2008;371:1839-1847.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e77-e137.

Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2014;35:2383-2431.

Mangano DT, Layug EL, Wallace A, et al. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. *N Engl J Med*. 1996;335:1713-1720.

Poldermans D, Boersma E, Bax JJ, et al; for Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. *N Engl J Med*. 1999;341:1789-1794.

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Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: pulmonary embolism prevention (PEP) trial. *Lancet*. 2000;355:1295-1302.

Schouten O, Boersma E, Hoeks SE, et al. Fluvastatin and perioperative events in patients undergoing vascular surgery. *N Engl J Med*. 2009;361:980-989.

Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after noncardiac surgery. *Anesthesiology*. 2004;101:284-293.

A.7. Based on his MI, would you recommend that the surgery be postponed for a certain period of time? If so, why?

The arbitrary delaying of a surgical procedure is not supported by the ACC/AHA guidelines. According to these guidelines, an acute MI (≤7 days) or recent MI (>7 days but ≤1 month) with evidence of important ischemic risk by clinical symptoms or noninvasive study is a

major predictor of PMI. A discharge database analysis showed that patients with a recent MI who were revascularized before surgery had an approximately 50% decreased rate of reinfarction (5.1% vs. 10.0%). Thirty-day (5.2% vs. 11.3%) and 1-year mortality (18.3% vs. 35.8%) was also decreased in the revascularized patients. Current management of MI provides for risk stratification during the convalescence period. If a recent stress test does not indicate residual myocardium at risk, the likelihood of reinfarction after noncardiac surgery is low. Although there are no adequate clinical trials on which to base firm recommendations, it appears reasonable to wait 60 days after MI in a nonrevascularized patient to perform elective surgery due to the decrease in incidence of fatal arrhythmias and ventricular rupture after this period of time. However, the guidelines do not recommend that routine coronary revascularization be performed before noncardiac surgery exclusively to reduce perioperative cardiac events (class III, level of evidence B).

Devereaux PJ, Chan MT, Alonso-Coello P, et al. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *JAMA*. 2012;307:2295-2304.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:e278-e333.

A.8. Would you recommend that this elective colectomy be postponed, if the patient underwent placement of a right coronary artery, second-generation DES, and is taking aspirin and clopidogrel (Plavix)?

Coronary stents are particularly predisposed to stent thrombosis. Typically, stent thrombosis is defined according to the time of occurrence: (1) acute, within 24 hours; (2) early, 2 to 30 days; (3) late, >1 month to <1 year; and (4) very late, >1 year. Both bare metal stents (BMS) and DES are predisposed to stent thrombosis and require prolonged DAPT after stent placement: BMS, 4 to 6 weeks; DES, 12 months; and stents placed after acute coronary syndrome (ACS), 12 months. Second-generation DESs may require a minimum of 6 months DAPT after stent placement; however, data in this area is still evolving.

The cumulative incidence of noncardiac surgery after coronary stenting is more than 10% at 1 year and more than 20% at 2 years. Patients with a coronary stent pose a special challenge in the perioperative period. Bleeding is the major risk of continuing DAPT during the perioperative period. Surgical blood loss is increased 2.5% to 20% by aspirin alone and 30% to 50% by aspirin and clopidogrel—but with no increased risk of bleeding-related mortality, except during intracranial surgery. When surgery was performed within 180 days, discontinuation of DAPT was associated with an increased risk of stent thrombosis. Extremely high mortality rates (up to 20%) have been reported secondary to acute stent thrombosis if surgery is performed within weeks after coronary stenting with discontinuation of DAPT. Thus, the risks of stent thrombosis and bleeding should be balanced. Antiplatelet therapy should generally be continued throughout the perioperative period, except in cases where the risk of morbidity or mortality from bleeding significantly outweighs the risk of acute stent thrombosis, as in procedures likely to be associated with “major” blood loss or performed in a closed space.

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Current recommendations for DAPT after percutaneous coronary intervention (PCI) with stenting (BMS) is that patients should take aspirin and other $P2Y_{12}$ platelet inhibitor (clopidogrel, prasugrel, ticagrelor) for at least 30 to 45 days to prevent restenosis and allow reendothelialization of the stent to be completed. Therefore, it is prudent to postpone the elective surgery for a minimum of 30 days and ideally for up to 3 months after BMS implantation (ESC guidelines). Importantly, whenever possible, aspirin should be continued throughout surgery. A large meta-analysis, including 41 studies in 49,590 patients, which compared periprocedural withdrawal versus bleeding risks of aspirin, concluded that the risk of bleeding complications with aspirin therapy was increased by 50%, but that aspirin did not lead to greater severity of bleeding complications. In subjects at risk of—or with proven—IHD, nonadherence/withdrawal of aspirin tripled the risk of MACE.

Although DES delays in-stent thrombosis, their major drawback is the need for prolonged DAPT by aspirin and $P2Y1_2$ platelet inhibitors for at least 12 months. It is generally

recommended that after DES implantation, elective surgery should not take place until after at least 12 months of continuous DAPT. Even after 12 months, patients should be sent for noncardiac surgery with continuation of at least aspirin therapy. If the risk of surgical delay is greater than risk of thrombosis, in view of recent data that second-generation DES may require 6 months of DAPT, the guidelines suggest to proceed with surgery on aspirin (unless patient is scheduled for surgery associated with high risk of bleeding or consequence of bleeding). Typically, $P2Y_{12}$ platelet inhibitors should be stopped 5 days (clopidogrel, ticagrelor) or 7 days (prasugrel) before scheduled surgery and restarted as soon as possible.

In this patient, with a DES placed 5 months before surgery in the setting of acute coronary syndrome, the discontinuation of DAPT increases the risk of stent thrombosis appreciably. Furthermore, this is not high-risk surgery (laparoscopic colectomy), although risk of bleeding will be appreciably increased if patient is maintained on DAPT. This is a clinical situation where careful “case-by-case” consideration is advisable and discussion between the anesthesiologist, the surgeon, and the treating cardiologist is recommended.

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Culkin DJ, Exaire EJ, Green D, et al. Anticoagulation and antiplatelet therapy in urological practice: ICUD/AUA review paper. *J Urol*. 2014;192:1026-1034.

Darvish-Kazem S, Gandhi M, Marcucci M, et al. Perioperative management of antiplatelet therapy in patients with a coronary stent who need noncardiac surgery: a systematic review of clinical practice guidelines. *Chest*. 2013;144(6):1848-1856.

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Hawn MT, Graham LA, Richman JS, et al. Risk of major adverse cardiac events following noncardiac surgery in patients with coronary stents. *JAMA*. 2013;310(14):1462-1472.

Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur J Anaesthesiol*. 2014;35:2383-2431.

Oprea AD, Popescu WM. Perioperative management of antiplatelet therapy. *Br J Anaesth*. 2013;111(suppl 1):i3-i17.

Stefanini GG, Holmes DR Jr. Drug-eluting coronary-artery stents. *N Engl J Med*. 2013;368(3):254-265.

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how can we hit a moving target? *BMC Anesthesiol*. 2014;14:73.

Vetter TR, Short RT III, Hawn MT, et al. Perioperative management of the patient with a coronary artery stent. *Anesthesiology*. 2014;121(5):1093-1098.

Wolf AM, Pucci MJ, Gabale SD, et al. Safety of perioperative aspirin therapy in pancreatic operations. *Surgery*. 2014;155(1):39-46.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient's cardiac condition? What laboratory tests would you like to order?

The initial history, physical examination, and electrocardiographic assessment should focus on the identification of potentially serious cardiac disorders such as CAD (e.g., prior MI, angina pectoris), CHF, and symptomatic arrhythmias and valvular heart disease. In addition to identifying the presence of preexisting heart disease, it is essential to define disease severity, stability, and prior treatment. For patients who have been revascularized, it is also important to determine the presence or absence of any coronary syndrome/symptoms after coronary revascularization and any results of stress test results post-MI/revascularization. The initial history should also elicit presence of other components of RCRI, that is, history of cerebrovascular accident (stroke or transient ischemic attack), presence of diabetes, or renal insufficiency.

This patient is an insulin-dependent diabetic. Diabetes is associated with a twofold to fourfold increase in the risk of developing CAD. The risk of an MI in patients with diabetes and no evidence of CAD match that of patients without diabetes who have had a previous MI.

In patients with CAD and diabetes, the mortality rate can be up to 70% in 10 years. In addition, patients will have a worse outcome for any CAD manifestation.

Other factors that help determine cardiac risk include functional capacity, age, comorbid conditions (peripheral vascular disease, chronic pulmonary disease, and pulmonary hypertension), and type of surgery (vascular procedures and prolonged, complicated thoracic, abdominal, and head and neck procedures are considered elevated risk procedures) (see section B.3). Poor exercise tolerance has been associated by some with twofold higher odds for postoperative complications. It is a good indicator of global cardiopulmonary functional status of the patient, which can have direct impact on perioperative outcomes.

For this patient, the preoperative laboratory workup should include a hemoglobin/hematocrit (Hgb/Hct), prothrombin time, partial thromboplastin time, electrolytes, creatinine, blood urea nitrogen, and an ECG. The preoperative ECG may provide a useful baseline standard against which to measure changes in the postoperative period. The value of the preoperative 12-lead ECG is likely to increase with the risk of the surgical procedure, particularly for patients with known coronary heart disease, arrhythmias, peripheral arterial disease, cerebrovascular disease, or other significant structural heart disease.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e77-e137.

B.2. Would you recommend further cardiac testing or coronary revascularization before surgery?

Successful perioperative evaluation and treatment of cardiac patients undergoing noncardiac surgery requires careful teamwork and communication between patient, primary care physician, cardiologist, anesthesiologist, and surgeon. In general, indications for further cardiac testing and treatment are the same as those in the nonoperative setting, but their timing is dependent on factors such as the urgency of noncardiac surgery, the patient's risk factors, and specific surgical considerations. Preoperative testing should be limited to circumstances in which the results will affect patient treatment and outcomes. A conservative approach to the use of expensive tests and treatments is recommended. Coronary revascularization before noncardiac surgery to enable the patient to “get through” the noncardiac procedure is inappropriate. However, in a high-risk subset of patients, such as those with left main or severe multivessel disease,

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severe AS, and ejection fraction less than 20%, revascularization or valve replacement may be indicated. Currently, there is overwhelming agreement that aggressive medical management to provide myocardial protection during the perioperative period is a very important element in the reduction of perioperative cardiovascular complications.

Several studies have suggested that a stepwise approach to the assessment of CAD is both efficacious and cost-effective. The patient sustained MI 5 months ago and was managed with a DES and is scheduled for hemicolectomy, which is considered an intermediate-risk procedure. If the patient has more than 4 metabolic equivalents (METs) of physical activity (e.g., washing dishes, climbing one flight of stairs with a bag of groceries, walking on level ground at 4 miles per hour) without chest pain or shortness of breath, if no new cardiac symptoms are present since the revascularization, and if the resting ECG showed no new changes compared to 5 months ago, the patient can undergo anesthesia and surgery without further testing. If any of these factors are positive, then stress test is recommended. If the ischemic area is small, surgery is permissible with recommended aggressive medical therapy management. If the ischemic area is moderate to large, with a suspicion of new or severe coronary stenosis, cardiac catheterization is recommended before the planned surgery. Also see Chapter 10, section B.2, Figure 10.3.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e77-e137.

McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. *N Engl J Med*. 2004;351:2795-2804.

B.3. How would you classify the cardiac risk according to the type of surgery?

Surgery-specific cardiac risk of noncardiac surgery is related to two important factors: the type of surgery and the degree of hemodynamic stress associated with the procedure(s). The duration and intensity of coronary and myocardial stressors can be helpful in estimating the likelihood of perioperative cardiac events, particularly for emergency surgery. Surgeryspecific risk for noncardiac surgery can be stratified as high, intermediate, and low.

- *High-risk* surgery (cardiac risk >5%) includes major emergency surgery, particularly in the elderly; aortic and other major vascular surgery; peripheral vascular surgery; and anticipated prolonged procedures associated with large fluid shifts and/or blood loss.
- *Intermediate-risk* (cardiac risk <5%) procedures include carotid endarterectomy, head and neck surgery, intraperitoneal and intrathoracic, orthopedic, and prostate surgery. Endovascular aortic stent procedures also are included in this category.
- *Low-risk* (cardiac risk <1%) procedures include endoscopic and superficial procedures, cataract surgery, and breast surgery.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e77-e137.

B.4. What is the role of exercise or pharmacologic stress test for this patient?

The aim of functional cardiovascular testing is to elicit evidence and severity of CAD by subjecting the heart to physiologic stress. Noninvasive diagnostic testing must be used judiciously. Ideally, testing should be accurate, add useful information to the overall risk assessment, and avoid unnecessary delays in surgery. Noninvasive tests of myocardial perfusion are classified by the type of stress applied to elicit transient and reversible ischemia or by the mode of detecting the ischemic area. Myocardial stress can be induced by exercise (e.g., treadmill), by a pharmacologic agent that increases heart rate and myocardial contraction (e.g., dobutamine, atropine), or by a pharmacologic agent that can cause redistribution of coronary blood flow (e.g., dipyridamole). Physiologic exercise provides an estimate of functional capacity, provides blood pressure and heart rate response, and detects myocardial ischemia through ECG ST-segment or other imaging

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technique changes. The accuracy of exercise ECG varies significantly among studies. Preexisting ST-segment abnormalities at rest, especially in precordial leads V_5 and V_6, hamper reliable ST-segment analysis. However, most of these studies are dated and do not reflect the current protocols and contemporary practice. Meta-analysis of studies using treadmill testing in vascular surgery patients showed a rather low sensitivity (74%) and specificity (69%) to detect myocardium at risk, comparable with daily clinical practice.

A significant fraction of the high-risk population cannot exercise to an adequate level and will require pharmacologic stress testing. Pharmacologic stress testing with dobutamine stress echocardiography (DSE), dipyridamole/adenosine/regadenoson myocardial perfusion imaging with thallium-201, and/or technetium-99m and rubidium-82 can be used in patients undergoing noncardiac surgery who cannot perform exercise to detect stress-induced myocardial ischemia and CAD. Reversible wall motion abnormalities on echocardiography, or reversible perfusion defects on radionuclide imaging suggest reversible ischemia.

The myocardial perfusion imaging and DSE before vascular surgery predict PMI or death, with a positive predictive value of only 12% to 14% and a negative predictive value of 88% and 94%, respectively. However, the large majority of the cited thallium studies involved older planar imaging technology that is no longer used. The newer nuclear imaging studies have higher sensitivity for detecting IHD, and patients with normal scans have excellent prognosis. Cardiovascular magnetic resonance (CMR) imaging can also be used for detection of myocardial ischemia. Although its accuracy in assessment of myocardial ischemia is high, there is practically no data in the setting of preoperative risk stratification. Computed tomography can be used to detect coronary calcium, which reflects coronary atherosclerosis; however, currently, there is no data available in the setting of preoperative risk stratification.

Selection of the noninvasive stress test should be based primarily on patient characteristics, local availability, and expertise in interpretation. DSE is the preferred test if there is an additional question regarding valvular function or LV dysfunction.

Akhtar S. Ischemic heart disease. In: Hines RL, Marshall K, eds. *Stoelting's Anesthesia and Co-existing Diseases*. 6th ed. Philadelphia, PA: Elsevier; 2012:1-30.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e77-e137.

B.5. Would you discontinue any medication before surgery?

Patients with CAD are usually on a variety of medications. All antianginal drugs, especially *β*-blockers and statins, should be continued up to the time of surgery. Sudden withdrawal of antianginal drugs may produce rebound tachycardia and hypertension that may precipitate acute myocardial ischemia or infarction.

Current management of hypertensive patients suggests the continuation of antihypertensive therapy up to the day of surgery. In particular, *β*-blockers, calcium channel blocker, and nitrates should be continued. There is continued controversy about withholding angiotensinconverting enzyme (ACE) inhibitors and angiotensin-2 receptor blockers (ARBs) 24 hours prior to surgery. Prolonged hypotension has been observed in patients who are undergoing general anesthesia and who have chronically been treated with ACE inhibitors. A meta-analysis demonstrated hypotension in 50% of patients taking ACE inhibitors or ARBs on the day of surgery but no change in cardiovascular outcomes such as death, MI, stroke, and renal failure. It is prudent to withhold ACE inhibitors and ARBs for 24 hours prior to surgical procedures involving major body fluid shifts on significant blood loss. If ACE inhibitors are withheld, it is important to restart them as soon as possible. Hypotension attributed to ACE inhibitors is frequently responsive to fluid and/or administration of sympathomimetic drugs, such as phenylephrine and ephedrine. If hypotension is refractory to these measures, treatment with vasopressin or its long-acting analogue, terlipressin, may be effective.

Bertrand M, Godet G, Meersschaert K, et al. Should the angiotensin II antagonists be discontinued before surgery? *Anesth Analg*. 2001;92:26-30.

Rosenman DJ, McDonald FS, Ebbert JO, et al. Clinical consequences of withholding versus administering renin-angiotensin-aldosterone system antagonists in the preoperative period. *J Hosp Med*. 2008;3:319-325.

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Turan A, You J, Shiba A, et al. Angiotensin converting enzyme inhibitors are not associated with respiratory complications or mortality after noncardiac surgery. *Anesth Analg*. 2012;114:552-560.

B.6. How would you premedicate this patient?

The classical teaching has been to adequately sedate the patient prior to bringing to the operating room to avoid anxiety-induced tachycardia and hypertension. Benzodiazepines are typically used for this purpose. However, benzodiazepines have been associated with delirium, especially in elderly patients. Indiscriminate use of benzodiazepines is discouraged and should only be used in selected patients.

Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med*. 2013;41(1):263-306.

Maurice-Szamburski A, Auquier P, Viarre-Oreal V, et al. Effect of sedative premedication on patient experience after general anesthesia: a randomized clinical trial. *JAMA*. 2015;313(9):916-925.

B.7. Is there a role for α2-agonist in premedication?

The α_2-agonists stimulate prejunctional α receptors and decrease norepinephrine release from prejunctional terminals, thereby decreasing noradrenergic central nervous system transmission, producing sedation, anxiolysis, and analgesia. Studies have shown that clonidine as a premedication reduces hypertension, tachycardia, and norepinephrine levels in patients undergoing aortic reconstruction. Clonidine also suppresses the normal postoperative increase in fibrinogen levels and antagonizes epinephrine-induced platelet aggregation. It has also been shown to decrease intraoperative myocardial ischemia. A small study evaluating the prophylactic use of

clonidine showed a significant reduction in intra- and postoperative myocardial ischemia when compared to placebo. However, a much larger POISE-2 trial did not show any difference in rate of death or nonfatal MI. The rate of nonfatal cardiac arrest and significant hypotension was increased in the clonidine group. Both ACC and ESC guidelines do not advocate prophylactic use of clonidine to decrease MACE, in patients scheduled for noncardiac surgery.

Devereaux PJ, Sessler DI, Leslie K, et al. Clonidine in patients undergoing noncardiac surgery. *N Engl J Med*. 2014;370(16):1504-1513.

Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2014;35:2383-2431.

Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after non-cardiac surgery. *Anesthesiology*. 2004;101:284-293.

C. Intraoperative Management

C.1. What are the intraoperative predictors for perioperative MACE?

Intraoperative Predictors

Classic intraoperative predictors for perioperative MACE include emergency surgery, major vascular surgery, and prolonged (>3 hours) thoracic or upper abdominal surgery. Among the dynamic predictors, both hypotension and tachycardia predict PCM. In a recent systematic review, the intraoperative predictors include a fall in mean arterial blood pressure >20 mm Hg for >60 minutes, an increase in baseline systolic pressure >30%, or tachycardia in the recovery room (>30 beats per minute from baseline) for >5 minutes. However, the most consistent factor that independently predicted greater risk of perioperative event was intraoperative blood transfusion. Most MIs occur early after surgery and are commonly associated with ST-segment depression. Prolonged duration of myocardial ischemia (>20 to 30 minutes or

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cumulative duration of >1 to 2 hours) seems to be the important factor associated with adverse cardiac outcome.

Biccard BM, Rodseth RN. What evidence is there for intraoperative predictors of perioperative cardiac outcomes? A systematic review. *Perioper Med (Lond)*. 2013;2:14.

Grocott MP, Dushianthan A, Hamilton MA, et al. Perioperative increase in global blood flow to explicit defined goals and outcomes following surgery. *Cochrane Database Syst Rev*. 2012;(11):CD004082.

Kheterpal S, O'Reilly M, Englesbe MJ, et al. Preoperative and intraoperative predictors of cardiac adverse events after general, vascular, and urological surgery. *Anesthesiology*. 2009;110(1):58-66.

Priebe HJ. Perioperative myocardial infarction—aetiology and prevention. *Br J Anaesth*. 2005;95:3-19.

Sprung J, Abdelmalak B, Gottlieb A, et al. Analysis of risk factors for myocardial infarction and cardiac mortality after major vascular surgery. *Anesthesiology*. 2000;93(1):129-140.

C.2. How would you monitor the patient in the operating room?

The patient should be monitored using the following American Society of Anesthesiologists standard guidelines:

- *ECG*—simultaneous leads V_5 and II
- *Blood pressure*—noninvasive automatic Doppler sphygmomanometer and an invasive arterial catheter
- *End-tidal carbon dioxide*—to determine continuous end-tidal CO_2 analysis
- *Oxygen saturation of arterial blood*—to assess arterial oxygenation
- *Fractional inspired oxygen concentration*—to determine inspired fraction of oxygen
- *Respiratory rate*—which determined by multiple monitors
- *Availability of esophageal/bladder temperature probe*— to determine temperature changes

In addition to these monitors, this patient will also require the monitoring of urine output with a Foley catheter.

American Society of Anesthesiologists. *Standards for Basic Anesthetic Monitoring*. Schaumburg, IL: American Society of Anesthesiologists; 2005.

C.3. What electrocardiogram (ECG) leads would you monitor? Why V_5?

ECG ST-segment changes are most commonly used for detection of intraoperative myocardial ischemia. Multiple-lead ECG monitoring provides the best clinically available method of detecting perioperative ischemia, primarily by combining leads II, V_3, V_4, and V_5 (detection of ischemia is 80% with leads II/V_5 and 96% with leads II/V_4 and V_5).

Landesberg et al. were able to correlate the duration of ischemia observed in the STsegment analysis of a continuously monitoring 12-lead ECG throughout the perioperative period with the incidence of postoperative MI. They also found that ischemia is transient even in patients who will develop an infarct.

Certain prerequisites must be met to use the ECG effectively:

- The diagnostic mode allows detection of ST-segment changes that are filtered out by the monitoring mode.
- The number of ECG leads and their location affects detection of ischemic events.
- Immediate availability of a hard copy of the ECG leads for more detailed analysis.
- Studies have reported that even trained observers recognize only 15% to 40% of electrocardiographic ischemic events displayed on the monitor.

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- The introduction of ST-segment trending helps as an early warning detection system but should not replace examination of the ECG printout.

Landesberg G, Beattie WS, Mosseri M, et al. Perioperative myocardial infarction. *Circulation*. 2009;119:2936-2944.

Landesberg G, Mosseri M, Wolf Y, et al. Perioperative myocardial ischemia and infarction: identification by continuous 12-lead electrocardiogram with online ST-segment monitoring. *Anesthesiology*. 2002;96:264-270.

London MJ, Hollenberg M, Wong MG, et al. Intraoperative myocardial ischemia: localization by continuous 12-lead electrocardiography. *Anesthesiology*. 1988;69:232-241.

C.4. Would you use a pulmonary artery catheter (PAC)?

Right heart catheterization is not recommended for monitoring patients for intraoperative ischemia. Large observational study and a randomized multicenter trial did not show benefit associated with the use of right heart catheterization after major noncardiac surgery. A meta-analysis of randomized controlled trials showed that the use of PAC neither increased mortality nor conferred any benefits to critically ill patients. A recent Cochrane review that included 13 studies (5,686 patients) concluded that use of a PAC did not alter the mortality and general intensive care unit (ICU) or hospital length of stay. PAC is a diagnostic and hemodynamic monitoring tool but not a therapeutic intervention. A number of studies report that PAC is an insensitive monitor for myocardial ischemia and should not be inserted with this as a primary indication.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e77-e137.

Rajaram SS, Desai NK, Kalra A, et al. Pulmonary artery catheters for adult patients in intensive care. *Cochrane Database Syst Rev*. 2013;(2):CD003408.

C.5. Would you use transesophageal echocardiography (TEE) as a monitor?

TEE is a very sensitive diagnostic method of new onset myocardial ischemia. The echocardiographic diagnosis of myocardial ischemia is based on the development of new regional wall motion abnormalities, decreased systolic wall thickening, and ventricular dilation. Usually, a cross-sectional view (transgastric mid-short axis) of the LV is imaged because this view displays the myocardial perfusion territories of the three major coronary arteries. TEE was found to be twice as predictive as ECG in identifying coronary artery bypass graft (CABG) patients who have an MI. In CABG patients, postbypass regional wall motion abnormalities were related to adverse clinical outcome.

However, practitioners should realize certain limitations of TEE. One, preintubation events are missed, as are the ischemic events that can occur frequently at the end of the surgery, when tachycardia and hypertension appear as part of the emergence from general anesthesia.

Notwithstanding TEE's limitations, ESC and the AHA guidelines recommend the use of TEE intraoperatively or perioperatively to determine the cause of an acute, persistent, and life-threatening hemodynamic abnormality (class IIa recommendation). However, its use as an ischemia monitor in noncardiac surgery is less validated and may only be considered in patients at high risk for developing myocardial ischemia who undergo major noncardiac surgery (class IIb recommendation by ESC). The routine use of intraoperative TEE during noncardiac surgery to screen for cardiac abnormalities or to monitor for myocardial ischemia is *not* recommended in patients without risk factors, or procedural risks for significant hemodynamic, pulmonary, or neurologic compromise.

American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Practice guidelines for perioperative transesophageal echocardiography. An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on transesophageal echocardiography. *Anesthesiology*. 2010;112(5):1084-1096.

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Porter TR, Shillcutt SK, Adams MS, et al. Guidelines for the use of echocardiography as a monitor for therapeutic intervention in adults: a report from the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2015;28(1):40-56.

C.6. Is regional anesthesia better than general anesthesia for patients with cardiac disease?

A number of studies in patients with cardiac disease have compared the effects of regional versus general anesthetics on the incidence of perioperative infarction, dysrhythmias, and CHF. No distinct advantage is apparent between them when considering PCM and mortality in patients undergoing peripheral vascular surgery. There is some evidence to support regional anesthesia over general anesthesia in an effort to optimize graft patency if the regional technique is extended into the postoperative period to provide neuraxial analgesia. The Multicenter Australian Study of Epidural Anesthesia (MASTER) trial randomized 915 patients undergoing major abdominal surgery to receive either combined general and epidural anesthesia/epidural analgesia or general anesthesia with opioid analgesia. Epidural anesthesia/analgesia did not decrease death or cardiovascular outcomes but modestly improved pulmonary outcomes compared with the general anesthesia group. A retrospective analysis, published in 2013, of nearly 400,000 patients undergoing total hip or knee arthroplasty, observed a significantly lower incidence of major morbidity and mortality in patients receiving neuraxial anesthesia. The most recent meta-analysis stated that, when epidurals or spinals were used to replace general anesthesia, there was a significant 29% decrease in the risk of dying during surgery. In both situations, there was a significant decrease in the risk of pneumonia. However, neuraxial anesthesia failed to decrease the risk of MI. A 2011 Cochrane review meta-analysis of four studies examining neuraxial anesthesia versus general anesthesia for lower limb revascularization found an overall 4% MI rate in both groups. Thus, the current guidelines recommends that the choice of anesthesia is best left to the discretion of the anesthesia care team, which will consider the need for postoperative ventilation; pulmonary/neuromuscular comorbidities; cardiovascular effects, including myocardial depression; sympathetic blockade consequences; and dermatomal level of the procedure.

Barbosa FT, Jucá MJ, Castro AA, et al. Neuraxial anaesthesia for lower-limb revascularization. *Cochrane Database Syst Rev*. 2013;(7):CD007083.

Gogarten W, Vandermeulen E, Van Aken H, et al. Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. *Eur J Anaesthesiol*. 2010;27:999-1015.

Leslie K, Myles P, Devereaux P, et al. Neuraxial block, death and serious cardiovascular morbidity in the POISE trial. *Br J Anaesth*. 2013;111:382-390.

Mauermann WJ, Shilling AM, Zuo Z. A comparison of neuraxial block versus general anesthesia for elective total hip replacement: a meta-analysis. *Anesth Analg*. 2006;103:1018-1025.

Memtsoudis SG, Sun X, Chiu YL, et al. Perioperative comparative effectiveness of anesthetic technique in orthopedic patients. *Anesthesiology*. 2013;118:1046-1058.

Norris EJ, Beattie C, Perler BA, et al. Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. *Anesthesiology*. 2001;95:1054-1067.

C.7. How will you induce general anesthesia?

It is essential to prevent hypotension, hypertension, and tachycardia, which can precipitate myocardial ischemia. Different induction techniques may be employed to achieve this goal. For example, while the patient is being preoxygenated, fentanyl (up to 5 μg per kg) is given slowly to achieve drowsiness and to attenuate the sympathetic response to direct laryngoscopy and intubation of the trachea. Then, using lower doses of thiopental, propofol, or etomidate, unconsciousness is achieved. Succinylcholine or an intermediate duration nondepolarizing relaxant is administered to

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facilitate tracheal intubation. A few minutes before intubation, the use of a short-acting β-blocker (esmolol) could help to further attenuate the sympathetic response to intubation if necessary. Various techniques to induce general anesthesia have been used and tested in the past. High-dose opioid-based anesthesia was previously popularized because of cardiovascular stability; however, because of the need for prolonged postoperative mechanical ventilation and ICU stay, this technique is no longer considered the technique of choice. On the other hand, in patients undergoing cardiac surgery, volatile anesthetics have been shown to decrease troponin release, enhance LV function compared with propofol, midazolam, or balanced anesthesia technique with opioids. However, no real difference between volatile inhalational anesthesia versus intravenous anesthesia has been shown in randomized controlled trials or meta-analyses. A meta-analysis of more than 6,000 patients undergoing noncardiac surgery failed to demonstrate a difference in MI rates between patients who received volatile anesthesia and patients who received total intravenous anesthesia. The current AHA guidelines state that "use of either a volatile anesthetic agent or total intravenous anesthesia is reasonable for patients undergoing noncardiac surgery, and the choice is determined by factors other than the prevention of myocardial ischemia and MI."

Bignami E, Greco T, Barile L, et al. The effect of isoflurane on survival and myocardial infarction: a metaanalysis of randomized controlled studies. *J Cardiothorac Vasc Anesth*. 2013;27:50-58.

Martin DE, Rosenberg H, Aukburg SJ, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesth Analg*. 1982;61:680-684.

C.8. Would you induce anesthesia with etomidate? Why?

Although etomidate has a negative inotropic effect on failing and nonfailing human heart muscle in doses that exceed the clinical dose, it appears to have a better hemodynamic profile than other commonly used induction agents, especially in the setting of coronary heart disease; with an induction dose of 0.2 to 0.3 mg per kg, there are minimal changes in heart rate, stroke volume, or cardiac output, and the blood pressure may decrease up to 15% because of decrease of systemic vascular resistance. Etomidate does suppress adrenocortical function, cause myoclonus, and prolong duration of seizure when used for electroconvulsive therapy.

Flood P, Rathmell JP, Shafer S. *Stoelting's Pharmacology and Physiology in Anesthetic Practice* . 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2015.

Haessler R, Madler C, Klasing S, et al. Propofol/fentanyl versus etomidate/fentanyl for the induction of anesthesia in patients with aortic insufficiency and coronary artery disease. *J Cardiothorac Vasc Anesth*. 1992;6:173-180.

Sprung J, Ogletree-Hughes ML, Moravec CS, et al. The effects of etomidate on the contractility of failing and nonfailing human heart muscle. *Anesth Analg*. 2000;91:68-75.

C.9. What is the best choice of anesthetic agents for maintenance of anesthesia? Why?

There appears to be no one best myocardial protective agent or technique. The knowledge of physiologic and pharmacologic effects of anesthetic agents in patients with cardiac disease will allow flexibility in their selection. The use of inhalation versus opioid anesthesia in patients with cardiac disease is still debated, although the cardiovascular effects of both techniques and the physiologic differences between them are well documented. However, most outcome studies have not demonstrated a difference between the techniques. Studies of more than 3,000 noncardiac surgical patients with CAD have concluded that anesthetic type does not affect outcome.

Inhalation anesthetics are thought to possess ischemic preconditioning properties. Most investigations of anesthetic ischemic preconditioning have been done in patients undergoing

cardiac surgery, but maybe there are potential beneficial effects in the high-risk cardiac patients undergoing noncardiac surgery as well. However, none of the trials to date were powered to evaluate MI or death as an outcome. The current consensus is that use of either a volatile anesthetic agent or total intravenous anesthesia is reasonable for patients undergoing noncardiac surgery.

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The use of nitrous oxide in patients with history of CAD has been questioned since the early 1990s, when animal and human studies showed the increase in peripheral vascular resistance, diastolic dysfunction, and subsequently myocardial ischemia. Badner et al. demonstrated the increase on homocysteine plasma levels of patients during carotid endarterectomy when nitrous oxide was administered and the correlation of those levels with increased incidence of myocardial ischemia. However, the Evaluation of Nitrous Oxide in the Gas Mixture for Anaesthesia (ENIGMA-II) trial, which enrolled 7,110 patients, showed that nitrous oxide did not increase the risk of death and cardiovascular complications or surgical site infection.

The objectives during maintenance are not dissimilar to any other patient: amnesia, unconsciousness, and analgesia. These goals are constrained by the hemodynamic effect of each agent in order to provide heart rate control, coronary pressure perfusion, and effects on LV function. The preferred anesthetic technique will be a balanced anesthetic approach: opioids, with low/moderate doses of volatile anesthetics and benzodiazepines.

Badner NH, Beattie WS, Freeman D, et al. Nitrous oxide-induced increased homocysteine concentrations are associated with increased postoperative myocardial ischemia in patients undergoing carotid endarterectomy. *Anesth Analg*. 2000;91(5):1073-1079.

Imberger G, Orr A, Thorlund K, et al. Does anaesthesia with nitrous oxide affect mortality or cardiovascular morbidity? A systematic review with meta-analysis and trial sequential analysis. *Br J Anaesth*. 2014;112(3):410-426.

Ko H, Kaye AD, Urman RD. Nitrous oxide and perioperative outcomes. *J Anesth*. 2014;28(3):420-428.

Leslie K, Myles P, Devereaux PJ, et al. Nitrous oxide and serious morbidity and mortality in the POISE trial. *Anesth Analg*. 2013;116(5):1034-1040.

Myles PS, Leslie K, Chan MT, et al. The safety of addition of nitrous oxide to general anaesthesia in atrisk patients having major non-cardiac surgery (ENIGMA-II): a randomised, single-blind trial. *Lancet*. 2014;384(9952):1446-1454.

Nigro Neto C, Landoni G, Cassarà L, et al. Use of volatile anesthetics during cardiopulmonary bypass: a systematic review of adverse events. *J Cardiothorac Vasc Anesth*. 2014;28:84-89.

Sanders RD, Graham C, Lewis SC, et al. Nitrous oxide exposure does not seem to be associated with increased mortality, stroke, and myocardial infarction: a non-randomized subgroup analysis of the General Anaesthesia compared with Local Anaesthesia for carotid surgery (GALA) trial. *Br J Anaesth*. 2012;109(3):361-367.

C.10. You notice a new 3-mm ST-segment depression in lead V_5. How would you treat it?

ST-segment depression can be an indicator of myocardial ischemia. Initial efforts should be focused on determining its etiology. Management of ischemia should include pharmacologic manipulation of the determinants of myocardial oxygen supply and demand.

The crucial aspect of such management includes the following:

- Heart rate control and adequate coronary perfusion pressure. If ST-segment depression is associated with tachycardia and hypertension, the most common cause during surgery is inadequate anesthesia. Therefore, adequate levels of anesthesia should be achieved first. Heart rate control can also be achieved by the use of β-blockers. Caution should be exerted in patients with known contraindications and hemodynamic instability. The calcium channel blockers are considered the drug of choice if coronary spasm is suspected.
- Avoidance of hypotension and use of vasopressors to sustain coronary perfusion pressure
- The use of nitrates is advocated as long as it does not compromise coronary perfusion pressure. Nitrates decrease myocardial oxygen demand by decreasing preload, intracavitary pressure, and myocardial wall tension. In addition, NTG increases the ratio of endocardial to epicardial blood flow.
- Oxygen delivery should be increased by correcting significant anemia (<7 g per dL) and increasing the fraction of

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inspired oxygen.

- Oxygen demand also could be reduced by correction of hypothermia and/or shivering, if present.
- Secondary therapies should consider the use, if feasible, of antiplatelet therapy such as aspirin.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e77-e137.

C.11. Would you give prophylactic intravenous NTG to prevent myocardial ischemia?

There are no randomized data that support the use of prophylactic intraoperative intravenous NTG in patients at high risk. NTG should be used only when ischemia is detected and the hemodynamic effects of other agents in use are considered.

Beattie WS. Evidence-based perioperative risk reduction. *Can J Anaesth*. 2005;52(suppl 1):R3.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e77-e137.

C.12. What is the significance of tight control of the heart rate intraoperatively?

Numerous studies have shown that intraoperative tachycardia and the duration of tachycardia could cause myocardial ischemia. Therefore, control of heart rate intraoperatively could significantly reduce the risk of perioperative myocardial events. It is clear that heart rate should be maintained to less than 100 beats per minute; however, the optimal heart rate for all patients has not been determined. Some recommend maintaining the heart rate between 60 to 70 beats per minute in high-risk patients. Slogoff et al. in the 1980s were able to correlate tachycardia with the occurrence of intraoperative myocardial ischemia. Raby et al. demonstrated that by identifying the high-risk patients, whose preoperative Holter tracing showed signs of ischemia, and controlling the heart rate 20% below the ischemia threshold or approximately 60 beats per minute with esmolol, during vascular surgeries could reduce the risk of perioperative myocardial ischemia. Feringa et al. demonstrated that tight heart rate control instead of just the use of β-blockers reduced perioperative myocardial ischemia and improved long-term outcome in vascular surgery patients.

Biccard BM, Sear JW, Foëx P. Meta-analysis of the effect of heart rate achieved by perioperative beta-adrenergic blockade on cardiovascular outcomes. *Br J Anaesth*. 2008;100:23-28.

Feringa H, Bax J, Boersma E, et al. High-dose beta-blockers and tight heart rate control reduce myocardial ischemia and troponin T release in vascular surgery patients. *Circulation*. 2006;114:344-349.

Landesberg G, Beattie WS, Mosseri M, et al. Perioperative myocardial infarction. *Circulation*. 2009;119:2936-2944.

Raby KE, Brull SJ, Timimi F, et al. The effect of heart rate control on myocardial ischemia among high-risk patients after vascular surgery. *Anesth Analg*. 1999;88:477-482.

Slogoff S, Keats AS. Myocardial ischemia revisited. *Anesthesiology*. 2006;105:214-216.

C.13. When would you extubate the trachea in this patient? What could you do to prevent hypertension and tachycardia during extubation and emergence?

At the end of surgery, assuming no intraoperative complications, the trachea would be extubated when the patient is fully

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awake, breathing adequately, and neuromuscular blockade is fully reversed. To prevent tachycardia and hypertension associated with extubation and emergence, low doses of medications such as 1 mg per kg of lidocaine or esmolol, or 0.015 to 0.03 mg per kg of nicardipine, or 0.1 mg per kg of labetalol or diltiazem, before emergence in order to reduce sympathetic response of emergence and extubation can be administered.

Atlee JL, Dhamee MS, Olund TL, et al. The use of esmolol, nicardipine, or their combination to blunt hemodynamic changes after laryngoscopy and tracheal intubation. *Anesth Analg*. 2000;90:280-285.

Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2014;35:2383-2431.

Mikawa K, Nishina K, Maekawa N, et al. Attenuation of cardiovascular responses to tracheal extubation: verapamil versus diltiazem. *Anesth Analg*. 1996;82:1205-1210.

D. Postoperative Management

D.1. What are the postoperative predictors of perioperative MACE?

In noncardiac surgical patient, the highest risk of cardiac morbidity is in the postoperative period. It is during this period where up to 67% of the ischemic events occur. This period is characterized by increase in heart rate, blood pressure, sympathetic discharge, and hypercoagulability. Heart rate commonly increases postoperatively by 25% to 50% over intraoperative values, and tachycardia occurs in 10% to 25% of patients. Postoperative myocardial ischemia occurs in 27% to 41% of high-risk patients. Most of these events (50% or higher) are silent (without angina). Postoperative MI is usually preceded by prolonged ST-segment depression. This change on ECG is easily missed if ECG is not continuously monitored because most of the changes will revert completely to baseline. However, routine continuous postoperative ECG monitoring is not recommended, and even routine daily ECG for 3 days is no longer advocated. In a study involving 337 vascular surgery patients in whom troponin I levels were collected within 48 hours of surgery and 12-lead ECGs were performed daily for 3 postoperative days, although 40% of the subjects had elevated troponin levels, only 6% of the patients had ischemic changes on the ECG. PMI may be associated with tachycardia and pain. Studies involving large numbers of patients suggest that postoperative ischemia is the most important marker of immediate and long-term adverse cardiovascular events. It is associated with a 2.8-fold increase in the odds of all adverse cardiac outcomes.

The highest incidence of troponin elevation, a biochemical marker of ischemia, frequently occurs 8 to 24 hours after the surgical procedure; even mild elevations are associated with postoperative cardiac ischemia and they could help to categorize the short- and long-term risk of the surgical patient as they are independent predictors of mortality. Postoperative MI has also been associated with other clinical conditions as postoperative hypothermia, hypercoagulability, postoperative pain, and anemia.

Akhtar S. Ischemic heart disease. In: Hines RL, Marshall K, eds. *Stoelting's Anesthesia and Co-existing Diseases*. 6th ed. Philadelphia, PA: Elsevier; 2012:1-30.

Garcia S, Marston N, Sandoval Y, et al. Prognostic value of 12-lead electrocardiogram and peak troponin I level after vascular surgery. *J Vasc Surg*. 2013;57:166-172.

Le Manach Y, Perel A, Coriat P, et al. Early and delayed myocardial infarction after abdominal aortic surgery. *Anesthesiology*. 2005;102:885-891.

Nagele P, Brown F, Gage BF, et al. High-sensitivity cardiac troponin T in prediction and diagnosis of myocardial infarction and long-term mortality after noncardiac surgery. *Am Heart J*. 2013;166(2):325-332.

D.2. How would you control postoperative pain?

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The postoperative period can be stressful due to the onset of pain during emergence from anesthesia, fluid shifts, temperature changes, and alteration of respiratory function. Marked changes occur in plasma catecholamine concentration, hemodynamics, ventricular function, and coagulation following noncardiac surgery, particularly in patients with preexisting cardiac disease. These stressors place the patient at increased risk for development of adverse cardiac outcome. Severe postoperative pain reported in 5% to 10% of patients. The effective pain management is essential to prevent adverse outcome and promote early recovery. Intravenous patient-controlled analgesia and/or patient-controlled epidural analgesia are popular methods for reducing postoperative pain. Several studies suggest that effective pain management leads to a reduction in postoperative catecholamine surges and hypercoagulability. A meta-analysis published in 2013, which analyzed the impact of epidural analgesia versus systemic analgesia, concluded that epidural analgesia was associated with a 40% decrease in mortality and a significant decrease in the risk of atrial fibrillation, supraventricular tachycardia, deep vein thrombosis, respiratory depression, atelectasis, pneumonia, ileus, and postoperative nausea and vomiting, and also improved recovery of bowel function. However, epidural analgesia also significantly increased the risk of arterial hypotension, pruritus, urinary retention, and motor blockade.

Norris EJ, Beattie C, Perler BA, et al. Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. *Anesthesiology*. 2001;95:1054-1067.

Pöpping DM, Elia N, Van Aken HK, et al. Impact of epidural analgesia on mortality and morbidity after surgery: systematic review and meta-analysis of randomized controlled trials. *Ann Surg*. 2014;259(6):1056-1067.

D.3. Is postoperative anemia associated with adverse cardiac outcome?

Patients with IHD may be adversely affected by anemia. Based on existing literature, the evidence is sufficient to state that transfusions are rarely beneficial if the Hgb level exceeds 10 g per dL (Hct >30%) in the absence of acute blood loss. It is also reasonable to state that the patient may benefit from a transfusion if the Hgb level falls below 7 g per dL. The controversy remains between Hgb concentrations of 8.0 to 10.0 g per dL. The 2012 American Association of Blood Banks Guideline, which is based on expert opinion and studies, recommends a restricted transfusion strategy (Hgb <7 to 8 g per dL) in asymptomatic, hemodynamically stable patients without CAD. The guideline also recommends adherence to a restrictive transfusion strategy in hospitalized patients with cardiovascular disease and consideration of transfusion for patients with symptoms (e.g., chest pain, orthostasis, CHF) or Hgb less than 8 g per dL. In postoperative patients, the recommended maintenance Hgb concentration is 8 g per dL or more, unless the patient exhibits symptoms. There were no specific recommendations for hemodynamically stable patients with ACS because of the lack of high-quality evidence for either a liberal or a restrictive transfusion strategy in these patients. The consensus of those experts recommended a symptom-guided approach to evaluating an Hgb level to determine whether to transfuse a patient with anemia.

Beattie WS, Karkouti K, Wijeysundera DN, et al. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. *Anesthesiology*. 2009;110:574-581.

Carson JL, Grossman BJ, Kleinman S, et al. Red blood cell transfusion: a clinical practice guideline from the AABB. *Ann Intern Med*. 2012;157(1):49-58.

Qaseem A, Humphrey LL, Fitterman N, et al. Treatment of anemia in patients with heart disease: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2013;159(11):770-779.

Simmons JW, Pittet JF. Revealing the real risks of perioperative transfusion: rise of the machines! *Anesthesiology*. 2015;122(1):1-2.

D.4. Is postoperative hypothermia associated with postoperative myocardial ischemia?

Hypothermia is common during anesthesia and surgery owing to anesthetic-induced inhibition of thermoregulatory control. The principal initial cause of hypothermia is core-toperipheral redistribution of body heat.

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Perioperative hypothermia is associated with numerous complications; it triples the incidence of adverse myocardial outcomes in high-risk patients, increases blood loss. Even mild hypothermia has been associated with an increased incidence of wound infection following colon resection. Also, it adversely affects oxygen availability in tissues, changes the kinetics and action of some anesthetic agents and muscle relaxants, and is associated with delayed postanesthetic recovery. It causes immune dysfunction and increased transfusion requirements.

Core hypothermia may increase circulating catecholamines levels, leading to tachycardia, hypertension, systemic vasoconstriction, and an imbalance between oxygen demand and supply. Frank et al. studied 100 patients undergoing lower extremity vascular surgery. They found that unintentional hypothermia (sublingual temperature less than 35°C [95°F]) on arrival to postoperative ICU is associated with a significantly higher incidence of myocardial ischemia (36% vs. 13%), angina (18% vs. 15%), and PaO_2 less than 80 mm Hg (52% vs. 30%) during the early postoperative period. However, a subsequent trial involving 1,000 patients with subarachnoid hemorrhage, which were randomized to perioperative hypothermia or normothermia, did not show a difference in perioperative cardiac events. Maintenance of normothermia may be reasonable to reduce perioperative cardiac events in patients undergoing noncardiac surgery.

Frank SM, Beattie C, Christopherson R, et al. Unintentional hypothermia is associated with postoperative myocardial ischemia. *Anesthesiology*. 1993;78:468-476.

Todd MM, Hindman BJ, Clarke WR, et al. Mild intraoperative hypothermia during surgery for intracranial aneurysm. *N Engl J Med*. 2005;352(2):135-145.

D.5. How would you make a diagnosis of perioperative myocardial infarction (PMI)?

The definition of MI, according to the third universal definition of MI, is based on elevation of biomarkers, in conjunction with cardiac symptoms, ECG changes, new echocardiographic changes, or angiographic findings of intracoronary thrombus.

Most ischemic episodes occur after and not during the operation. This is probably because of the high postoperative stresses related to anesthesia and surgery. Several studies have examined the optimal method for diagnosing a PMI. Most patients suffering from PMI do not complain of chest pain and the value of routine serial postoperative ECG is limited. Cardiacspecific enzyme elevations such as troponin I (cTnI) and troponin T (cTnT) are currently the standard of care for biochemical diagnosis of a PMI because they demonstrate sensitivity and tissue specificity superior to other available biomarkers.

In the purest physiologic sense, any detectable necrosis is an acute MI; however, troponin elevation can be observed in many other conditions in which the heart is stressed. Even small elevations of specific markers of myocardial damage, such as cardiac troponins, should be acknowledged as indicative of myocardial injury. This has been categorized as myocardial injury in the third universal definition of MI and includes myocardial injury related to demand (type II) and related to plaque rupture (type I). From a clinical perspective, there is clear evidence that any amount of detectable cardiac troponin release is associated with an increased risk of new adverse cardiac events. Many investigators agree that the increase in cardiac troponins postoperatively, even if no cardiovascular signs and symptoms are present, carries poor long-term outcome.

Clinicians need to be sensitive to redundancy in testing. Some authors have demonstrated that routine cardiac troponin monitoring is an easy, effective, and inexpensive way to detect postoperative myocardial injury. However, the ACC/AHA guidelines reserves the use of this biomarkers for patients at high risk and those with clinical, ECG, or hemodynamic evidence of cardiovascular dysfunction. Routine measurement of postoperative troponins in asymptomatic or low-risk patients undergoing low-risk procedure is not warranted.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e77-e137.

Landesberg G, Shatz V, Akopnik I, et al. Association of cardiac troponin, CK-MB, and postoperative myocardial ischemia with long-term survival after major vascular surgery. *J Am Coll Cardiol*. 2003;42:1547-1554.

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Lopez-Jimenez F, Goldman L, Sacks DB, et al. Prognostic value of cardiac troponin T after noncardiac surgery: 6-month follow-up data. *J Am Coll Cardiol*. 1997;29:1241-1245.

White HD, Thygesen K, Alpert JS, et al. Clinical implications of the Third Universal Definition of Myocardial Infarction. *Heart*. 2014;100(5):424-432.

D.6. How would you manage the patient with a suspected PMI?

There is lack of control evidence regarding management of PMI in the postsurgical patient. PMI could include three different clinical scenarios/diagnosis: unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI).

The initial management should focus on the following diagnosis:

- Evaluation of chest pain if present
- 12-Lead ECG and determination of changes, if present
- Measurement of biomarkers of cardiac injury. A cardiac-specific troponin is the preferred marker.
- Immediate consultation of a cardiologist and risk stratification to determine high-risk patients

It is important to consider the recent surgical procedure and consultation with the surgical team regarding impact of aspirin and anticoagulant therapy.

Unless a contraindication exists, patients with an ACS of the type UA or NSTEMI should be treated with oxygen, aspirin (acetylene salicylic acid), sublingual/intravenous NTG for chest pain relief, as long as blood pressure is adequate, a *β*-blocker, unfractionated heparin or low molecular weight heparin, and/or a glycoprotein (GP) IIb/IIIa inhibitor.

The cardiology consultant should guide further management:

- Option 1 is a routine angiographic approach, in which coronary angiography and revascularization are performed unless a contraindication exists. Within this approach, the most

  common strategy advocates for a period of medical stabilization. A more aggressive approach calls for coronary angiography and revascularization performed within 24 hours of the onset of symptoms or diagnosis; the rationale for the more aggressive approach is the protective effect of carefully administered anticoagulant and antiplatelet therapy on reperfusion procedures outcome.
- The alternative approach, commonly referred to as the initially conservative strategy, is guided by ischemia, with angiography reserved for patients with recurrent ischemia despite medical therapy.

Regardless of the angiographic strategy, an assessment of LV function (echocardiography, ventriculogram, or nuclear ventriculography) should be strongly considered because of the importance of treating patients who have impaired LV function with ACE inhibitors, *β*-blockers, and surgical revascularization (CABG) when appropriate (e.g., three-vessel disease).

If the patient presents with a STEMI, recognized on the basis of the 12-lead ECG, the management will be initially similar to UA/NSTEMI (oxygen, acetylene salicylic acid, NTG, *β*-blockers), then one should attempt to complete restoration of flow in the infarct artery by PCI (balloon angioplasty with or without deployment of an intracoronary stent under the support of pharmacologic measures to prevent thrombosis), or surgical measures (CABG).

Evidence supports expeditious restoration of flow in the obstructed infarct artery after the onset of symptoms in patients with STEMI as a key determinant of short- and long-term outcomes. Early reperfusion of ischemic myocardium within the risk region of an occluded infarct-related artery interrupts the occurring necrosis, reduces ultimate infarct size, preserves regional and global ventricular function, and improves survival. A subset of patients will have severe three-vessel or left main disease or anatomic features unfavorable for PCI and may be candidates for urgent or emergency CABG.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64:e77-e137.

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Chapter 15
Intestinal Obstruction

Joseph Tjan

A 73-year-old woman with an acute abdomen was scheduled to undergo an emergency exploratory laparotomy. She complained of severe abdominal pain with periodic bouts of bilious vomiting. Her past surgical history included a right hemicolectomy for colon cancer. She had a blood pressure of 85/60 mm Hg, pulse of 115 beats per minute, and hematocrit of 45%.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis of the acute abdomen?
2. What are the causes of intestinal obstruction of the small bowel and of the large bowel?
3. Differentiate between simple and strangulated bowel obstruction.
4. Is it important to differentiate whether the bowel obstruction is located in the small bowel or large bowel? Why?
5. What are the signs and symptoms of intestinal obstruction?
6. What are the causes and effects of bowel distention?
7. Describe the fluid shifts during small bowel intestinal obstruction.
8. Discuss the systemic derangements that occur with intestinal obstruction.
9. Can there be actual losses of red cell mass?
10. What is an ileus? Discuss its causes and treatment.
11. What are the systemic effects from the absorption of bacteria and bacterial products?

B. Preoperative Evaluation and Preparation

1. Is it important to decompress the abdomen before surgical intervention? Why?
2. Describe the respiratory implications.
3. What are the implications of the tense abdominal wall?
4. Outline the methods of abdominal decompression.
5. Discuss the goals of fluid management.
6. What would you use as a guide to fluid volume replacement?

C. Intraoperative Management

1. What dangers are present during induction? How are they planned for?
2. Does the administration of antacids and/or histamine-2 (H2) blockers before the induction of anesthesia have a significant value in patients with small bowel obstruction?

3. In what position would you intubate this patient?
4. Is succinylcholine the best muscle relaxant to use for the rapid sequence induction?
5. Would you remove or leave the nasogastric tube (NGT) in place before inducing anesthesia?
6. Would you use nitrous oxide in this patient?
7. Are there any benefits to using a high concentration of inspired oxygen?

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D. Postoperative Management

1. What are the principles of postoperative care in this patient?
2. Are there any postoperative respiratory problems associated with factors other than aspiration?
3. If the patient did aspirate gastric contents, what are the possible sequelae of this event? What is the treatment?
4. What is gram-negative sepsis? Describe the clinical picture and treatment.

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis of the acute abdomen?

Intestinal obstruction accounts for approximately 15% to 20% of hospitalized patients with an acute abdomen. Abdominal pain can be divided into three categories: visceral, somatic (parietal), and referred. Visceral pain is transmitted through the autonomic nervous system through C fibers located intramurally in hollow viscera and in the capsule of abdominal organs. Visceral pain is dull, crampy, or aching in nature, and the factors that produce it include stretching and distention that result in increased wall tension, inflammation, ischemia, torsion, compression, and certain chemicals. Transmission of somatic pain occurs through C and A-δ fibers of spinal nerves to produce pain that is characteristically sharp, severe, and persistent. Somatic pain is caused by irritation of the parietal peritoneum and arises as a response to acute changes in pH or temperature, as seen with bacterial or chemical inflammation. Referred pain is that which is felt in a region of the body different from the point of its origin because of the sharing of common pathways for afferent neurons arising from different sites.

A proper history and physical examination with early diagnosis is of utmost importance in the management of the patient with an acute abdomen. In a review of over 1,100 patients with abdominal pain who presented to the emergency room, the most common diagnosis overall was nonspecific abdominal pain. Appendicitis, intestinal obstruction, urologic disorders, and gallstones were the most common surgical causes in order of decreasing frequency. In 47% of the patients, surgical intervention was required. The gastrointestinal and intraperitoneal causes of abdominal pain are listed in Table 15.1. There are many extraperitoneal causes of abdominal pain, and these include pulmonary, cardiac, neurologic, metabolic, toxic, infectious, vascular, and hematologic conditions.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

A.2. What are the causes of intestinal obstruction of the small bowel and of the large bowel?

Intestinal obstruction can be of extraluminal (e.g., adhesions, hernias, or carcinomatosis), intraluminal (e.g., gallstones or foreign bodies), or intramural (e.g., Crohn disease or tumors) origin. The term *mechanical bowel obstruction* denotes an actual physical barrier that interferes with the normal progression of intestinal contents. The most common cause of small bowel obstruction is postoperative adhesions, followed by incarcerated hernias and malignant tumors. Postoperative adhesions make up approximately 75% of cases of small bowel obstruction. Alternatively, neoplasms account for most large bowel obstruction. Other causes of large bowel obstruction include diverticulitis and volvulus.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

TABLE 15.1 Gastrointestinal and Intraperitoneal Causes of Abdominal Pain

I. Inflammation/infection

A. Peritoneum

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1. Chemical and nonbacterial peritonitis— perforated peptic ulcer, gallbladder, ruptured ovarian cyst, mittelschmerz
2. Bacterial peritonitis
   a. Primary peritonitis—pneumococcal, streptococcal tuberculous
   b. Perforated hollow viscus—stomach, intestine, biliary tract

B. Hollow intestinal organs
1. Appendicitis
2. Cholecystitis
3. Peptic ulceration
4. Gastroenteritis
5. Regional enteritis
6. Meckel's diverticulitis
7. Colitis—ulcerative, bacterial, amebic
8. Diverticulitis

C. Solid viscera
1. Pancreatitis
2. Hepatitis
3. Hepatic abscess
4. Splenic abscess

D. Mesentery
1. Lymphadenitis

E. Pelvic organs
1. Pelvic inflammatory disease
2. Tuboovarian abscess
3. Endometritis

II. Mechanical (obstruction, acute distention)

A. Hollow intestinal organs
1. Intestinal obstruction—adhesions, hernia, tumor, volvulus, intussusception
2. Biliary obstruction—calculi, tumor, choledochal cyst, hematobilia

B. Solid viscera
1. Acute splenomegaly
2. Acute hepatomegaly—cardiac failure, Budd-Chiari syndrome

C. Mesentery
1. Omental torsion

D. Pelvic organs
1. Ovarian cyst
2. Torsion or degeneration of fibroid
3. Ectopic pregnancy

III. Vascular

A. Intraperitoneal bleeding
1. Ruptured liver
2. Ruptured spleen
3. Ruptured mesentery
4. Ruptured ectopic pregnancy
5. Ruptured aortic, splenic, or hepatic aneurysm

B. Ischemia
1. Mesenteric thrombosis
2. Hepatic infarction—toxemia, purpura
3. Splenic infarction
4. Omental ischemia

IV. Miscellaneous

A. Endometriosis

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From Schwartz SI, Shires GT, Spencer FC, et al, eds. *Principles of Surgery*. 7th ed. New York: McGraw-Hill; 1999:1036, with permission.

A.3. Differentiate between simple and strangulated bowel obstruction.

Simple obstruction occurs when the lumen is obstructed and the blood supply remains normal. Occlusion of the blood supply to the obstructed bowel results in a strangulated obstruction. Toxic fluid is discharged into the bowel lumen, bowel wall, and peritoneal cavity when venous outflow obstruction occurs. It is important to recognize strangulation preoperatively because the implications are more serious and the mortality rate is high at between 8% and 25%. Conversely, the mortality rate for nonstrangulating bowel obstruction is under 5%, mostly in the elderly. A closed-loop obstruction is present when both limbs of the loop are obstructed. This leads rapidly to strangulation, occasionally even before clinical evidence of intestinal obstruction appears.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 13th ed. New York: McGraw-Hill; 2010:451-463, 621-657.

A.4. Is it important to differentiate whether the bowel obstruction is located in the small bowel or large bowel? Why?

Yes. Simple mechanical obstruction of the small bowel results in altered bowel motility, bowel distention with progressive accumulation of fluid and gas, and systemic derangements. If the obstruction is not relieved promptly, strangulation ensues, leading to bowel necrosis and the

leakage of blood, fluid, and toxic substances into the bowel and peritoneal cavity. Approximately 60% to 80% of intestinal obstructions occur in the small bowel.

Although the signs and symptoms may be similar, large bowel obstruction is usually more insidious than small bowel obstruction. Except for a volvulus, large bowel obstruction has less of a propensity to strangulate. The colon is essentially a storage organ and has little secretory and absorptive functions. Therefore, systemic derangements are less severe with large bowel obstruction. The most important complication is progressive distention and rupture of the colon, especially in the presence of a competent ileocecal valve. The cecum is the usual site of rupture.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

A.5. What are the signs and symptoms of intestinal obstruction?

The four cardinal signs and symptoms of intestinal obstruction are crampy abdominal pain, nausea and vomiting, obstipation, and abdominal distention. Intestinal activity initially increases in an effort to overcome the obstruction, leading to colicky pain and diarrhea. The colicky pain often is diffuse and alternates with quiescent periods. The duration of the quiescent period depends on the site of intestinal obstruction. With a high obstruction, the duration is approximately 4 to 5 minutes, and with lower ileal obstruction, the duration is 15 to 20 minutes. Steady, severe abdominal pain usually indicates strangulation.

Vomiting commonly occurs immediately after the onset of bowel obstruction, followed by a variable quiescent period before recurrence. Vomiting becomes more frequent and bilious the higher the level of obstruction, and with the exception of a volvulus, it is uncommon in colonic obstruction. Abdominal distention is a late finding that may be absent in high small bowel obstruction that is associated with frequent bouts of emesis. Other signs of intestinal obstruction include localized tenderness, fever, tachycardia, and leukocytosis. White blood cell counts of 15,000 to 25,000 per μL is strongly suggestive

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of strangulation, but this is not a sensitive test because 40% of patients with strangulation have normal white blood cell counts. The presence of acidosis also will increase the likelihood of strangulation. With the development of dehydration, serum chemistries will change, hemoconcentration occurs, and urine output will diminish and become concentrated.

A partial bowel obstruction is more likely to be present if the patient is able to pass stool and/or gas 6 to 12 hours after the onset of symptoms.

The most important initial diagnostic procedures are plain x-ray films of the abdomen in the supine and upright positions with upright and lateral chest x-ray films. In intestinal obstruction, gas-fluid levels are seen on the radiographs. Although normal within the stomach and colon, intestinal gas is usually minimal and infrequent in the small bowel. Therefore, gas-fluid levels are indicative of obstruction but also may be seen in gastroenteritis, severe constipation, sprue, and severe aerophagia. The radiologic findings and those features that differentiate simple mechanical obstruction from an ileus are summarized in Table 15.2.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

A.6. What are the causes and effects of bowel distention?

Intestinal obstruction results in the sequestration of fluid and gas within the bowel lumen proximal to the site of obstruction. Accumulation of fluid accounts for most of the bowel distention. As intraluminal pressure increases, the secretory function of the bowel increases progressively. Prostaglandin release seems to mediate this hypersecretion of fluid. In addition, reabsorption is impaired once intraluminal pressure exceeds 20 cm H2O. The basic composition of the intestinal gas is that of swallowed air. As bowel distention continues from the ongoing gas and fluid accumulation, intraluminal and intramural pressures rise. The increased

intramural pressures lead to progressive interference with the mesenteric blood supply, resulting in a strangulated obstruction with its associated morbidity and mortality.

TABLE 15.2 Radiologic Signs in Intestinal Obstruction

SIGN	SIMPLE MECHANICAL OBSTRUCTION	ADYNAMIC ILEUS
Gas in intestine	Large bow-shaped loops in ladder pattern	Copious gas diffusely through intestine
Gas in colon	Less than normal	Increased, scattered through colon
Fluid levels in intestine	Definite	Often very large throughout
Tumor	None	None
Peritoneal exudate	None	Present with peritonitis; otherwise absent
Diaphragm	Somewhat elevated; free motion	Elevated: diminished motion

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Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

A.7. Describe the fluid shifts during small bowel intestinal obstruction.

Normally, approximately 7 to 9 L of fluid are secreted daily into the upper gastrointestinal tract. The secretions include saliva (500 to 2,000 mL), gastric juice (1,000 to 2,000 mL), bile (300 to 600 mL), pancreatic juice (300 to 800 mL), and succus entericus (2,000 to 4,000 mL) (Table 15.3). Because of small intestinal reabsorption, only 400 mL passes the ileocecal valve.

In small bowel obstruction, several mechanisms contribute to fluid and electrolyte loss. The most important is the accumulation of fluid in the bowel lumen because the obstructed bowel becomes overly secretory instead of absorptive. Sequestration of fluid within the bowel wall accounts for the edematous appearance of the bowel. This, in turn, results in free peritoneal fluid because of transudation of fluid across the serosal surface of the bowel. Fluid accumulation above the obstruction can be remarkable. In early small bowel obstruction, 1,500 mL of fluid accumulates in the bowel. Once intestinal obstruction is well established and vomiting occurs, 3,000 mL of fluid may be present. When the patient becomes hypotensive and tachycardic, indicating circulatory instability, as much as 6,000 mL of fluid is in the abdomen. Lastly, vomiting and/or nasogastric suctioning further increase fluid losses.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1767-1810.

TABLE 15.3 Volume and Composition of Gastrointestinal Fluids

	24-hr VOLUME (mL)	NA^+ (mEq/L)	K^+ (mEq/L)	CL^- (mEq/L)	HCO_3^- (mEq/L)
Saliva	500-2,000	2-10	20-30	8-18	30
Stomach	1,000-2,000	60-100	10-20	100-130	0
Pancreas	300-800	135-145	5-10	70-90	95-120
Bile	300-600	135-145	5-10	90-130	30-40
Jejunum	2,000-4,000	120-140	5-10	90-140	30-40
Ileum	1,000-2,000	80-150	2-8	45-140	30
Colon	—	60	30	40	—

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A.8. Discuss the systemic derangements that occur with intestinal obstruction.

The systemic derangements that occur can be categorized as follows: hemodynamic changes, electrolyte abnormalities, and disturbances in acid-base balance.

Hemodynamically, if fluid and electrolyte losses are not corrected, central venous pressure will fall. Hypotension and tachycardia will follow as the vascular volume decreases in relation to the size of the vascular bed. The shock state develops as the body calls forth sympathomimetic amines to increase cardiac output and decrease the size of the vascular bed.

Small bowel obstruction results in the loss of vast quantities of isotonic extracellular fluid. The extent of extracellular fluid loss may be monitored by serial hematocrit determinations. A rise in the hematocrit is proportionate to the amount of fluid loss. For example, if the hematocrit has risen to 55%, approximately 40% of plasma and extracellular fluid volume has been lost.

As the obstruction continues, there is a gradual decrease in the plasma sodium and chloride concentrations. Hyponatremia will aggravate hypovolemic hypotension, and confusion and somnolence will ensue. Hypokalemia will be manifested in delayed ventricular conduction, ST-T segment changes, and ventricular arrhythmias. With respect to acid-base balance, the most common occurrence is metabolic acidosis because of the effects of dehydration, starvation, ketosis, and loss of alkaline secretions. Metabolic alkalosis is rare and is the result of marked loss of acidic gastric fluid. Monitoring includes serial determinations of sodium, potassium, chloride, and carbon dioxide.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1767-1810.

A.9. Can there be actual losses of red cell mass?

Yes. In long-standing intestinal obstruction, especially when it is associated with strangulation, increased permeability of the bowel wall occurs with loss of red blood cells into the bowel and peritoneal cavity. Whole blood or packed red blood cells may be needed to restore circulating red blood cells.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

A.10. What is an ileus? Discuss its causes and treatment.

An ileus is a functional failure of normal aboral intestinal transit. Except for the discomfort of abdominal distention, it is usually not painful. The pathogenesis of ileus is poorly understood, but stimulation of the inhibitory adrenergic neurons may play an important role. Classification of ileus is as follows:

- *Adynamic or inhibition ileus*—diminished or absent motility from neuromuscular inhibition
- *Spastic ileus*—contracted bowel musculature with resultant uncoordinated motility
- *Ileus of vascular occlusion*—disordered motility secondary to ischemia

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Adynamic ileus is the most common form because it is present following every intra-abdominal operation. Postoperative ileus affects different parts of the gastrointestinal tract differently. Small bowel function recovers within 24 hours, whereas gastric motility may take 24 to 48 hours to return. The colon is the most severely affected, where an ileus may persist for as long as 3 to 5 days.

If postoperative ileus is prolonged, other contributing causes should be sought that include the following:

- *Metabolic*—hypokalemia, hyponatremia, hypomagnesemia
- *Drugs*—narcotics, antacids, anticoagulants, phenothiazines, ganglionic blockers
- *Other*—intraperitoneal inflammation (e.g., acute appendicitis or acute pancreatitis), sepsis, hematoma, wound infection, ureteral colic, spine or rib fractures, basal pneumonia

Spastic ileus is rare and occurs with heavy metal poisoning, porphyria, and uremia. Management of ileus involves treatment of the underlying cause, nasogastric decompression, intravenous hydration, correction of metabolic abnormalities, and nutritional support if needed. No specific drug therapy has been shown to be effective.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

A.11. What are the systemic effects from the absorption of bacteria and bacterial products?

The normal mucosa is impermeable to bacteria and toxins produced by bacterial degradation, but permeability is affected when there is impairment of the blood supply in a strangulated segment of bowel. Intestinal obstruction also can lead to a change in the bacterial flora within the bowel. Subsequent transperitoneal absorption of bacteria and toxins can result in bacteremia and septic shock.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

B. Preoperative Evaluation and Preparation

B.1. Is it important to decompress the abdomen before surgical intervention? Why?

Yes, it is because of the respiratory and circulatory complications that ensue.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

B.2. Describe the respiratory implications.

The distended bowel produces pressure on the diaphragm, limiting its downward movement which results in inadequate ventilation and an increased work of breathing in a patient who already may be malnourished. The decrease in tidal volume and the reduction in functional residual capacity (FRC) result in a low PaO_2 and an elevated $PaCO_2$. It is especially true if the stomach also is distended. An additional reason for gastric decompression is to remove fluid and air from the stomach to decrease the likelihood of aspiration of gastric contents into the tracheobronchial tree during the induction of anesthesia. A long-standing obstruction and its associated respiratory compromise will result in a gasping,

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dusky, cyanotic, semicomatose patient.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

B.3. What are the implications of the tense abdominal wall?

The first is related to the higher incidence of reverse peristalsis. Second, the stretched abdominal wall requires deeper anesthesia and more muscle relaxant to provide adequate operating conditions. These implications may increase morbidity. The distended abdomen, also, significantly affects venous return by two mechanisms. First, distention decreases negative intrathoracic pressure and thereby decreases venous return. The second is due to direct vena caval compression from intraperitoneal tension. In long-standing intestinal obstruction, a large volume of intraperitoneal fluid may be present in the abdominal cavity. At the time of surgical incision, care must be taken to prevent the fluid from escaping rapidly from the abdomen to minimize severe hypotension. As fluid is slowly released from the abdominal cavity, the blood pressure should be checked frequently and the rate of fluid release adjusted to minimize a fall in blood pressure.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

B.4. Outline the methods of abdominal decompression.

There are two types of tubes available for abdominal decompression: short tubes placed in the stomach and long tubes placed in the small intestine. To reduce the likelihood of regurgitation of gastric contents, it is important that the stomach be empty before induction of anesthesia. This is best done with a sump tube, which is more efficient than the simple Levin tube. The sump tube is composed of a double lumen, one for aspiration and the other to allow air into the stomach. The Miller-Abbott tube is a long intestinal tube that is initially passed into the stomach, and an incorporated balloon containing mercury at its tip aids in its passage through the pylorus into the small bowel.

Although gastric and intestinal tubes are employed to relieve abdominal distention, they do not function solely as definitive therapy for bowel obstruction except in postoperative ileus, partial small bowel obstruction, and intestinal obstruction resulting from inflammation that is expected to subside with conservative therapy. For all other bowel obstructions, the mainstay of therapy remains surgical intervention.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

B.5. Discuss the goals of fluid management.

Estimating the fluid deficit in a patient with an intestinal obstruction is extremely difficult and is often underestimated. There is significant sequestration of fluid within the bowel lumen, bowel wall, and transudation into the peritoneal cavity. Poor preoperative nutrition and protein loss into the bowel may lead to hypoalbuminemia and further fluid losses. The primary goal of fluid management is the initial restoration of intravascular volume to a state of normovolemia. This will lead to the optimization of oxygen delivery to the tissues and organs. The second goal is the correction of electrolyte disturbances, including acid-base derangements, which may exist. Because the fluid lost to an obstructed segment of bowel is similar to plasma in composition, a balanced salt solution, such as lactated Ringer's solution, is appropriate to use for fluid resuscitation.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-

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Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1767-1810.

B.6. What would you use as a guide to fluid volume replacement?

Fluid losses can be calculated knowing that the body turns over 17 to 18 L of fluid a day; this loss includes intestinal secretions, urine excreted by the kidneys, fluid loss through the feces, and insensible losses from the lungs and skin. As mentioned previously, there is tremendous fluid loss into the gut, which may amount to 4,500 to 9,000 mL of functional fluid loss, including the loss resulting from vomiting and nasogastric suctioning. If there is significant bowel wall edema and leakage of fluid into the peritoneal cavity because of peritonitis, an additional 7 L of fluid may be sequestered in the peritoneal space. Measurement of central venous pressure, hourly urine output, arterial blood pressure, heart rate, and skin turgor can be used to guide fluid replacement. In addition, there must be ongoing modifications in the management of fluid and electrolytes to achieve the desired physiologic goals.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1137-1174.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1767-1810.

C. Intraoperative Management

C.1. What dangers are present during induction? How are they planned for?

Regurgitation of stomach contents and subsequent aspiration into the tracheobronchial tree is the principal danger during induction of anesthesia for the patient with intestinal obstruction.

Mortality associated with aspiration of gastric contents ranges widely from 3% to 70%. Abdominal surgery in particular has been associated with up to 75% of the perioperative mortality resulting from aspiration pneumonitis. The incidence of aspiration for all anesthetics is almost 5 per 10,000 anesthetics. A rapid sequence induction intubation (RSII) has been traditionally recommended. An awake intubation might be preferred if a difficult intubation is anticipated.

For an awake intubation, the patient's lips, tongue, and pharynx should be sprayed with a topical anesthetic. Care must be taken to avoid anesthetizing the larynx because the defense mechanism for laryngeal closure will be lost in the event that regurgitation or vomiting should occur. Therefore, a superior laryngeal nerve block or a transtracheal injection is not warranted in these patients. Sedation should be limited or avoided altogether.

The goal of RSII is to complete the tracheal intubation with a cuffed endotracheal tube in the shortest possible time after the patient loses consciousness. Intuitively, this should decrease the risk of aspiration. Scientific evidence fails to support it or refute it. A search of 184 randomized controlled trials since 1966 failed to find any study that evaluated the effect of RSII on the incidence and prevention of pulmonary aspiration of gastric contents. As a result, controversy exists today regarding its use as well as some of the components of the RSII technique. According to Sellick, cricoid pressure, if applied, should not be released until the cuff is inflated and correct placement of the endotracheal tube has been verified by measures including auscultation and capnometry. There is growing controversy on the usefulness of cricoid pressure itself. Some studies show that cricoid pressure is associated with an increased rate of failed intubation, whereas others found no difference. Radiologic studies have shown that the esophagus is displaced laterally rather than occluded in over 50% of cases and reflex relaxation of the lower esophageal sphincter (LES) in response to cricoid pressure may provoke regurgitation. However, cricoid pressure has also been shown to completely occlude the hypopharynx, making lateral

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displacement of the esophagus irrelevant in the prevention of regurgitation of gastric contents. Observational studies have shown that cricoid pressure is frequently applied incorrectly and it is difficult to clinically teach application of 40 N of pressure. Other areas of controversy include the best induction drug choice, the optimal drug for muscle relaxation, the rapidity with which drugs are delivered during RSII, the best preoxygenation technique, the ideal patient position during RSII, and even the avoidance of positive pressure ventilation prior to intubation of the trachea. Should the patient remain hemodynamically unstable following fluid and electrolyte resuscitation, ketamine or etomidate is preferable for induction of anesthesia.

Brimacombe JR, Berry AM. Cricoid pressure. *Can J Anaesth*. 1997;44:414-425.

El-Orbany M, Connolly LA. Rapid sequence induction and intubation: current controversy. *Anesth Analg*. 2010;110:1318-1325.

Gobindram A, Clarke S. Cricoid pressure: should we lay off the pressure? *Anaesthesia*. 2008;63:1258-1259.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1647-1683.

Neilipovitz DT, Crosby ET. No evidence for decreased incidence of aspiration after rapid sequence induction. *Can J Anaesth*. 2007;54:748-764.

Rice MJ, Mancuso AA, Gibbs C, et al. Cricoid pressure results in compression of the postcricoid hypopharynx: the esophageal position is irrelevant. *Anesth Analg*. 2009;109:1546-1552.

Sellick BA. Cricoid pressure to control regurgitation of stomach contents during induction of anaesthesia. *Lancet*. 1961;2:404-406.

Smith KJ, Dobranowski J, Yip G, et al. Cricoid pressure displaces the esophagus: an observational study using magnetic resonance imaging. *Anesthesiology*. 2003;99:60-64.

Tournadre JP, Chassard D, Berrada KR, et al. Cricoid cartilage pressure decreases lower esophageal sphincter tone. *Anesthesiology*. 1997;86:7-9.

C.2. Does the administration of antacids and/or histamine-2 (H2) blockers before the induction of anesthesia have a significant value in patients with small bowel obstruction?

The volume and pH of gastric contents and the presence or absence of particulate matter appear to be the three most important factors in determining the degree of pulmonary injury following aspiration. The classical term *at risk* is thought to imply a gastric volume greater than 25 mL with a pH less than 2.5. Approximately 40% of emergency surgical patients have a gastric pH below 2.5. The more critical factor involved in determining the degree of lung injury appears to be the pH of gastric contents. Therefore, outcomes are better with aspirations of large volumes of nonacidic material compared with that of small volumes of acidic material. Normally, clear, nonparticulate antacids (0.3 M sodium citrate) are effective in raising gastric pH and H2 blocking agents are effective in reducing gastric volume and acidity. However, because of the large volumes of fluid sequestered in the bowel, antacids and/or H2 blockers have little or no value in high mechanical intestinal obstruction. When there is time to prepare the patient, these agents may be of some value in partial small bowel obstruction to reduce both gastric volume and acidity.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:601-603, 1568-1569.

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C.3. In what position would you intubate this patient?

Because gravity will aid in keeping gastrointestinal contents within the stomach, the headup position is likely to decrease the incidence of regurgitation and thereby lessen the risk of pulmonary aspiration. Some clinicians advise that the patient be intubated in the supine position for fear that if the patient did vomit and was in the sitting or semisitting position, there would be a greater tendency to aspirate. However, we believe the head-up position is preferable. Should massive reverse peristalsis and regurgitation occur, vigorous suctioning and the head-down position are the best methods of preventing soilage of the tracheobronchial tree. The head-down position must be at least 10 degrees to prevent aspiration into the lungs.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:781-783.

El-Orbany M, Connolly LA. Rapid sequence induction and intubation: current controversy. *Anesth Analg*. 2010;110:1318-1325.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1647-1683.

C.4. Is succinylcholine the best muscle relaxant to use for the rapid sequence induction?

Succinylcholine is still the only ultrarapid onset/ultrashort duration muscle relaxant for use in the rapid sequence induction technique despite the known complications associated with the use of this drug. Several studies have advocated the use of large doses of nondepolarizing muscle relaxants for rapid sequence induction of anesthesia using the priming principle. The technique recommends the use of a small dose of a nondepolarizing muscle relaxant (usually about 20% of the ED95), followed 2 to 4 minutes later by a second dose, the intubating dose. These authors claim that patients can be intubated significantly earlier, by approximately 30 to 60 seconds, than if they are given a single intubating dose of a nondepolarizing muscle relaxant. With use of the priming principle, tracheal intubation can be achieved approximately 90 seconds following the second intubating dose of muscle relaxant. However, some argue that 90 seconds is not fast enough for a rapid sequence induction technique, and furthermore, intubating conditions at 90 seconds may not be as ideal as that achieved at 60 seconds following succinylcholine administration. In addition, one should keep in mind that large doses of nondepolarizing muscle relaxants will result in a longer duration of neuromuscular blockade and may increase the potential for side effects. Another consideration of the priming technique that is especially relevant to the bowel-obstructed patient is the risk of aspiration due to the variable degree of neuromuscular blockade produced by the priming dose.

With the availability of rocuronium and the previously stated concerns, the use of the priming technique has diminished at the present time. See Table 15.4 for the priming dose and intubating dose of various muscle relaxants.

TABLE 15.4 Rapid Tracheal Intubation[a] with Succinylcholine or Nondepolarizing Relaxants[b]

DRUG	PRIMING DOSE[c] (mg/kg)	INTUBATING DOSE[d] (mg/kg)	CLINICAL DURATION[e]	FULL RECOVERY[f]
Succinylcholine	None	1.0	5-10	12-15
Succinylcholine	Nondepolarizer pretreatment	1.5	5-10	12-15
Rocuronium	None	0.6-1.0	30-60	60-120

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Mivacurium	0.02	0.25-0.3	15-20	25-35
Vecuronium	0.01	0.2	60-75	90-120
Vecuronium	None	0.3-0.4	90-150	120-180
Cisatracurium	0.01	0.25	55-75	75-100
Cisatracurium	None	0.4	75-100	100-120

[a]Intubation within 60 to 90 seconds following injection of the intubating dose of the relaxant.

[b]The administration of adequate dosage of intravenous anesthetic is assumed.

[c] This dose is given as preoxygenation is begun.

[d] This dose is given 2 to 4 minutes following the priming dose. For atracurium and mivacurium, slower injection (30 seconds) is recommended to minimize circulatory effects.

[e] Minutes from injection of the intubating dose to recovery of twitch to 25% of control.

[f] Minutes from injection of the intubating dose to recovery of twitch to 95% of control and train-of-four of 0.70.

From Miller RD, ed. *Anesthesia*. 5th ed. New York: Churchill Livingstone; 2000:427, with permission.

El-Orbany M, Connolly LA. Rapid sequence induction and intubation: current controversy. *Anesth Analg*. 2010;110:1318-1325.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:958-994, 1647-1683.

Neilipovitz DT, Crosby ET. No evidence for decreased incidence of aspiration after rapid sequence induction. *Can J Anaesth*. 2007;54:748-764.

C.5. Would you remove or leave the nasogastric tube (NGT) in place before inducing anesthesia?

The decision of whether to remove or leave the NGT in place before induction of general anesthesia is somewhat controversial. The case for leaving the NGT in is that it allows gastric decompression, reduces intragastric pressure, and thereby reduces the chances of regurgitation. However, the presence of NGT during induction does not reliably ensure an empty stomach but renders the LES incompetent by preventing complete closure of the LES. The LES usually is 2 to 3 cm long and functions as the major impediment to reflux of gastric contents into the esophagus. An incompetent LES will increase the likelihood of regurgitation and aspiration of gastric contents into the tracheobronchial tree. Further, an indwelling NGT also may interfere with visualization of the larynx during laryngoscopy and endotracheal intubation.

Atlee JL, ed. *Complications in Anesthesia*. 2nd ed. Philadelphia, PA: Saunders Elsevier; 2007:641-643.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:781-783.

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C.6. Would you use nitrous oxide in this patient?

Nitrous oxide should be avoided because its administration is associated with an undesirable increase in intraluminal gas volume and pressure that may lead to detrimental consequences. The blood-to-gas partition coefficient of nitrous oxide is 34 times that of nitrogen. Therefore, nitrous oxide in the blood can enter gas-filled cavities 34 times more rapidly than nitrogen can leave those cavities to enter the blood. When this happens during abdominal

surgery, bowel distention will occur. The amount of distention will depend on the amount of gas already within the bowel and the duration of nitrous oxide administration. Normally, the bowel contains approximately 100 mL of gas that is mostly swallowed air, and nitrous oxide use results in a slow increase in bowel distention and intraluminal pressure. However, with bowel obstruction, the volume of gas within the bowel is greatly increased. Under these conditions, the increased intraluminal pressure associated with nitrous oxide administration may lead to bowel ischemia and necrosis. More commonly, it will cause difficulties with abdominal closure at the conclusion of surgery. Therefore, anesthesia should be maintained with oxygen, air, a volatile agent, and increments of opioids and muscle relaxants as needed.

Akca O, Lenhardt R, Fleischmann E, et al. Nitrous oxide increases the incidence of bowel distension in patients undergoing elective colon resection. *Acta Anaesthesiol Scand*. 2004;48(7):894-898.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1263-1264.

Orhan-Sungur M, Apfel C, Akça O. Effects of nitrous oxide on intraoperative bowel distension. *Curr Opin Anaesthesiol*. 2005;18(6):620-624.

C.7. Are there any benefits to using a high concentration of inspired oxygen?

It has been suggested that administration of a high concentration of inspired oxygen may lead to a reduction in the incidence of surgical wound infections. Wound infections are a serious complication of surgery that can prolong hospitalization, thereby increasing morbidity and medical costs. The factors that may play a role in producing surgical wound infections include the site and complexity of surgery, the tissue oxygen tension, the presence of any underlying illness, prophylactic antibiotic use, the intravascular volume status, the patient's body temperature, and postoperative pain control. Compared with the administration of 30% inspired oxygen, those patients receiving 80% inspired oxygen had approximately half the number of postoperative surgical wound infections in one study; however, others have failed to reproduce these results. Timely use of prophylactic antibiotics and maintenance of normothermia in the perioperative period probably are more effective in decreasing surgical site infections.

Greif R, Akça O, Horn EP, et al. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. *N Engl J Med*. 2000;342:161-167.

D. Postoperative Management

D.1. What are the principles of postoperative care in this patient?

The principles of postoperative management are the same as those in the preoperative care of the patient, namely, fluids and electrolytes, antibiotics, and gastrointestinal decompression. In the immediate postoperative period, there continues to be significant ongoing fluid loss, mostly secondary to “third spacing.” However, this fluid loss gradually diminishes over time and usually by about the third postoperative day reverses in direction as fluid is transferred back into the vascular compartment. The significant autoinfusion that ensues must, therefore, be accounted for in the computations of the daily fluid requirements for the patient. Otherwise, congestive heart failure may follow, especially because patients with intestinal obstruction are often older adults with limited reserves in several organ systems. As electrolyte loss continues postoperatively, serial determinations of serum sodium and potassium levels may be necessary. Hyponatremia and hypokalemia are factors that contribute to a prolonged postoperative ileus. Because return of normal intestinal motility usually is prolonged after surgical relief of bowel obstruction, abdominal decompression often must be continued for 5 or 6

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days postoperatively, whereas bowel function returns on about the third postoperative day after a routine abdominal operation.

The long-held practice of liberal intravenous fluid administration during the perioperative period of major abdominal surgery has been questioned. There is growing evidence to suggest that a restricted perioperative fluid regimen will lead to a decrease in complications, including a shorter duration of postoperative ileus following abdominal surgery, and to a reduction

in the length of hospital stay. Regardless of the fluid regimen instituted, tissue perfusion must be adequately maintained. Finally, postoperative management also may include frequent monitoring of hemodynamic parameters, hemoglobin concentration, and urine output.

Brandstrup B, Tønnesen H, Beier-Holgersen R, et al. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial. *Ann Surg*. 2003;238:641-648.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:65-83, 1138-1153.

Doherty GM, ed. *Current Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015.

Lobo DN, Bostock KA, Neal KR, et al. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomized controlled trial. *Lancet*. 2002;359:1812-1818.

Luckey A, Livingston E, Taché Y. Mechanisms and treatment of postoperative ileus. *Arch Surg*. 2003;138(2):206-214.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1767-1810.

Noblett SE, Snowden CP, Shenton BK, et al. Randomized clinical trial assessing the effect of Doppler-optimized fluid management on outcome after elective colorectal resection. *Br J Surg*. 2006;93:1069-1076.

D.2. Are there any postoperative respiratory problems associated with factors other than aspiration?

The postoperative respiratory problems are related to hypoventilation. Although the intestinal obstruction has been relieved, there still may be significant abdominal distention that will inhibit diaphragmatic motion, and the patient may develop hypoxia and hypercarbia. In addition, abdominal pain and the residual effects of inhaled anesthetics, intravenous anesthetics, and neuromuscular blockers may contribute to respiratory inadequacy. The 15% to 20% reduction in FRC associated with general anesthesia continues into the postoperative period, and following upper abdominal surgery, vital capacity remains abnormal for more than a week. In summary, several pulmonary changes occur, including reductions in the following parameters: tidal volume, vital capacity, FRC, residual volume, and forced expiratory volume in 1 second (FEV1). For these reasons, the endotracheal tube may be left in place to decrease anatomic dead space and make it possible to ventilate the patient during the immediate postanesthesia period. Leaving the endotracheal tube in place also is desirable for those patients with previous respiratory disease or in the morbidly obese individual. In both of these situations, the respiratory support will decrease residual atelectasis in the basilar portions of the lung. This will decrease any pulmonary shunting and lessen the need for high inspired oxygen concentrations (FIO2). For those patients not requiring ventilator support, a T-piece delivering an increased FIO2 attached to the endotracheal tube will maintain the PaO2 at an acceptable level. As the patient gradually regains respiratory adequacy (as shown by measuring inspiratory force and vital capacity), ventilation returns to normal and the patient can be safely extubated.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1563-1569.

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Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:444-472.

D.3. If the patient did aspirate gastric contents, what are the possible sequelae of this event? What is the treatment?

Aspiration of gastric contents produces a chemical pneumonitis characterized initially by hypoxemia, bronchospasm, and atelectasis. In addition, the patient may exhibit signs of tachypnea, tachycardia, coughing, cyanosis, and shock. Arterial hypoxemia is the earliest and most reliable sign of aspiration. Even saline, when aspirated, causes significant hypoxemia.

Destruction of pneumocytes, lung parenchyma, and pulmonary microvasculature ensues, resulting in decreased surfactant activity, interstitial and alveolar edema, alveolar hemorrhage, and pulmonary hypertension (which results from hypoxic pulmonary vasoconstriction). The clinical picture may resemble that of adult respiratory distress syndrome. Radiographic

findings are variable and may not appear for several hours. In at least 10% of cases, the radiographic films are normal. Positive findings usually consist of diffuse infiltrates bilaterally located in either the perihilar or basal regions.

Once vomiting or regurgitation occurs, immediate lateral head positioning, vigorous suctioning, and the head-down position should be instituted. To avoid disseminating the aspirated material further distally, the trachea is suctioned before beginning positive pressure ventilation. Bronchoscopy is indicated only for those patients who have aspirated solid material resulting in significant airway obstruction. Use of bronchial irrigation with saline or sodium bicarbonate solution is of little value and may actually be more detrimental than beneficial. Management includes keeping the patient intubated and well ventilated, following arterial blood gases, and obtaining serial chest x-ray films. Depending on the arterial blood gases, regulation of the inspired oxygen concentration and the amount of ventilation to maintain PaO_2 and $PaCO_2$ within normal limits will be necessary. If the fraction of inspired oxygen (FIO_2) has to be maintained above 60%, the use of positive end-expiratory pressure may be necessary to recruit additional alveoli and improve oxygenation. The best positive end-expiratory pressure will have the least effect on venous return and at the same time allow FIO_2 to be reduced to a safe level (40% or lower), thereby decreasing the likelihood of oxygen toxicity. It is important to realize that although a patient may look well and have a clear chest without rhonchi or wheezes in the immediate postanesthetic period following aspiration, respiratory distress still may develop. It may take as long as 6 to 12 hours before the syndrome manifests. The patient should be observed closely over 24 to 48 hours for the development of aspiration pneumonitis. Corticosteroid therapy remains controversial, and the routine use of prophylactic antibiotics is not recommended because it may alter the normal flora of the respiratory tract and promote colonization by resistant organisms. However, antibiotics should be administered to those patients who show clinical signs of a secondary bacterial pulmonary infection with positive Gram stain and cultures or to those patients known to have aspirated gross fecal material, as with lower intestinal obstruction.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1568-1569.

D.4. What is gram-negative sepsis? Describe the clinical picture and treatment.

Gram-negative sepsis frequently leads to a shock state caused by endotoxins from the cell walls of gram-negative bacteria circulating in the blood. The earliest signs of a gram-negative infection include an elevated temperature above 101°F (38.33°C), the development of shaking chills, mild hyperventilation, respiratory alkalosis, and an altered sensorium. The hemodynamic abnormalities of gram-negative sepsis are not understood clearly but seem to follow two distinct hemodynamic patterns, depending on the patient's volume status.

The first is a hyperdynamic circulatory pattern associated with early septic shock that occurs in patients who are normovolemic before the onset of sepsis. These patients present with hypotension, high cardiac output, normal or increased blood volume, normal or high central venous pressure, decreased peripheral resistance, warm and dry extremities, hyperventilation, and respiratory alkalosis. However, in a patient who is hypovolemic before the onset of sepsis as with a strangulated obstruction of the small bowel, a hypodynamic pattern is seen characterized by hypotension, low cardiac output, high peripheral resistance, low central venous pressure, and cold, clammy extremities. Both types of patterns will have a better outcome if early treatment is begun, but if therapy is delayed or unsuccessful, cardiac and circulatory failure ensues associated with a low, fixed cardiac output and a resistant metabolic acidosis.

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Definitive therapy of gram-negative sepsis includes the administration of appropriate antibiotics and early surgical debridement or drainage of the source of infection when indicated. Supportive measures are provided by fluid replacement and the use of vasoactive drugs. Corticosteroid administration as part of the treatment regimen for sepsis is still a controversial issue. Direct arterial blood pressure monitoring and insertion of a pulmonary artery catheter may be necessary for proper management.

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Chapter 16
Liver Transplantation

L. Hannah Bell

Vivek K. Moitra

A 66-year-old woman with a history of alcoholic cirrhosis and portal hypertension is admitted to the intensive care unit with altered mental status and low urine output. She has ascites and encephalopathy. Her kidney injury is acute with a creatinine clearance of 30 mL per minute. Her international normalized ratio (INR) is 3.0. Her hemoglobin level is 10.2 g per dL. She has a model for end-stage liver disease (MELD) score of 28 points. Her respiratory rate is 30 breaths per minute. She is scheduled for orthotopic liver transplantation.

A. Medical Disease and Differential Diagnosis

1. What are the potential graft options for liver transplantation?
2. What are the indications and contraindications for liver transplantation?
3. What is acute liver failure (ALF)?
4. What is the MELD score and how is it used in liver transplantation evaluation?
5. Describe the cardiovascular system of patients with end-stage liver disease (ESLD).
6. What causes acute kidney injury (AKI) in patients with cirrhosis?
7. What causes hyponatremia in patients with cirrhosis?
8. Discuss the neurologic manifestations of acute and chronic liver disease.
9. Why do patients with ESLD have abnormalities of hemostasis?
10. What is the differential diagnosis for hypoxemia in patients with cirrhosis?
11. What is portal hypertension? What are the sequelae of portal hypertension?

B. Preoperative Evaluation and Preparation

1. What preoperative workup is desirable?
2. How is ascites managed preoperatively?
3. How is hyponatremia managed preoperatively?
4. What is a transjugular intrahepatic portosystemic shunt (TIPS) procedure? What is the role of TIPS in the management of patients with ESLD?
5. How are hepatic encephalopathy and elevated intracranial pressure (ICP) treated?
6. Should this patient be transfused with fresh frozen plasma prior to surgery?

C. Intraoperative Management

1. What monitors would you use? Why?
2. What are the considerations for the induction of anesthesia?
3. How does liver disease affect intraoperative medication management?
4. What happens during the first stage (preanhepatic phase) of the liver transplant operation?
5. What happens during the second stage (anhepatic phase) of the liver transplant operation?

6. What physiologic disturbances should be anticipated during the second stage (anhepatic phase) of the liver transplant

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operation?

7. What is venovenous bypass? What are potential advantages and disadvantages of this procedure?
8. What surgical techniques anastomose the donor and recipient inferior vena cava?
9. What are the potential advantages of the “piggyback” (vena cava preservation) technique?
10. What hemodynamic changes are expected after removal of vascular clamps? What is postreperfusion syndrome?
11. How would you treat hyperkalemia?
12. Why should you anticipate hypocalcemia?
13. What happens during the third stage of the liver transplant operation?
14. What causes intraoperative bleeding during each phase of liver transplantation? How is coagulopathy monitored and treated? What are thromboelastography (TEG) and rotational thromboelastography (ROTEM)?
15. What are the complications of massive transfusion?
16. How are the complications of massive transfusion prevented?
17. How is hyperfibrinolysis managed?
18. When is intraoperative renal replacement therapy indicated?
19. What intraoperative signs suggest that the hepatic graft is working?

D. Postoperative Management

1. What are the goals of immediate postoperative care of the liver transplant patient?
2. What postoperative findings suggest that the hepatic graft is functioning?
3. What coagulation disturbances should be anticipated in the postoperative period?
4. Can renal function change after liver transplantation?
5. What vascular and biliary complications occur after liver transplantation?
6. What immunosuppressive agents will be given after liver transplantation? What are the major side effects?

A. Medical Disease and Differential Diagnosis

A.1. What are the potential graft options for liver transplantation?

Liver grafts are harvested from deceased or living donors. Cadaveric livers are procured after brain or cardiac death. Because of an increasing number of patients who die waiting for a transplant, efforts to expand the donor pool include donation after cardiac death (DCD), harvesting marginal organs from cadavers with extended donor criteria, and procuring partial livers from living donors. DCD is the fastest growing source of transplant organs in the United States. Upon cardiac death (defined as the irreversible cessation of circulatory and respiratory function), the liver is harvested after a mandatory waiting period of 1 to 5 minutes. Warm ischemic time begins when the waiting period starts and ends when the liver is flushed with cold preservative solution. Transplantation of a DCD-donor liver that has been exposed to a longer warm ischemic time than a graft from a brain-dead donor may be associated with perioperative complications such as vascular- and biliary-related lesions and early graft dysfunction. Ideal organs have shorter warm and cold ischemic times and are harvested from hemodynamically stable donors younger than 50 years of age who are free of hepatobiliary or renal disease, infection, and cancer.

Extending donor criteria (age older than 65 years; DCD; positive viral serology; split liver; hypernatremia; or prior carcinoma, steatosis, or high-risk behaviors) to harvest organs with initial poor function or primary nonfunction expands the donor pool.

A related or unrelated healthy individual may donate a portion of the liver for transplantation. Usually, the right hepatic lobe is removed from a healthy individual and transplanted

into an adult recipient. Transplantation of the smaller left hepatic lobe into pediatric or very small adults may decrease the incidence of complications in the donor. This chapter focuses on cadaveric liver transplantation into adult recipients.

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Saidi, RF. Utilization of expanded criteria donors in liver transplantation. *Int J Organ Transplant Med*. 2013;4:46-59.

Song G, Lee S. Living donor liver transplantation. *Curr Opin Organ Transplant*. 2014;19:217-222.

A.2. What are the indications and contraindications for liver transplantation?

Patients with acute liver failure (ALF), decompensated cirrhosis, or hepatocellular carcinoma are candidates for liver transplantation. In the United States, alcoholic liver disease is the most common cause of end-stage liver disease (ESLD), but cirrhosis from hepatitis C is the most common indication for orthotopic liver transplant. With the rise of the obesity epidemic, nonalcoholic steatohepatitis (NASH) is the third most common indication for liver transplantation. Specific indications for transplantation include recurrent cholangitis in patients with primary sclerosing cholangitis or intractable pruritus in patients with primary biliary cirrhosis. Uncommon indications for liver transplantation include hepatic tumors such as carcinoid tumors and hepatic adenoma, metabolic disorders such as α_1-antitrypsin deficiency, vascular disorders such as Budd-Chiari syndrome, cystic fibrosis, hemochromatosis, amyloidosis, sarcoidosis, hyperoxaluria, and adult polycystic liver disease. Biliary atresia is the most common indication for pediatric liver transplantation.

Most surgeons will not offer transplantation to patients with severe cardiopulmonary or neurologic disease, significant hemodynamic instability, sepsis, extrahepatic malignancy, active alcohol or drug use, or unfavorable psychosocial circumstances. The decision to offer transplantation considers age and infection with human immunodeficiency virus.

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A.3. What is acute liver failure (ALF)?

In the absence of transplantation, ALF leads to death. ALF is defined by the absence of chronic liver disease, acute hepatitis (elevation in transaminases with an elevation in INR), encephalopathy, and illness less than 26 weeks. The most common causes of ALF are acetaminophen toxicity (39%), indeterminate (18%), idiosyncratic (19%), and acute viral hepatitis (12%, usually hepatitis B). Other etiologies include drugs (phenytoin and halothane), autoimmune disease, Wilson disease, Budd-Chiari syndrome, HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count), acute fatty liver of pregnancy, toxins (i.e., trichloroethylene and tetrachloroethane in cleaning solvents and sniffed glue), and *Amanita phalloides*, the “deathcap” mushroom that grows wild in parts of the United States.

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Stravitz RT, Kramer AH, Davern T, et al. Intensive care of patients with acute liver failure: recommendations of the U.S. Acute Liver Failure Study Group. *Crit Care Med*. 2007;35:2498-2508.

A.4. What is the MELD score and how is it used in liver transplantation

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evaluation?

Grafts from deceased donors are offered to patients with the highest risk of death. Since 2002, the Model for End-stage Liver Disease (MELD), a validated and widely used prognostic tool that estimates disease severity and 3-month survival in patients with chronic liver disease, prioritizes organ allocation (Fig. 16.1). The MELD score ranges from 6 to 40 points and is calculated from the patient's serum bilirubin, serum creatinine, and INR.

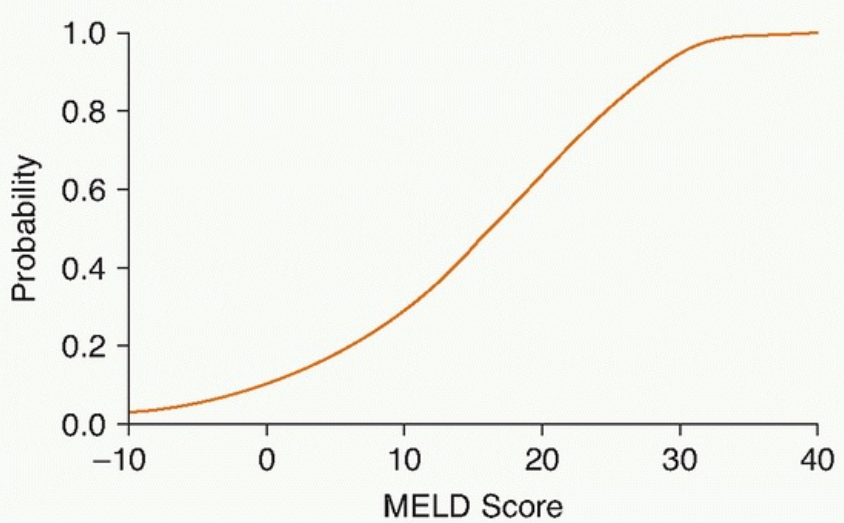


FIGURE 16.1 Relation between MELD score and 3-month mortality in patients with cirrhotic liver disease. MELD, model for end-stage liver disease. (From Wiesner RH, Mc-Diarmid SV, Kamath PS, et al. MELD and PELD: application of survival models to liver allocation. *Liver Transpl*. 2001;7:567-580.)

Formula 16.1

MELD Score = 11.2 × ln (INR) + 9.57 × ln (creatinine, milligrams per deciliter) + 3.78 × ln (bilirubin, milligrams per deciliter) + 6.43 (an intercept). The score is rounded to the nearest whole number.

There is a lower limit of 1 for all variables.

The maximum creatinine value is 4 mg per dL. For patients who receive dialysis, creatinine is set to 4 mg per dL.

Patients with a high score rank high on the transplant list and have a greater short-term risk of dying from liver disease than patients with lower scores. The incorporation of hyponatremia, an important prognostic factor in patient with cirrhosis, into the MELD score may provide better calibration and discrimination of the risk of death among patients awaiting liver transplantation.

Exceptions to the MELD classification exist for patients with fulminant hepatic failure and life expectancy of less than 7 days without a liver transplant. These patients are classified as *status 1* and rank highest on the waiting list. This group includes patients who develop ALF without a history of liver disease, suffer from primary graft nonfunction or hepatic artery thrombosis within 7 days of a liver transplant, or have acutely decompensated Wilson disease. Special case exceptions also exist for patients with hepatocellular carcinoma, hepatopulmonary syndrome, familial amyloidosis, and primary oxaluria.

Pediatric patients younger than 12 years of age are ranked on the transplant waiting list according to the pediatric end-stage liver disease (PELD) model. The PELD score is similar in derivation to the MELD but does not consider creatinine and incorporates bilirubin, INR, albumin, age, and growth failure into the formula.

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Martin P, DiMartini A, Feng S, et al. Evaluation for liver transplantation in adults: 2013 practice guidelines by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Hepatology*. 2014;59:1144-1165.

A.5. Describe the cardiovascular system of patients with end-stage liver disease (ESLD).

The cardiovascular system of patients with ESLD mimics the hyperdynamic circulatory changes of patients with sepsis. Tachycardia, elevated cardiac output, low arterial blood pressure, and low systemic vascular resistance are characteristic. Enhanced endogenous production or diminished hepatic clearance of vasodilating substances, such as nitric oxide, carbon monoxide, and endogenous cannabinoids, and the inflammatory response to bacterial

translocation cause splanchnic arterial vasodilation. Increased venous capacitance from formation of portosystemic shunts because of portal hypertension increases venous capacitance and contributes to a hyperdynamic circulation. During the perioperative period, the patient's circulatory system may be challenged with shunt insertion or greater afterload from surgical stress, unmasking an underlying cirrhotic cardiomyopathy. Echocardiography shows impaired myocardial function similar to that found in septic patients. This condition is also characterized by QT prolongation and systolic and diastolic dysfunction. Reduced *β*-receptor function may explain these findings.

Systemic conditions such as hemochromatosis (ventricular hypertrophy with increased end-diastolic and end-systolic volumes), amyloidosis (restrictive cardiomyopathy), Wilson disease (supraventricular extrasystolic beats), and alcoholism (systolic and diastolic dysfunction) can affect liver and cardiac function. Patients with portal hypertension may develop portopulmonary hypertension and right ventricular dysfunction. A mean pulmonary artery pressure greater than 25 mm Hg at rest and a pulmonary vascular resistance greater than 240 dynes/sec/cm^{-5} define portopulmonary hypertension.

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Zardi EM, Abbate A, Zardi DM, et al. Cirrhotic cardiomyopathy. *J Am Coll Cardiol*. 2010;56:539-549.

A.6. What causes acute kidney injury (AKI) in patients with cirrhosis?

Patients with AKI and cirrhosis have more complications and increased risk of mortality after liver transplantation than those without renal failure. Gastrointestinal bleeding, diarrhea from infection or lactulose administration, and diuretic medications change circulatory function via hypovolemia and can cause renal injury. As cirrhosis progresses, a reduction in systemic vascular resistance causes compensatory activation of the renin-angiotensin and sympathetic nervous systems, which leads to ascites, edema, and vasoconstriction of the intrarenal circulation and renal hypoperfusion.

Hepatorenal syndrome (HRS) is caused by functional renal vasoconstriction in response to splanchnic arterial vasodilation. Although histologic findings and diagnostic tests for HRS are lacking, diagnostic criteria are used to categorize two types of HRS. Criteria for HRS include (1) cirrhosis with ascites, (2) serum creatinine greater than 1.5 mg per dL, (3) no improvement of creatinine after 2 days of diuretic withdrawal and volume expansion with albumin, (4) absence of shock, (5) no current or recent treatment with nephrotoxic drugs, and (6) absence of parenchymal kidney disease. Type I HRS involves rapid and progressive impairment of renal function (usually the result of an acute insult such as spontaneous bacterial peritonitis or a large volume paracentesis) with a doubling of the initial serum creatinine to a level greater than 2.5 mg per dL or a 50% reduction in the 24-hour creatinine clearance to lower than 20 mL per minute in less than 2 weeks. The development of type I HRS is associated with a short-term mortality of more than 50%. Patients with type II HRS have impaired renal function and a serum creatinine greater than 1.5 mg per dL and do not meet the criteria for type I HRS. Compared with patients diagnosed with prerenal failure, patients with HRS lack a renal response

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to a 1.5-L volume challenge. Distinguishing between HRS and acute tubular necrosis is difficult. A fractional excretion of sodium less than 1% suggests tubular function and favors a diagnosis of HRS. The presence of renal tubular epithelial cells in urinary sediment favors a diagnosis of acute tubular necrosis.

The administration of terlipressin, a vasopressin analogue, along with intravenous albumin has been shown to have some benefit in patients with type I HRS. Medical management of HRS is marginally effective, but liver transplantation can reverse HRS. Kidneys transplanted from patients with HRS function normally in new hosts, suggesting the essential role of hepatic disease in the pathogenesis. Up to 40% of patients with HRS do not recover

kidney function after transplantation. In these cases, systemic inflammation with hyperbilirubinemia may contribute to irreversible structural damage to the kidney.

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Gludd LL, Christensen K, Christensen E, et al. Terlipressin for hepatorenal syndrome. *Cochrane Database Syst Rev*. 2012;(9):CD005162.

Meltzer J, Brentjens TE. Renal failure in patients with cirrhosis: hepatorenal syndrome and renal support strategies. *Curr Opin Anaesthesiol*. 2010;23:139-144.

Salerno F, Gerbes A, Ginès P, et al. Diagnosis, prevention and treatment of hepatorenal syndrome in cirrhosis. *Gut*. 2007;56:1310-1318.

A.7. What causes hyponatremia in patients with cirrhosis?

Patients with advanced cirrhosis have decreased effective blood volume and then circulatory dysfunction. They develop hypervolemic hyponatremia from increased secretion of antidiuretic hormone, which acts on the vasopressin-2 receptors of the renal tubular collecting duct to impair excretion of solute-free water. These patients have expanded extracellular volume, ascites, and edema.

Patients who develop hypovolemic hyponatremia via loss of extracellular fluid from the kidneys (overdiuresis) or gastrointestinal tract rarely have ascites or edema. These patients may have prerenal failure from low plasma volume and dehydration or hepatic encephalopathy from a rapid reduction in serum osmolality.

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A.8. Discuss the neurologic manifestations of acute and chronic liver disease.

Hepatic encephalopathy is a neuropsychiatric complication of acute and chronic liver disease with features that range from mild confusion to cerebral edema with intracranial hypertension. Patients have disturbances in consciousness, cognitive abilities, behavior, neuromuscular function, concentration, reaction time, memory, and/or electroencephalogram readings. The pathogenesis of hepatic encephalopathy is not understood, but most theories implicate elevated levels of ammonia, a gut-derived neurotoxin, which is shunted to the systemic circulation from the portal system. Bacteria in the gut produce ammonia, which crosses the blood-brain barrier into astrocytes that detoxify it to glutamine. Astrocytes regulate neurotransmission, but their function is decreased when they swell because of increased concentrations of intracellular glutamine. High serum ammonia levels characterize patients with hepatic encephalopathy, even though the degree of

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elevation of ammonia does not correlate with neurologic severity. This observation suggests that other factors, such as hyponatremia, gastrointestinal bleeding, and infection contribute to the development of hepatic encephalopathy. Left untreated, cerebral edema can progress to intracranial hypertension and herniation of the brain. Multiple grading scales assess the severity of hepatic encephalopathy. The most common scales are the West Haven Criteria (Conn Score), which has grades 0 through 4 and the Glasgow Coma Scale (GCS).

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Sakamoto M, Perry W, Hilsabeck RC, et al. Assessment and usefulness of clinical scales for semiquantification of overt hepatic encephalopathy. *Clin Liver Dis*. 2012;16:27-42.

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A.9. Why do patients with ESLD have abnormalities of hemostasis?

Patients with ESLD have hemostatic changes that promote both bleeding and thrombosis. Inadequate synthesis of all coagulation factors (except for von Willebrand factor), thrombocytopenia, platelet function defects, dysfibrinogenemia, and elevated tissue plasminogen activator (tPA) levels cause bleeding. Elevations of von Willebrand factor and factor VIII and decreased levels of a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS-13), protein C, protein S, antithrombin, α2-macroglobulin, plasminogen, and heparin cofactor II favor thrombosis.

Factors VII, X, V, II (prothrombin), and I (fibrinogen) have a short half-life (hours to days) and are synthesized solely in the hepatocytes making possible a “semi-real time” evaluation of the liver's synthetic function. Although patients with liver disease can have abnormal prothrombin times (PTs) from decreased production of procoagulant factors, the rebalanced state of pro- and anticoagulants in patients with liver disease makes the PT an unreliable tool for evaluating tendency to bleed or clot.

Levels of fibrinogen, an acute phase reactant, are normal or increased in liver disease. Patients with severe hepatic dysfunction, however, may synthesize fibrinogen poorly, which increases the risk of bleeding. Although high concentrations of fibrinogen are found in patients with chronic hepatitis, cholestatic jaundice, and hepatocellular carcinoma, clot formation is not enhanced because fibrinogen is dysfunctional. Hyperfibrinolysis (from increased levels of tPA and reduced levels of thrombin-activatable fibrinolysis inhibitor [TAFI] and plasmin inhibitor) has been observed in cirrhotic patients, but its association with bleeding is unclear. Hypofibrinolysis (from increased levels of plasminogen activator inhibitor [PAI] and reduced levels of plasminogen) may restore the balance of fibrinolysis.

Thrombocytopenia and platelet dysfunction are characteristic of ESLD. Thrombocytopenia results from several factors: hypersplenism, which sequesters platelets; consumption of platelets during systemic intravascular coagulation; and impaired hepatic synthesis of thrombopoietin, which produces platelets in the bone marrow. Defective signal transduction; uremia from AKI; and intrinsic defects of adenosine diphosphate (ADP), arachidonic acid, collagen, and thrombin prevent platelet aggregation.

There may be little evidence of deranged coagulation when normal hepatic parenchyma is preserved, such as in an isolated hepatoma.

Northup P, Caldwell S. Coagulation in liver disease: a guide for the clinician. *Clin Gastroenterol Hepatol*. 2013;11:1064-1074.

Tripodi A, Mannucci PM. The coagulopathy of chronic liver disease. *N Engl J Med*. 2011;365:147-156.

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Weeder P, Porte R, Lisman T. Hemostasis in liver disease: implications of new concepts for perioperative management. *Transfus Med Rev*. 2014;28:107-113.

A.10. What is the differential diagnosis for hypoxemia in patients with cirrhosis?

Potential causes of preoperative hypoxemia and respiratory failure in patients with cirrhosis includes atelectasis from the compressive effects of ascites, hepatic hydrothorax, hepatopulmonary syndrome (HPS), and underlying chronic pulmonary disease. Muscle wasting and intra-abdominal hypertension from ascites increase the work of breathing.

Ascites fluid can enter the pleural space through small channels in the diaphragm to cause a hepatic hydrothorax (usually on the right side). Negative intrathoracic pressure during inspiration facilitates movement of fluid from the peritoneum to the pleural space to minimize ascites.

A diagnosis of HPS is considered in patients without cardiopulmonary disease who have a PaO_2 less than 60 mm Hg.

The triad of liver disease and/or portal hypertension, widened age-corrected alveolar-arterial oxygen gradient (more than 15 to 20 mm Hg) while breathing room air, and documented intrapulmonary vascular dilation (IPVD) define HPS. Enhanced production or impaired hepatic clearance of endogenous vasodilators (i.e., nitric oxide, carbon monoxide, vasodilator prostaglandins, substance P) or inhibition of vasoconstrictive substances (i.e., tyrosine, serotonin, and endothelin) by a damaged liver may cause IPVD. IPVD causes hypoxemia via ventilation/perfusion mismatching, intrapulmonary shunt physiology, and diffusion limitation. Patients with HPS often complain of dyspnea and fatigue; they

may have clubbing and spider angiomata on physical examination. Patients may experience platypnea (dyspnea in the upright position relieved by recumbency) or have orthodeoxia (arterial oxyhemoglobin desaturation in the upright position). Preferential perfusion of IPVD (while the patient is upright) may cause these clinical manifestations. Contrast-enhanced echocardiography or perfusion lung scanning with technetium-99m-labeled macroaggregated albumin detects intrapulmonary shunting suggestive of IPVD. Medical therapy for HPS has, to date, been relative ineffective. Currently, the only known treatment option for patients with HPS is a liver transplant.

Hemprich U, Papadakos PJ, Lachmann B. Respiratory failure and hypoxemia in the cirrhotic patient including hepatopulmonary syndrome. *Curr Opin Anaesthesiol*. 2010;23:133-138.

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Zhang J, Fallon MB. Hepatopulmonary syndrome: update on pathogenesis and clinical features. *Nat Rev Gastroenterol Hepatol*. 2012;9:539-549.

A.11. What is portal hypertension? What are the sequelae of portal hypertension?

The normal portosystemic gradient between the portal vein and hepatic vein is less than 5 mm Hg. Intrahepatic vascular resistance and portal venous blood flow increase this gradient and characterize portal hypertension. Liver fibrosis, regenerative nodules, collagen deposition in the space of Disse, endothelial dysfunction, and an imbalance between endogenous vasoconstrictors (e.g., norepinephrine, thromboxane A, endothelin I, angiotensin II, leukotrienes) and vasodilators, such as nitric oxide, increase vascular resistance in the liver. As the pressure gradient between the portal vein and the hepatic vein increases, collaterals such as gastroesophageal and hemorrhoidal varices develop to decompress the portal system. Portal hypertension produces endogenous vasodilators that cause splanchnic vasodilation. Splanchnic vasodilation in turn increases portal blood flow and exacerbates portal hypertension.

Complications of portal hypertension include gastrointestinal bleeding from expansion and rupture of varices, intraoperative bleeding from intra-abdominal collaterals, and formation of ascites and pleural effusions.

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B. Preoperative Evaluation and Preparation

B.1. What preoperative workup is desirable?

Anesthesiologists face several preoperative challenges when patients with ESLD need surgery. Surgical and anesthetic management is complicated for patients with an encephalopathy, AKI, electrolyte abnormalities, ascites, myocardial and pulmonary dysfunction, or coagulopathy. Physiologic perturbations during the perioperative period may precipitate multisystem organ failure. To anticipate and prevent complications from transplantation, underlying conditions should be thoroughly evaluated before surgery. A multidisciplinary team including an anesthesiologist, hepatologist, and surgeon should be involved in preoperative preparation. Consultations may be requested with cardiology, pulmonary, infectious diseases, and nephrology (especially if renal replacement therapy is considered) for patients with comorbidities.

Echocardiography is useful to detect cardiac dysfunction. The chest radiograph rules out pulmonary edema or cardiomegaly in patients with signs and symptoms of pulmonary edema or heart failure. Electrolyte levels, blood urea nitrogen, creatinine levels, albumin levels, bilirubin levels, complete blood count, coagulation parameters, and glucose values should be obtained. In cases of altered mental status, a head computed tomography (CT) scan often is indicated to evaluate intracranial bleeding, herniation, and/or the extent of cerebral edema. Patients who may have received multiple previous transfusions, such as patients

with a history of gastrointestinal bleeding, should be evaluated in advance for crossmatching large quantities of blood products for a transplant operation.

Patients of advanced age or those with risk factors may undergo cardiopulmonary testing for myocardial ischemia (e.g., dobutamine stress echocardiography), cardiac dysfunction (e.g., transthoracic echocardiography), or lung disease (e.g., pulmonary function tests).

Risk factors for adverse cardiac outcomes after liver transplantation include history of stroke, coronary artery disease, and increased intraventricular thickness. Preoperative myocardial evaluation is recommended, typically with functional stress echocardiography and dobutamine. The heart rate must reach 85% of the maximum predicted heart rate for the stress test to be considered adequate. A vasodilatory (e.g., adenosine, persantine) myocardial stress test is less useful because in patients with ESLD, the resting vascular tone is so low that provoking vasodilation with drugs is impossible. Transthoracic echocardiography is useful to estimate right ventricular systolic pressure as a gauge of pulmonary artery pressure. If elevated, pretransplant right heart catheterization may be warranted.

If intraoperative renal replacement (continuous venovenous hemofiltration) therapy is a consideration, a nephrologist should be consulted.

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Sandberg WS, Raines D. Anesthesia for liver surgery. In: Longnecker DE, Tinker JH, Morgan GE, eds. *Principles and Practice of Anesthesiology*. 3rd ed. St. Louis, MO: Mosby; 2007:1338-1377.

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Sharma P, Rakela J. Management of pre-liver transplant patients—part 2. *Liver Transpl*. 2005;11:249-260.

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Wiklund RA. Preoperative preparation of patients with advanced liver disease. *Crit Care Med*. 2004;32: S106-S115.

B.2. How is ascites managed preoperatively?

Ascites is initially managed with a low-sodium diet (<2 g per day) and diuretic therapy. Patients with ascites refractory to treatment with diuretics may require large volume paracentesis and albumin replacement to prevent hypotension and HRS. Large-volume paracentesis is a risk factor for the development of HRS. Patients with ascites should avoid nephrotoxic agents such as nonsteroidal anti-inflammatory drugs (NSAIDs), aminoglycosides, angiotensin-converting enzyme (ACE) inhibitors, and α_1-blockers. Patients may be treated with a transjugular intrahepatic portosystemic shunt (TIPS) in refractory cases of ascites or hepatic hydrothorax.

European Association for the Study of the Liver. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. *J Hepatol*. 2010;53:397-417.

Liou I. Management of end-stage liver disease. *Med Clin North Am*. 2014;98:119-152.

B.3. How is hyponatremia managed preoperatively?

Hyponatremia is associated with HRS, ascites, death from liver disease, and postoperative mortality after transplantation. Distinguishing between hypervolemic and hypovolemic hyponatremia guides treatment. Hypervolemic hyponatremia is managed with fluid restriction (1 to 1.5 L per day) and withholding of diuretics. Vaptans, medications that block the vasopressin-2 receptor, increase solute-free water excretion dose dependently and may preclude water restriction so that diuretics can be continued. Patients with hypovolemic hyponatremia are not given diuretics; instead, saline is administered to increase plasma volume.

Patients who undergo orthotopic liver transplantation are at risk for central pontine myelinolysis (CPM) perioperatively. CPM is a neurologic condition characterized by symmetric noninflammatory demyelinating lesions in the basis pontis. The etiology of CPM is uncertain, but osmotic stress on central nervous system cells is theorized, and CPM correlates with rapid correction of hyponatremia. Rapid changes in concentration of serum sodium cannot be predicted and a “safe” rate of correction of hyponatremia has not been definitively established; some experts recommend sodium correction at a rate less than 12 mEq/L/day.

Preoperative correction of hyponatremia may prevent a rapid rise in serum sodium intraoperatively and postoperatively. During intraoperative fluid replacement, high sodium loads may cause rapid swings in serum sodium, or even hypernatremia, by the end of the case. Sodium bicarbonate should be administered cautiously because it has a high concentration of sodium.

Bernal W, Auzinger G, Dhawan A, et al. Acute liver failure. *Lancet*. 2010;376:190-201.

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Teperman LW, Peyregne VP. Considerations on the impact of hepatic encephalopathy treatments in the pretransplant setting. *Transplantation*. 2010;89:771-778.

Zafirova Z, O'Connor M. Hepatic encephalopathy: current management strategies and treatment, including management and monitoring of cerebral edema and intracranial hypertension in fulminant hepatic failure. *Curr Opin Anaesthesiol*. 2010;23:121-127.

B.4. What is a transjugular intrahepatic portosystemic shunt (TIPS)

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procedure? What is the role of TIPS in the management of patients with ESLD?

During a TIPS procedure, an expandable stent is placed into the liver parenchyma for portosystemic exchange and to decrease portal hypertension. This intervention may prevent recurrent variceal bleeding and manage refractory ascites. The procedure is performed under local or general anesthesia as a "bridge" to liver transplantation in patients with severe liver disease. General anesthesia may be preferred because of the duration of the procedure and the potential for life-threatening events such as bleeding, infection, hemobilia, arrhythmias, liver ischemia, and stent migration. Preoperative evaluation of cardiac function (particularly right ventricular function) is essential because stent placement can rapidly increase venous return and cardiac output to unmask an underlying cardiomyopathy. Unlike older, surgically created portosystemic (e.g., splenorenal) and peritoneovenous (e.g., LeVeen shunt) shunts, a TIPS does not require abdominal operation or vascular diversion, both of which impose technical hazards to future liver transplantation.

Encephalopathy may worsen from enhanced systemic delivery of biogenic amines normally cleared by the liver. The long-term patency of a TIPS is poor, and revisions may be needed before liver transplantation.

Boyer TD, Haskal ZJ. The role of transjugular intrahepatic portosystemic shunt in the management of portal hypertension. *Hepatology*. 2005;41:386-400.

DeGasperi A, Corti A, Corso R, et al. Transjugular intrahepatic portosystemic shunt (TIPS): the anesthesiological point of view after 150 procedures managed under total intravenous anesthesia. *J Clin Monit Comput*. 2009;23:341-346.

Gaba RC, Khiatani VL, Knuttinen MG, et al. Comprehensive review of TIPS technological complications and how to avoid them. *AJR Am J Roentgenol*. 2011;196:675-685.

Scher C. Anesthesia for transjugular intrahepatic portosystemic shunt. *Int Anesthesiol Clin*. 2009;47:21-28.

B.5. How are hepatic encephalopathy and elevated intracranial pressure (ICP) treated?

Initial therapy for hepatic encephalopathy identifies and treats reversible triggers (i.e., gastrointestinal bleeding and infection) of this neuropsychiatric syndrome. Nonabsorbable disaccharides such as lactulose decrease absorption of ammonia from the gut via catharsis. Excessive dosing of lactulose causes dehydration. Oral antibiotics (rifaximin, neomycin, vancomycin, paromomycin, or metronidazole) reduce ammonia-producing enteric bacteria. Rifaximin, in combination with lactulose, may prevent episodes of hepatic encephalopathy.

Patients who develop fulminant hepatic failure are at risk for hepatic encephalopathy, cerebral edema with increased ICP, and a threat of herniation. In cases of altered mental status, a head CT scan is often indicated to evaluate intracranial bleeding, herniation, and/or the extent of cerebral edema. ICP monitoring should be seriously considered for patients with fulminant hepatic failure and encephalopathy, even given the bleeding risks associated with invasive monitors. Bleeding risk seems to be the greatest deterrent to ICP monitoring. There is a risk of approximately 10% for intracranial hemorrhage with insertion of a monitor.

To minimize the risk, epidural transducers are recommended rather than intradural monitors. With or without ICP monitoring, 30-day outcomes are similar. Alternate noninvasive ultrasonographic modalities such as transcranial Doppler and measurements of optic nerve sheath diameters estimate ICP.

ICP elevations to greater than 25 mm Hg should be treated with mannitol to achieve hyperosmolarity. Preoperative hyperventilation has not been shown to improve outcome, and corticosteroids are not indicated. Pentobarbital coma may be indicated for patients unresponsive to mannitol, but coma may worsen cerebral hypoperfusion by causing systemic hypotension. Many centers consider sustained cerebral hypoperfusion (cerebral perfusion pressure <40 mm Hg) a contraindication to transplant because of the high risk for brain death. In the future, transcranial Doppler ultrasonography, near-infrared spectrophotometry, and measurements of extracellular lactate via cerebral microdialysis may offer means of monitoring for elevated ICP in these patients. For anesthesia, drugs or conditions that exacerbate elevations in ICP should be avoided. Recent evidence shows that moderate hypothermia (32° to 33°C) may reduce cerebral edema and intracerebral hypertension; however, the side effects of the maneuvers are greater risk of infection, cardiac dysrhythmias, and coagulopathy.

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Bass NM, Mullen KD, Sanyal A, et al. Rifaximin treatment in hepatic encephalopathy. *N Engl J Med*. 2010;362:1071-1081.

Dmello D, Cruz-Flores S, Matuschak GM. Moderate hypothermia with intracranial pressure monitoring as a therapeutic paradigm for the management of acute liver failure: a systematic review. *Intensive Care Med*. 2010;36:210-213.

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Nielsen HB, Tofteng F, Wang LP, et al. Cerebral oxygenation determined by near-infrared spectrophotometry in patients with fulminant hepatic failure. *J Hepatol*. 2003;38:188-192.

Tofteng F, Jorgensen L, Hansen BA, et al. Cerebral microdialysis in patients with fulminant hepatic failure. *Hepatology*. 2002;36:1333-1340.

Zafirova Z, O'Connor M. Hepatic encephalopathy: current management strategies and treatment, including management and monitoring of cerebral edema and intracranial hypertension in fulminant hepatic failure. *Curr Opin Anaesthesiol*. 2010;23:121-127.

B.6. Should this patient be transfused with fresh frozen plasma prior to surgery?

Management of coagulopathy is challenging because blood tests such as PT and activated partial thromboplastin time (aPTT) do not predict bleeding during liver transplantation.

Patients who need an orthotopic liver transplant usually have severe perturbations in coagulation, but it is neither necessary nor possible to correct them preoperatively. Patients with active sites of bleeding should be transfused with fresh frozen plasma, packed red blood cells, cryoprecipitate, or platelets as dictated by clinical assessment and laboratory tests. In addition, desmopressin (1-deamino-8-D-arganine vasopressin [DDAVP]) may be considered for patients with concomitant renal dysfunction and uremic bleeding. Potentially curative transplant surgery should not be postponed to correct coagulation defects.

Findlay JY, Rettke SR. Poor prediction of blood transfusion requirements in adult liver transplantations from preoperative variables. *J Clin Anesth*. 2000;12:319-323.

Massicotte L, Beaulieu D, Thibeault L, et al. Coagulation defects do not predict blood product requirements during liver transplantation. *Transplantation*. 2008;85:956-962.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2274-2289.

C. Intraoperative Management

C.1. What monitors would you use? Why?

In addition to the monitors recommended by the American Society of Anesthesiologists (electrocardiogram, pulse oximetry, capnography, temperature, and noninvasive blood pressure), a radial arterial catheter is placed for beat-to-beat blood pressure monitoring and frequent sampling of blood. Pulse pressure variation, calculated from the invasive arterial tracing,

assesses fluid responsiveness. A second arterial catheter is placed in the femoral artery to measure central aortic blood pressure. Peripheral arterial pressures may not be reliable in a patient with vasoconstriction, vasodilation, or compression

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of the subclavian artery with rib retraction.

Central line access is established to measure right atrial pressure and to administer drugs. Central venous pressure monitoring does not reliably measure blood volume or change in blood volume. The use of a pulmonary artery catheter depends on local practice and the physiologic state of the patient. Mixed venous oxygen saturation values are measured to assess cardiac output, but these measurements also are influenced by changes in oxygencarrying capacity and oxygen consumption.

Transesophageal echocardiography (TEE) assesses ventricular filling, contractility, and function. Diagnoses such as myocardial ischemia, pulmonary embolism, pleural effusions, and inadequate inferior vena cava (IVC) reconstruction can be observed with TEE. The risk of rupture of esophageal varices with TEE is rare.

Krenn C, DeWolf AM. Current approach to intraoperative monitoring in liver transplantation. *Curr Opin Organ Transplant*. 2008;13:285-290.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2274-2289.

C.2. What are the considerations for the induction of anesthesia?

If there is evidence of tense ascites, recent food ingestion, or a propensity for delayed gastric emptying, a rapid sequence induction of general endotracheal anesthesia is performed. AKI with elevated potassium levels or prolonged immobilization may preclude the use of succinylcholine. Compressive atelectasis from ascites and pleural effusions reduce functional residual capacity and decrease the time to oxygen desaturation. Vasodilating anesthetic agents may cause hypotension if intravascular volume is depleted (i.e., overdiuresis or gastrointestinal losses).

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2274-2289.

C.3. How does liver disease affect intraoperative medication management?

The metabolic activity and clearance of anesthetic medications is impaired in patients with liver disease. Without adjusted doses of medications, duration of drug actions is extended and toxic levels result. Emergence from anesthesia may be delayed.

In the liver, metabolism takes place via two pathways: biotransformation via the cytochrome P450 system (which requires delivery of oxygen molecules via hepatic perfusion) and glucuronide conjugation. The first is decreased in liver disease; the second pathway is relatively spared when dysfunction begins. Many anesthetic drugs (i.e., opioids, barbiturates) bind to albumin in the circulation. Low albumin levels increase the free fraction of drug and can theoretically exaggerate the drug's effect. ESLD, however, alters many other aspects of normal pharmacokinetics such as drug volume of distribution, hepatic extraction and metabolism, renal excretion, and levels of serum proteins other than albumin. The net effect of these changes is unpredictable, making general recommendations for drug administration difficult. A safe approach in these patients is to titrate the drug to the desired effect.

Patients with hepatic dysfunction may be sensitive to sedatives such as midazolam and diazepam. In contrast, the pharmacokinetics of lorazepam, which undergoes glucuronidation, is less likely to be affected by liver disease. Benzodiazepines may precipitate hepatic encephalopathy, and flumazenil can reverse this condition. Conversely, patients who have a history of alcohol abuse may require large doses of benzodiazepines. Rapid redistribution of bolused propofol determines its duration of action, which is not affected by impaired liver metabolism.

The adverse effects of morphine may be more pronounced in patients with severe liver disease. Morphine is metabolized by glucuronidation in the liver, and its intermediate metabolites are eliminated renally. Although the pharmacokinetics of morphine may be

unaltered in patients with mild hepatic disease, a prolonged half-life is associated with a prolonged PT, hypoalbuminemia, encephalopathy, ascites, and jaundice. The elimination of morphine's metabolites can be prolonged in patients with HRS. Metabolism of fentanyl, sufentanil, and morphine, which have a high hepatic extraction ratio, is slowed by impaired hepatic

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blood flow.

In patients with liver disease and edema, muscle relaxant doses are increased because fluid retention increases volume of distribution. The duration of action of muscle relaxants that are metabolized by the liver (i.e., vecuronium and rocuronium) is prolonged. Liver disease reduces plasma cholinesterase activity, and prolonged neuromuscular blockade after succinylcholine has been reported.

Vasodilating anesthetic agents such as propofol and volatile anesthetics may cause hypotension if intravascular volume is depleted (i.e., overdiuresis or gastrointestinal losses) and reduce liver perfusion. In addition to perioperative hemorrhage and hypotension, volatile anesthetics can reduce hepatic blood flow and hepatic oxygen uptake. Compared to the vasoconstrictive effects of halothane, isoflurane and desflurane may improve hepatic blood flow and splanchnic perfusion via hepatic vasodilation.

Patients with ESLD often exhibit coagulation disorders. The presence of a coagulopathy is a contraindication to regional anesthesia, particularly epidural anesthesia.

Kiamanesh D, Rumley J, Moitra VK. Monitoring and managing hepatic disease in anaesthesia. *Br J Anaesth*. 2013;111(suppl 1):i50-i61.

Wiklund RA. Preoperative preparation of patients with advanced liver disease. *Crit Care Med*. 2004;32: S106-S115.

C.4. What happens during the first stage (preanhepatic phase) of the liver transplant operation?

The preanhepatic phase begins with induction of anesthesia and ends with clamping of the hepatic artery. The diseased liver is mobilized; the suprahepatic and infrahepatic vena cava, portal vein, and hepatic artery are isolated; and the bile duct is divided. The anesthesia team manages disorders of coagulation and hemodynamic disturbances. Large losses of ascites cause hypotension and require early fluid resuscitation. Albumin solution and fresh frozen plasma are often used to replete intravascular volume.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2274-2289.

C.5. What happens during the second stage (anhepatic phase) of the liver transplant operation?

The second stage of the liver transplant operation, the anhepatic phase, begins after removal of the diseased liver and ends with reperfusion of the new liver. If the IVC and portal vein are clamped, venous return to the heart and cardiac output decreases. In preparation for clamping and dividing the IVC, a test clamp maneuver (occlusion of the suprahepatic IVC) is performed to assess the resilience of the circulatory system. Hypotension is managed with vasoactive medications, fluid repletion, adjustment of anesthetic agents, correction of hypocalcemia, and venovenous bypass. Anastomoses between the recipient and donor liver are performed in the following order: caval, portal, hepatic artery, and biliary.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2274-2289.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant*. 2009;23:546-564.

C.6. What physiologic disturbances should be anticipated during the second stage (anhepatic phase) of the liver transplant operation?

Without a liver, the patient may develop acidosis and hypocalcemia because lactic acid and citrate are not cleared. Acidemia, reduced urine output, and the absence of hepatic uptake of potassium cause hyperkalemia. The liver regulates glucose levels, but in the anhepatic phase,

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gluconeogenesis is absent. Blood glucose levels are monitored for both hyperglycemia and hypoglycemia.

Merritt WT. Metabolism and liver transplantation: review of perioperative issues. *Liver Transpl*. 2000; 6(4 suppl 1):S76-S84.

C.7. What is venovenous bypass? What are potential advantages and disadvantages of this procedure?

Some centers routinely use venovenous bypass to divert blood flow from the portal circulation and IVC to the right atrium. A Y-shaped tubing is used. One limb of the tubing is inserted into the recipient's portal vein to drain the splanchnic beds. Another limb of the tubing is placed, through a groin cut, down into an iliac vein or the distal IVC. The outflow tubing passes through a pump. Blood returns to the patient through a cutdown access to an axillary vein or through percutaneous access to an internal jugular or subclavian vein (Fig. 16.2).

Potentially, venovenous bypass can decompress the portal circulation and reduce congestion of the gut, decrease hemodynamic instability during clamping of the IVC, maintain normothermia via continuous warming of the bypass circuit, manage blood volume overload, preserve renal perfusion pressure, and improve surgical exposure during dissection. Disadvantages include the complications of venous cannula placement (bleeding, air, or thrombotic embolism); release of proinflammatory mediators; activation of complement, which may contribute to tissue injury and organ failure; and the time and cost of an expensive procedure.

The efficacy and benefits of routine use of venovenous bypass remain controversial. However, portal decompression clearly improves surgical visualization in certain circumstances,

such as in Budd-Chiari syndrome. Other centers reserve venovenous bypass for situations in which interrupted venous return through the IVC depresses the recipient's circulating system.

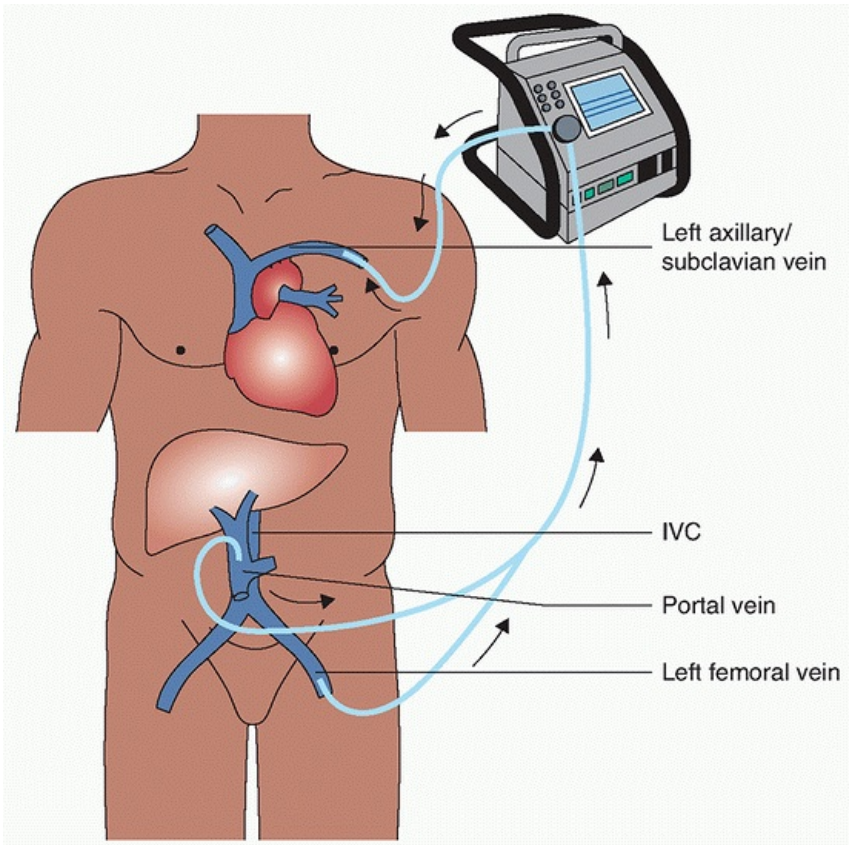


FIGURE 16.2 Schematic diagram of venovenous bypass circuit during liver transplantation. Venous return comes from the femoral and portal veins connected with the tubing connected together into a single venous return line. The centrifugal pump returns the blood into the axillary or subclavian vein. IVC, inferior vena cava.

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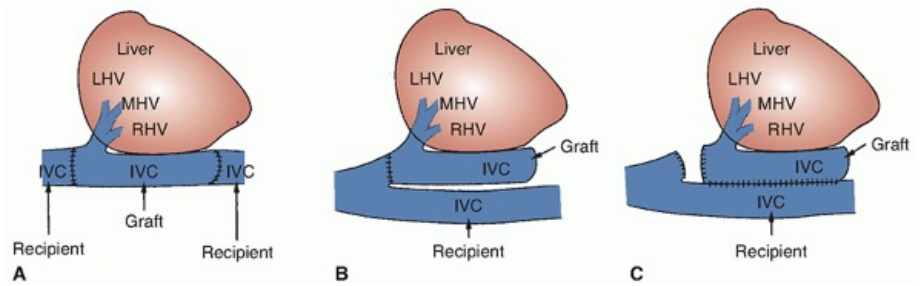


FIGURE 16.3 Three different techniques to reconstruct the hepatovenous outflow. **A.** End-to-end interposition of the donor vena cava to the recipient vena cava. **B.** End-to-end anastomosis of the vena cava to the hepatic veins. **C.** Side-to-side cavo-cavostomy. IVC, inferior vena cava; LHV, left hepatic vein; MHV, middle hepatic vein; RHV, right hepatic vein. (Modified from Hesse UJ, Berrevoet F, Troisi R, et al. Hepato-venous reconstruction in orthotopic liver transplantation with preservation of the recipients' inferior vena cava and veno-venous bypass. *Langenbecks Arch Surg*. 2000;385:350-356.)

Barnett R. Pro: veno-veno bypass should routinely be used during liver transplantation. *J Cardiothorac Vasc Anesth*. 2006;20:742-743.

Hilmi IA, Planinsic R. Con: venovenous bypass should not be used in orthotopic liver transplantation. *J Cardiothorac Vasc Anesth*. 2006;20:744-747.

Hoffmann K, Weigand MA, Hillebrand N, et al. Is veno-venous bypass still needed during liver transplantation? A review of the literature. *Clin Transplant*. 2009;23:1-8.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant*. 2009;23:546-564.

C.8. What surgical techniques anastomose the donor and recipient inferior vena cava?

There are several techniques to anastomose the donor and recipient IVC. Conventionally, blood flow through the IVC is completely interrupted and a cylinder of the recipient's IVC is removed with the diseased liver. An end-to-end anastomosis is created between the donor's and the recipient's IVC (Fig. 16.3A). In the piggyback method, the diseased liver is dissected off the IVC. The recipient's IVC is preserved, and blood flow is not completely interrupted. One end of the graft's segment of IVC is oversewn, and the orifice of the hepatic veins (the liver's venous outflow) is anastomosed to the preserved recipient's suprahepatic IVC (Fig. 16.3B). A third technique creates a side-to-side cavo-caval anastomosis (Fig. 16.3C).

Mehrabi A, Fonouni H, Müller SA, et al. Current concepts in transplant surgery: liver transplantation today. *Langenbecks Arch Surg*. 2008;393:245-260.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant*. 2009;23:546-564.

C.9. What are the potential advantages of the "piggyback" (vena cava preservation) technique?

Potential advantages of the piggyback technique for vascular reconstruction include hemodynamic stability because

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cardiac filling is preserved; protected perfusion pressure; nonneed for the surgical interventions associated with venovenous bypass; reduced need for retrocaval dissection, which lessens the likelihood of damage to the adrenal vein; and shorter anhepatic time and warm ischemia time. A disadvantage of the technique is that outflow obstruction results in hepatic congestion. Unfavorable anatomy in the recipient may preclude the piggyback technique.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant*. 2009;23:546-564.

C.10. What hemodynamic changes are expected after removal of vascular clamps? What is postreperfusion syndrome?

Removal of the suprahepatic IVC clamp is not associated with hemodynamic changes. Unclamping the infrahepatic IVC restores venous return.

After unclamping of the portal vein, desaturated blood from the obstructed portal circulation, inflammatory mediators such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), potassium, protons, and cold components are released into the systemic circulation. Hemodynamic instability, characterized by a decrease in blood pressure, heart rate, systemic vascular resistance, cardiac output, and an increase in pulmonary arterial pressures, may follow unclamping of the portal vein and reperfusion of the liver. Careful flushing of the graft just before completion of the anastomoses attenuates reperfusion disturbances by removing the cold hyperkalemic preservative solution. A sustained 30% decrease in mean arterial blood pressure for more than 1 minute during the first 5 minutes after reperfusion defines postreperfusion syndrome. A prolonged cold ischemic time and the absence of portocaval shunting are associated with the development of postreperfusion syndrome. Before reperfusing the new graft, the following measures should be considered: (1) preemptive administration of calcium to correct hypocalcemia; (2) sodium bicarbonate, dichloroacetate, or tris-hydroxymethyl aminomethane to adjust pH; and (3) inotropes or vasopressors for circulatory support. The surgical and anesthesia teams must be prepared to diagnose and treat dysrhythmias or cardiac arrest.

Paugam-Burtz C, Kavafyan J, Merckx P, et al. Postreperfusion syndrome during liver transplantation for cirrhosis: outcome and predictors. *Liver Transpl*. 2009;15:522-529.

C.11. How would you treat hyperkalemia?

Hyperkalemia is treated with diuretics, β-adrenergic agonists, insulin in combination with glucose, and alkalinization via administration of sodium bicarbonate or hyperventilation. Dysrhythmic effects of elevated potassium may be countered with calcium. Rarely, when hyperkalemia is refractory to the preceding treatments, continuous venovenous hemofiltration may reduce the elevated serum potassium level.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2274-2289.

Xia VW, Ghobrial RM, Du B, et al. Predictors of hyperkalemia in the prereperfusion, early postreperfusion, and late postreperfusion periods during adult liver transplantation. *Anesth Analg*. 2007;105:780-785.

C.12. Why should you anticipate hypocalcemia?

The principal reason to anticipate hypocalcemia is a failure to clear citrate, which normally is metabolized by the liver. This calcium-chelating agent accumulates in patients who receive transfusions of citrated blood products.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2274-2289.

C.13. What happens during the third stage of the liver transplant operation?

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The third stage of the liver transplant operation, the neohepatic phase, follows reperfusion of the new liver. In the neohepatic phase, the biliary drainage system is constructed. Reconstruction may be straightforward, with an anastomosis between the graft's common bile duct and the biliary stump of the recipient. More complex reconstructions are sometimes required, such as the creation of a choledochojejunostomy. A donor cholecystectomy generally is performed. A T-tube is placed in the reconstructed biliary outflow system, with external drainage. An intraoperative cholangiogram, with contrast dye instilled through the T-tube, is used to assess the patency and integrity of the biliary reconstruction. The third stage ends with closure of all wounds and transport to the intensive care unit.

During the third stage of the procedure, an insidious coagulopathy may develop, requiring transfusion.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant*. 2009;23:546-564.

C.14. What causes intraoperative bleeding during each phase of liver transplantation? How is coagulopathy monitored and treated? What are thromboelastography (TEG) and rotational thromboelastography (ROTEM)?

The etiology of intraoperative bleeding during liver transplantation is multifactorial. Patients with ESLD have serious hemostatic defects, and coagulation is affected by alterations in body temperature, tissue perfusion, acid-base balance, and fluid balance.

During the preanhepatic phase, bleeding from the surgical technique is influenced by the patient's underlying coagulopathy. Excessive fluid administration may cause a dilutional coagulopathy and increase venous congestion of the splanchnic area, leading to more bleeding at the surgical site. Bleeding may be minimal in a hypercoagulable state such as hepatocellular carcinoma or cholestatic cirrhosis.

During the anhepatic phase, there is a net increase in systemic tPA derived from endothelial cells, which is normally cleared by the liver. Although PT and aPTT values may not change, hyperfibrinolysis is possible. Hyperfibrinolysis is confirmed by a decrease in α_2-antiplasmin and plasminogen activity and an increase in fibrin and fibrinogen degradation products.

Nonsurgical and insidious bleeding during reperfusion can be profound. Disseminated intravascular coagulation, increased fibrinolysis, release of heparin or heparin-like substances, and trapped platelets in the graft cause coagulopathy.

The coagulation status should always be monitored by inspection of the surgical field. Routine laboratory tests (PT, aPTT, platelet count, fibrinogen levels) are used in some centers for evaluating the coagulation status and directing treatment. Measurements from the TEG or ROTEM assess the viscoelastic properties of a whole blood sample as a function of time to reflect the function and interaction of the plasma, blood cells, and platelets. These measurements detects a hypercoagulable state and distinguishes hyperfibrinolysis from other causes of coagulopathy, such as factor depletion or thrombocytopenia to offer a complete composite picture of the entire clotting cascade (also see Chapter 12, section A.22 and Chapter 57, section C.25). Heparinase may be used to help diagnose coagulopathy resulting from the presence of heparinoids.

Clevenger B, Mallett SV. Transfusion and coagulation management in liver transplantation. *World J Gastroenterol*. 2014;20:6146-6158.

Dalmau A, Sabaté A, Aparicio I. Hemostasis and coagulation monitoring and management during liver transplantation. *Curr Opin Organ Transplant*. 2009;14:286-290.

Krzanicki D, Sugavanam A, Mallett S. Intraoperative hypercoagulability during liver transplantation as demonstrated by thromboelastography. *Liver Transpl*. 2013;19:852-861.

Tripodi A, Mannucci PM. The coagulopathy of chronic liver disease. *N Engl J Med*. 2011;365:147-156.

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C.15. What are the complications of massive transfusion?

Uncontrolled hemorrhage and massive transfusion may cause the lethal triad of acidosis, coagulopathy, and hypothermia. Left uncorrected, each of these abnormalities can exacerbate the other, creating a "blood vicious cycle." Additional early complications of massive transfusion include (1) acute hemolytic transfusion reactions, (2) febrile nonhemolytic transfusion reactions, (3) transfusion-related acute lung injury, (4) transfusion-associated circulatory overload, (5) allergic reactions, (6) bacterial sepsis, (7) hypocalcemia, (8) hyperkalemia, and (9) transfusion-related immunomodulation.

Sihler KC, Napolitano LM. Complications of massive transfusion. *Chest*. 2010;137:209-220.

C.16. How are the complications of massive transfusion prevented?

Warming the room, applying forced warming systems on the patient's body, administering blood products and fluids through a fluid warmer, and heating and humidifying inspired gases reduce the risk of hypothermia. Dilutional coagulopathy and thrombocytopenia may be prevented by transfusing packed red blood cells, fresh frozen plasma, and platelets in a 1:1:1 ratio. Occasionally, recombinant factor VIIa is administered. Potassium, magnesium, and calcium levels are frequently monitored to correct abnormal levels. Metabolic acidosis

is managed by improving hemodynamic parameters, adjusting minute ventilation, and administering sodium bicarbonate or tromethamine for severe metabolic acidosis. The risk of transfusion-related acute lung injury may be reduced by minimizing transfusions and transfusing packed red blood cells with a short storage time and fresh frozen plasma from men or nulliparous women.

Sihler KC, Napolitano LM. Complications of massive transfusion. *Chest*. 2010;137:209-220.

C.17. How is hyperfibrinolysis managed?

tPA has been implicated as a causal agent in hyperfibrinolysis. A functioning graft liver will eventually clear excess tPA from the circulation. Pharmacologic therapy with antifibrinolytic agents (tranexamic acid, ε-aminocaproic acid [Amicar]) blocks fibrin degradation by plasmin, but the full spectrum of their actions remains incompletely defined. The use of prophylactic antifibrinolytic agents in liver transplant surgery has been advocated, but this use is controversial. Potential disadvantages of antifibrinolytic agents include development of thromboses that may be catastrophic.

Groenland TH, Porte RJ. Antifibrinolytics in liver transplantation. *Int Anesthesiol Clin*. 2006;44:83-97.

Ortmann E, Besser MW, Klein AA. Antifibrinolytic agents in current anaesthetic practice. *Br J Anaesth*. 2013;111:549-563.

Xia VW, Steadman RH. Antifibrinolytics in orthotopic liver transplantation: current status and controversies. *Liver Transpl*. 2005;11:10-18.

C.18. When is intraoperative renal replacement therapy indicated?

Managing patients with low urine output, renal dysfunction, or preoperative hyperkalemia who undergo liver transplantation is challenging. Continuous renal replacement therapy may be used intraoperatively to manage volume shifts, acid-base balance, and electrolyte disturbances. Patients who are receiving dialysis and patients who have AKI should have intraoperative continuous renal replacement therapy.

Townsend DR, Bagshaw SM, Jacka MJ, et al. Intraoperative renal support during liver transplantation. *Liver Transpl*. 2009;15:73-78.

C.19. What intraoperative signs suggest that the hepatic graft is working?

Good texture and color of the graft, evidence of bile production, and hemodynamic stability are signs that the graft is

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working. Hypocalcemia often resolves quickly as the graft metabolizes citrate during the final phases of the procedure. Metabolic alkalemia can develop as a result of citrate metabolism. Potassium levels tend to normalize with the onset of hepatocyte function. A number of recipients exhibit hyperglycemia resistant to insulin.

D. Postoperative Management

D.1. What are the goals of immediate postoperative care of the liver transplant patient?

After liver transplantation, patients are admitted to the intensive care unit for monitoring of organ function, management of intraoperative complications, correction of coagulopathy, evaluation of graft function, and initiation of immunosuppression. Although many patients are extubated within 6 hours after the operation, the lungs of liver transplant patients often are mechanically ventilated for 24 to 48 hours.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2274-2289.

D.2. What postoperative findings suggest that the hepatic graft is functioning?

Clearance of lactic acid, production of glucose, resolution of encephalopathy, normothermia, normalization of coagulopathy, decreasing total bilirubin levels, production of bile (through the biliary tube), and adequate urine output suggest a functioning graft. Preservation injury

causes transaminases to rise immediately after surgery, but enzyme levels usually fall within 24 to 48 hours. New synthesis of coagulation factors will not correct factor depletion for hours to days after the transplant.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2274-2289.

D.3. What coagulation disturbances should be anticipated in the postoperative period?

Typically, heparin effects, disseminated intravascular coagulation, or hyperfibrinolysis have been resolved in the operating room. However, dilutional coagulopathy, along with ongoing platelet and factor consumption in the early postoperative phase and poor graft function, may contribute to clinical bleeding. Postoperative uremia compromises platelet function. A functioning graft liver may not produce substantial levels of clotting factors for several days. Therefore, plasma, cryoprecipitate, and/or platelets may be needed in the early postoperative period.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2274-2289.

D.4. Can renal function change after liver transplantation?

Postoperative renal function is correlated with preoperative glomerular filtration rate, and approximately 10% of liver transplant patients require postoperative dialysis. For patients on renal replacement therapy prior to surgery, rate of renal recovery is negatively associated with increasing age, presence of diabetes, and duration of renal replacement therapy greater than 8 weeks. For patients with cirrhosis who have HRS resistant to diuretics, renal function may improve after transplantation. Postoperatively, sepsis and the nephrotoxic calcineurin inhibitors such as cyclosporin A and FK-506 (tacrolimus) may contribute to renal dysfunction. Balanced immunosuppression with steroids, mycophenolate mofetil, anti-CD25 (basiliximab/daclizumab), and antithymoglobulin can minimize posttransplant renal dysfunction. Chronic allograft nephropathy in patients who have received liver, heart, lung, or kidney transplants is now the third most common reason for patients to be on the waiting list for a kidney transplant.

Ginès P, Schrier RW. Renal failure in cirrhosis. *N Engl J Med*. 2009;361:1279-1290.

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Razonable R, Findlay J, O'Riordan A, et al. Critical care issues in patients after liver transplantation. *Liver Transpl*. 2011;17:511-527.

Trotter J, Kahn B. Renal dysfunction and the liver transplant recipient; novel strategies for determination of reversibility and renal protective therapies pretransplant and posttransplant. *Curr Opin Organ Transplant*. 2012;17:225-229.

D.5. What vascular and biliary complications occur after liver transplantation?

Arterial and venous vascular complications include anastomotic bleeding leading to hypovolemia, acute stenosis or occlusion from thrombosis or kinking of the graft vessels, and development of an aneurysm or pseudoaneurysm. Thrombosis of the portal vein or hepatic artery compromises viability of the graft. Abdominal Doppler ultrasound is used to assess the hepatic vessels. Hepatic artery thrombosis, which is more common than portal vein thrombosis, may cause severe liver failure from necrosis. Portal vein thrombosis may cause liver dysfunction, tense ascites, and variceal bleeding.

Biliary complications include bile leak, bile duct stricture, ductal stones, and sphincter of Oddi dysfunction and are associated with the use of T-tubes, Roux-en-Y anastomoses, ischemia-reperfusion injury, cytomegalovirus infection, and hepatic artery thrombosis (leading to duct ischemia). Patients with bile leaks experience fever, abdominal pain, and peritoneal irritation. Bile leaks develop early in the postoperative course and may be identified by ultrasonography showing abdominal fluid collections or cholangiography. Bile leaks are managed with endoscopic placement of a biliary stent or relaparotomy.

Kochhar G, Parungao JM, Hanouneh IA, et al. Biliary complications following liver transplantation. *World J Gastroenterol*. 2013;19:2841-2846.

Mehrabi A, Fonouni H, Müller SA, et al. Current concepts in transplant surgery: liver transplantation today. *Langenbecks Arch Surg*. 2008;393:245-260.

TABLE 16.1 Adverse Effects of Immunosuppressant Medications

MEDICATION	ADVERSE EFFECTS
Cyclosporine	Nephrotoxicity Hypertension
FK-506 (tacrolimus)	Nephrotoxicity Hypertension
Mycophenolate mofetil	Hypertension Leukopenia Abdominal pain Diarrhea Vomiting
Azathioprine	Leukopenia Anemia Thrombocytopenia
Prednisone	Glucose intolerance Osteoporosis

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	Peptic ulcer disease Adrenal suppression
OKT3	Symptoms of cytokine release (fever, chills, dyspnea, wheezing, chest pain) Leukopenia
Antithymocyte globulin	Fever Chills Leukopenia Thrombocytopenia
Basiliximab	Gastrointestinal upset
Daclizumab	Gastrointestinal upset

D.6. What immunosuppressive agents will be given after liver transplantation? What are the major side effects?

The risk of organ rejection is balanced against the adverse side effects (i.e., neurotoxicity, nephrotoxicity, infection, metabolic abnormalities, malignancy, and recurrence of pretransplant conditions such as hepatitis C virus, hepatocellular carcinoma, and sclerosing cholangitis) of immunosuppressive medications. Although protocols vary from center to center, newer regimens have reduced the degree of immunosuppression. A usual induction regimen includes a calcineurin inhibitor such as cyclosporine or FK-506 (tacrolimus), an antimetabolite such as azathioprine or mycophenolate mofetil, and a steroid such as methylprednisolone or prednisone. Antibodies directed against T-cell lymphocytes (e.g., OKT3 or antithymocyte globulin) or the interleukin-2 (IL-2) receptor (basiliximab) or mammalian target of rapamycin (mTOR) inhibitors (e.g., everolimus or sirolimus) may be substituted for cyclosporine or tacrolimus in patients with renal dysfunction or used in short courses to treat rejection. After 6 months to a year, many patients can be weaned to calcineurin inhibitor monotherapy. New drugs for immunosuppression in liver transplantation are monoclonal antibodies to IL-2 receptors (CD25) of T lymphocytes (basiliximab and daclizumab). The adverse effects of these medications are listed in Table 16.1.

Gotthardt D, Bruns H, Weiss KH, et al. Current strategies for immunosuppression following liver transplantation. *Langenbecks Arch Surg*. 2014;399:981-988.

Moser MA. Options for induction immunosuppression in liver transplant recipients. *Drugs*. 2002;62:995-1011.

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Chapter 17
Brain Tumor and Craniotomy

June M. Chan

Kane O. Pryor

A 47-year-old woman who was previously healthy presents with a 4-month history of headache, with intermittent diplopia and gait disturbance developing over the last month. She is admitted after her family witnesses an acute episode of profound lethargy, altered cognition, and vomiting. Neurologic examination is remarkable for abnormal right-sided cranial nerve V, VII, and VIII function, nystagmus, and ataxic gait. Magnetic resonance imaging (MRI) shows a large, right posterior fossa mass that is only slightly hyperintense on T2-weighted images but is clearly demarcated after the intravenous injection of gadolinium contrast. The impression is of a petroclival meningioma, with mass effect on the pons and fourth ventricle. Magnetic resonance angiogram shows a highly vascular tumor drawing principal blood supply from the ascending pharyngeal branch of the ipsilateral external carotid artery. The patient improves clinically following the administration of dexamethasone and mannitol, and the infusion of 2% sodium chloride and is monitored in the neurosurgical intensive care unit (ICU). The day after admission, the patient undergoes uneventful cerebral angiography and partial embolization of the tumor under general anesthesia. She is now scheduled for posterior fossa craniotomy and resection of the tumor.

A. Medical Disease and Differential Diagnosis

1. What is the pathology of intracranial tumors?
2. What is intracranial pressure (ICP), and what are its determinants?
3. How does the presence of a mass alter the ICP in this patient, and what are the clinical manifestations of these alterations?
4. What is cerebral blood flow (CBF), and what are its determinants?
5. What are the cerebral steal syndromes?
6. Are there any issues specific to posterior cranial fossa pathology?
7. What is the role of preoperative embolization therapy?

B. Preoperative Evaluation and Preparation

1. What are the special considerations in preoperative evaluation of the patient scheduled for posterior fossa craniotomy?
2. In a patient who presents with intracranial hypertension, what management might have already been initiated preoperatively, and what are the implications for anesthetic management?

3. What are the types of intraoperative neurophysiologic monitoring (IOM) that would likely be used for this procedure, and how will they affect the anesthetic management plan?
4. What are the options for patient positioning during posterior fossa surgery?
5. What are the principal disadvantages associated with the common posterior fossa craniotomy positions?
6. How does the sitting position affect your preoperative assessment and planning?
7. How should the patient position ultimately be determined?
8. Should this patient receive premedication?

C. Intraoperative Management

1. What are the anesthetic goals for craniotomy?
2. What monitors should be used during craniotomy?

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3. Would you monitor for venous air embolism (VAE)? What are the monitoring options?
4. What specific risks are associated with induction of anesthesia?
5. How would you induce anesthesia?
6. What are the effects of anesthetics on cerebral metabolic rate of oxygen ($CMRO_2$), CBF, and ICP? With this in mind, how would you maintain anesthesia?
7. How would you manage ventilation and maintain arterial carbon dioxide?
8. How would you approach diuretic therapy?
9. How would you manage serum glucose?
10. How would you approach fluid management?
11. Once the bone plate is removed and the dura retracted, the surgeon reports that the brain is still “tight.” What would be your response?
12. If deliberate hypotension is indicated, how will you achieve it?
13. While the surgeon is resecting tumor from near the brainstem, the patient's heart rate suddenly drops to 20 beats per minute. What is your assessment and management?
14. Are there any measures you can take to prevent VAE?
15. During the procedure, the precordial Doppler becomes loud and turbulent. The endtidal CO_2 ($ETCO_2$) drops from 31 mm Hg to 13 mm Hg, and the systemic pressure from 121/63 mm Hg to 64/32 mm Hg. What is your assessment and management plan?
16. What is your approach to emergence? What if the patient does not wake up?

D. Postoperative Management

- What postoperative complications are of greatest concern? What level of monitoring is required?
- What is your approach to postoperative pain control?
- In the ICU, the patient's neurologic status deteriorates and ICP monitoring is instituted. What are the different methods of monitoring ICP, and what are their limitations?

A. Medical Disease and Differential Diagnosis

A.1. What is the pathology of intracranial tumors?

Intracranial tumors may be primary neoplasms or secondary to metastases, infection, inflammation, or vascular disruption. Primary cancers can be classified according to their cell origin, or according to their anatomic location (see Table 17.1). In the United States between 2006 and 2010, meningiomas were the most common (35.8%), followed by gliomas (28%) and pituitary tumors (15.8%). Secondary metastases are far more common than primary intracranial tumors, although the exact incidence is unknown, and most likely originate from lung cancer, breast cancer, and melanoma.

TABLE 17.1 Classification of Intracranial Tumors

Anatomic classification	**Supratentorial**	**Infratentorial**
	• Glioma • Pituitary • Craniopharyngioma • Pineal • Lymphoma • Metastases	• Schwannoma • Medulloblastoma • Ependymoma • Hemangioblastoma • Glioma

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Cell origin	Primary	Secondary

	• Neuroepithelial
	  ◦ Astrocytoma
	  ◦ Oligodendroglioma
	  ◦ Ependymoma
	• Neuronal/mixed neuronal-glial
	• Pineal
	• Embryonal
	  ◦ Medulloblastoma, PNET
	• Cranial and paraspinal nerves
	  ◦ Schwannoma, neurofibroma
	• Meningioma
	• Primary CNS lymphoma
	• Germ cell
		• Metastases
		  ◦ Lung
		  ◦ Breast
		  ◦ Genitourinary
		  ◦ Melanoma
		  ◦ Gastrointestinal
		• Infection
		  ◦ Abscess
		  ◦ Toxoplasmosis
		  ◦ Tuberculosis
		• Inflammation
		  ◦ Sarcoidosis
		• Vascular
		  ◦ Hemorrhage
		  ◦ Giant aneurysm

CNS, central nervous system; PNET, primitive neuroectodermal tumor.

Although the cause of primary intracranial neoplasms remains unclear, there are genetic conditions that predispose to tumor development. There is, for instance, a clear association between meningiomas and neurofibromatosis type 2. Other conditions linked with the development of brain tumors include neurofibromatosis type 1 and 2, von Hippel-Lindau syndrome, tuberous sclerosis, Li-Fraumeni syndrome, and Turcot syndrome. These conditions are associated with extra-tumor manifestations that should be carefully considered during preoperative evaluation (see Table 17.2).

Kufe DW, Pollock RE, Weichselbaum RR, et al, eds. *Holland-Frei Cancer Medicine*. 6th ed. Hamilton, Canada: BC Decker; 2003. http://www.ncbi.nlm.nih.gov/books/NBK13658/. Accessed January 30, 2015.

Nayak L, Lee EQ, Wen PY. Epidemiology of brain metastases. *Curr Oncol Rep*. 2012;14(1):48-54.

Ostrom QT, Gittleman H, Farah P, et al. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2006-2010. *Neuro Oncol*. 2013;15(suppl 2):ii1-ii56.

A.2. What is intracranial pressure (ICP), and what are its determinants?

Normal ICP is 5 to 15 mm Hg (6 to 20 cm H_2O). This pressure results from the physiologic interactions of intracranial structures within the rigid skull. Anatomically, these structures are enclosed within a cranial vault that is divided by tough dural partitions, the falx and tentorium cerebelli. Functionally, intracranial structures can be conceptualized as three compartments within a minimally compliant space:

- *Parenchyma*, consisting of cellular, extracellular, and intracellular fluid components, occupying 80% to 85% of total intracranial volume (˜1,400 mL in the average adult)
- *Cerebrospinal fluid* (CSF), occupying 10% of total intracranial volume (˜75 mL in the cisterns, 50 mL in the subarachnoid space, and 25 mL in the ventricles)
- *Intracranial blood volume*, consisting of both arterial and venous blood, which occupies 5% to 10% total intracranial volume (averaging 150 mL in the adult)

Without compensation, alterations in any one of these compartments will lead to increases in ICP. Monro (1783) and Kellie (1824) first hypothesized that an increase in the

volume of one compartment results a compensatory decrease in the other compartments, thereby preserving normal ICP. Initially, CSF can drain to the spinal CSF reservoir and venous blood to the extracranial veins. This minimizes the change

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in ICP during the early phases of intracranial volume expansion. However, this compensation is limited, especially if the expansion is rapid. At a critical point, these compensatory mechanisms are exhausted, and even small increases in intracranial volumes will result in significant increases in ICP.

TABLE 17.2 Genetic Conditions Associated with Intracranial Tumors

SYNDROME	CHROMOSOME	CHARACTERISTIC TUMOR	OTHER PATHOGNOMIC LESIONS
NF-1	17q11	Optic glioma Brainstem glioma	Café-au-lait spots, Lisch nodules
NF-2	22q12	Bilateral acoustic neuromas Multiple meningiomas	Subcutaneous schwannomas
Retinoblastoma	13q14	Trilateral retinoblastoma	
Von Hippel-Lindau	3p25	Cerebellar, retinal, and spinal hemangioblastoma	
Tuberous sclerosis	9q34	Subependymal astrocytoma Retinal astrocytoma	Ash-leaf spots Shagreen patch Adenoma sebaceum
Sturge Weber	9q21	Leptomeningeal angiomatosis Choroidal hemangioma	Port-wine nevus Glaucoma
Turcot	5q21	Glioblastoma Medulloblastoma	
Li-Fraumeni	17q	Malignant glioma PNET	

NF-1, neurofibromatosis type 1; NF-2, neurofibromatosis type 2; PNET, primitive neuroectodermal tumor.

Early signs of increased ICP include morning—classically occipital—headache, vomiting, minor behavioral changes, sedation, and cognitive slowing. Papilledema on funduscopy is an important sign that is often missed on examination. Further increases in ICP can eventually lead to compressive cranial neuropathies (typically CN VI, causing unilateral mydriasis) and herniation of brain tissue through a noncompliant partition—rapidly resulting in irreversible regional and global neuronal injury.

Kellie G. An account of the appearances observed in the dissection of two of three individuals presumed to have perished in the storm of the 3rd, and whose bodies were discovered in the vicinity of Leith on the morning of the 4th November 1821 with some reflection son the pathology of the brain. *Trans Med Chir Sci Edinburgh*. 1824;1:84-169. https://archive.org/details/transactionsmed00unkngoog. Accessed January 30, 2015.

Kurishima C, Tsuda M, Shiima Y, et al. Coupling of central venous pressure and intracranial pressure in a 6-year-old patient with Fontan circulation and intracranial hemorrhage. *Ann Thorac Surg*. 2011;91(5):1611-1613.

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2015:2158-2199.

Monro A. *Observations on the Structure and Functions of the Nervous System: Illustrated with Tables*. Edinburgh, Scotland: Creech and Johnson; 1783. http://digi.ub.uni-heidelberg.de/diglit/monro1783. Accessed January 30, 2015.

Ursino M, Lodi CA. A simple mathematical model of the interaction between intracranial pressure and cerebral hemodynamics. *J Appl Physiol*. 1997;82:1256-1269.

A.3. How does the presence of a mass alter the ICP in this patient, and what are the clinical manifestations of these alterations?

Within the constraints of the intracranial compliance model outlined earlier, there are certain characteristics of an intracranial mass that influence the degree of ICP alteration:

- *Size*: An intracranial mass exerts effects through its own intrinsic volume and any surrounding edema. Any space-occupying lesion within a relatively fixed intracranial compartment is compensated for through decreases in volume of other intracranial contents.

- *Rate of growth*: A rapidly expanding mass outpaces the rate in which compensatory volume shifts can occur, which leads to an increase in ICP.
- *Anatomic location*: The infratentorial space is notable for being highly susceptible to massrelated alterations in ICP. The area bound by the tentorium cerebelli and occiput is much lower in volume and compliance when compared with the supratentorial space. It also contains vital structures involved in CSF bulk flow between different compartments: the fourth ventricle, which communicates with the supratentorial ventricles and subarachnoid cisterns, and the foramen magnum, which communicates with the spinal column. Any volume shift within the infratentorial space may therefore precipitate a noncommunicating hydrocephalus, which further compromises compensatory mechanisms for intracranial hypertension.
- *Local tissue dysfunction*: The presence of an intracranial tumor causes local effects on surrounding tissue through invasive destruction, induction of neoangiogenesis through the release of oncogenic factors, or compression with ischemic cellular disruption. This results in an inflammatory response that causes further tissue edema and increases in ICP.

Taken together, these considerations account for the differences in the clinical presentation of intracranial masses. A slow-growing mass, particularly in the peripheral supratentorial space, can become sizable with minimal symptoms due to compensatory volume remodeling, whereas a small infratentorial lesion can obstruct the fourth ventricle and rapidly cause significant intracranial hypertension.

In this patient, a slow-growing meningioma has been able to attain a large size before becoming symptomatic. The patient's earliest signs and symptoms were most likely due to a localized mass effect. Nevertheless, the acute decompensation, with rapidly developing signs and symptoms of elevated ICP, probably represent the added component of CSF outflow obstruction at the fourth ventricle. Even with the clinical improvement provided by steroid therapy and osmotic diuresis, this patient certainly has very little volume reserve and intracranial compliance even small further increases in volume—such as an increase in cerebral blood volume (CBV) precipitated by a minimum alveolar concentration (MAC) of volatile anesthetic—have the potential to cause a precipitous spike in ICP.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2199.

Ropper AH. Lateral displacement of the brain and level of consciousness in patients with an acute hemispheral mass. *N Engl J Med*. 1986;314:953-958.

Schaller B, Graf R. Different compartments of intracranial pressure and its relationship to cerebral blood flow. *J Trauma*. 2005;59:1521-1531.

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A.4. What is cerebral blood flow (CBF), and what are its determinants?

The brain is only 2% of total adult body weight, yet receives 15% of the resting cardiac output via the carotid and vertebral arteries. This disproportionately high blood flow is due to the brain's metabolic requirement of oxygen (MRO_2), which consumes approximately 3.5 mL O_2/min/100 g brain tissue, or 20% of total body MRO_2. CBF is approximately 750 mL per minute in the adult, or 50 mL/min/100 g averaged across gray and white matter. Gray matter, which contains neuronal nuclei, is metabolically more active than white matter and consumes 75 versus 45 mL/min/100 g brain tissue.

CBF is determined by cerebral perfusion pressure (CPP), which describes the pressure gradient for blood flow across the cerebral vascular bed, and cerebral vascular resistance (CVR):

CBF = CPP / CVR

On a global level, CPP is the difference between the inflow and outflow pressures of the brain's blood supply. However, the cerebral circulation behaves as a Starling resistor: Its enclosure within the rigid cranial vault allows extravascular pressure (ICP) to compress and compromise venous outflow. Hence, CBF can be expressed as:

CBF = (mean arterial pressure [MAP] − outflow pressure) / CVR

where outflow pressure = CVP or ICP, whichever is higher.

CBF is highly regulated to ensure substrate delivery matches the metabolic demands of neural tissue and to prevent excess blood flow causing cerebral hyperemia. This is termed *flow-metabolism coupling* and is achieved through alterations in CVR via four overlapping mechanisms occurring on a regional and global cerebral level:

- *Vascular myogenic autoregulation*
  - CBF is maintained constant across MAPs of approximately 50 to 150 mm Hg. Based on recent studies in humans, the extremes of this range should be approached with caution, especially the lower boundary; CBF can decrease at MAPs of 60 or even 70 mm Hg. Chronic hypertension causes a rightward shift in the CBF-MAP relationship. Hypocapnia has been demonstrated to broaden the autoregulatory range, whereas hypercapnia and elevated ICP decreases the responsiveness of pressure autoregulation.
- *Metabolic autoregulation*
  - Carbon dioxide (CO_2): CO_2 is a potent cerebral vasodilator. It exerts its effects on the cerebral vasculature primarily by altering CSF pH, although there is evidence that CSF PCO_2 also has a direct effect on cerebral vascular smooth muscle. At normotensive ranges, CBF has a linear relationship with acute changes in $PaCO_2$ between 20 and 80 mm Hg, with CBF changing by 2% to 4% for every mm Hg change in $PaCO_2$. Beyond this range, further changes are limited by extremes in vascular diameter. This response is blunted by systemic hypotension and volatile anesthesia. It is important to note that prolonged hypocarbia or hypercarbia (beyond 6 to 8 hours) will ultimately have little effect on CVR, as CSF pH normalizes with active transport of bicarbonate over the blood-brain barrier. Further, subsequent correction of $PaCO_2$ would likely result in rebound cerebral hyper- or hypoperfusion.
  - Oxygen (O_2): Although variations in PaO_2 within the physiologic range do not affect CVR, acute hypoxemia below 50 mm Hg causes cerebral vasodilation, rapidly reaching maximal response at approximately 30 mm Hg. The exact mechanism of how this occurs is unclear, but it likely involves the direct effects of by-products from anaerobic metabolism and cellular ischemia, such as lactic acid and adenosine. This mechanism is also impaired in the presence of volatile anesthesia.
- *Neurogenic autoregulation*
  - Compared with myogenic and metabolic mechanisms, the autonomic nervous system plays a minor role in cerebral autoregulation. Both sympathetic innervation of cerebral arterioles and circulating sympathomimetics attenuate increases in CBF during severe hypertension, hypoxia, and hypercapnia.

As stated earlier, the presence of an intracranial mass induces dysfunction in surrounding neural tissue via several mechanisms, resulting in ischemia and inflammation. This acidic microenvironment promotes local vasodilatation and vasoplegia with subsequent narrowing of the pressure autoregulatory range. Regional CBF becomes dependent on MAP and ICP, with little ability to compensate for changes in systemic blood pressure. Mass effect alone can increase ICP enough to critically compromise CPP with apparently normal MAP.

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A conservative approach to the management of CPP would suggest that it should not be allowed to fall below 70 mm Hg for any extended period in the baseline normotensive patient. Although a more moderate approach targeting CPPs in the 60- to 70-mm Hg range is commonly used, most neuroanesthesiologists agree that sustained CPP values under 60 mm Hg place the brain at risk, despite the possible neuroprotection afforded by the presence of a GABAergic anesthetic agent.

Giulioni M, Ursino M. Impact of cerebral perfusion pressure and autoregulation on intracranial dynamics: a modeling study. *Neurosurgery*. 1996;39:1005-1014.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2199.

Sharma D, Bithal PK, Dash HH, et al. Cerebral autoregulation and CO_2 reactivity before and after elective supratentorial tumor resection. *J Neurosurg Anesthesiol*. 2010;22:132-137.

ter Laan M, van Dijk JM, Elting JW, et al. Sympathetic regulation of cerebral blood flow in humans: a review. *Br J Anaesth*. 2013;111(3):361-367.

Yoon S, Zuccarello M, Rapoport RM. pCO(2) and pH regulation of cerebral blood flow. *Front Physiol*. 2012;3:365.

A.5. What are the cerebral steal syndromes?

Any intracranial pathology, including marginal ischemia and inflammation surrounding a mass lesion, can cause localized dysfunction of normal cerebral autoregulation and an impaired response to vasoactive agents. The microvasculature in the pathologic region can have an essentially fixed resistance. In this case, if vasodilation occurs in other normal regions of the brain, the decreased vascular resistance in the normal tissue can theoretically shunt blood flow away from the pathologic regions, which are already most vulnerable. This phenomenon is known as *cerebral steal*.

In anesthesia management, cerebral steal is most relevant in the context of hypercapnia and the use of volatile anesthetics. Both of these cause vasodilation of normal vasculature and potentially cause decreased regional CBF in pathologic areas. For volatile anesthesia, cerebral vasodilatation is usually considered to be significant when given in doses of 1 MAC or greater, but as a dose-dependent effect, it may be clinically apparent at 0.5 MAC. During hypocapnia, when there is vasoconstriction in normal tissue, the opposite may occur. In this case, blood flow to pathologic regions can actually increase. This phenomenon is known as *inverse steal* or the *Robin Hood effect*. While both steal effects have been well reported in human literature, the clinical relevance of steal and inverse steal phenomena is unclear. Nonetheless, it is prudent to consider it in anesthetic management.

Alexandrov AV, Sharma VK, Lao AY, et al. Reversed Robin Hood syndrome in acute ischemic stroke patients. *Stroke*. 2007;38(11):3045-3048.

Darby JM, Yonas H, Marion DW, et al. Local “inverse steal” induced by hyperventilation in head injury. *Neurosurgery*. 1988;23:84-88.

McCulloch TJ, Thompson CL, Turner MJ. A randomized crossover comparison of the effects of propofol and sevoflurane on cerebral hemodynamics during carotid endarterectomy. *Anesthesiology*. 2007;106(1):56-64.

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A.6. Are there any issues specific to posterior cranial fossa pathology?

Surgery for tumors in the posterior fossa presents several challenges not seen with supratentorial surgery (Table 17.3). The posterior fossa is a tightly enclosed space in which tumors are often in direct contact with critical brainstem structures,

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including the cranial nerves and brainstem nuclei. The margin for error when operating near these structures is extremely

small, as can be the spatial reserve for postoperative inflammation. The patient with a posterior fossa tumor, especially one close to the brainstem, can worsen neurologically in the hours following surgery as a result of postsurgical inflammation causing edema.

TABLE 17.3 Specific Anesthetic Considerations in Posterior Fossa Craniotomy

SPECIFIC CHALLENGES	MANAGEMENT CONSIDERATIONS
Need for adequate surgical access	• High likelihood of nonsupine positioning - Sitting position - Prone/semiprone position • Reduced access to airway and precordium in case of emergency • Risk of disrupting airway, vascular access, and monitors during position changes • Specific hemodynamic effects of nonsupine positioning - Venous air embolism risk - Venous pooling in sitting position - External abdominal compression in prone position • Positioning-related nerve and soft tissue injury
Brainstem dysfunction	• Intraoperative autonomic instability • Postoperative central respiratory failure
Intraoperative neuromonitoring	• Limitations in the administration of volatile agents and neuromuscular blockade • Need to understand implications of pathologic alterations in intraoperative monitoring signals and the appropriate management response

In addition to the risk of neuronal damage, surgery in proximity to brainstem nuclei can trigger significant intraoperative autonomic and collateral hemodynamic instability, which can be extremely challenging to manage. The most common autonomic event is an acute increase in vagal tone, which in some instances can lead to a prolonged period of asystole, and can be immediately followed by a reflexive surge in sympathetic tone. Further, the risk to cranial nerves and other structures often demands IOM—such as somatosensory evoked potentials (SSEPs), brainstem auditory evoked potentials, or electromyography (EMG)—all of which can substantially restrict and dictate anesthetic management.

Finally, the posterior fossa cannot be accessed with the patient in the conventional supine position. In the past, the sitting position was highly favored by neurosurgeons and presented marked anesthetic challenges because of the increased risk of VAE. Although still common in some centers, the sitting position has fallen out of favor; nonetheless, all of the positions that permit access to the posterior fossa pose management difficulties that must be considered. The risk of VAE, although reduced, often still exists. Other considerations include loss of jugular outflow, deterioration of pulmonary compliance, strain on the cervical spine and brachial plexus, and a lack of access to central venous lines and the airway. In patients who are critically ill or otherwise at risk for life-threatening intraoperative events, it must be remembered that cardiopulmonary resuscitation will always require that the patient be rapidly returned to the supine position.

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Bullock MR, Chesnut R, Ghajar J, et al. Surgical management of posterior fossa mass lesions. *Neurosurgery*. 2006;58:S47-S55.

Gurol ME, St Louis EK. Treatment of cerebellar masses. *Curr Treat Options Neurol*. 2008;10:138-150.

Kan P, Couldwell WT. Posterior fossa brain tumors and arterial hypertension. *Neurosurg Rev*. 2006;29:265-269.

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A.7. What is the role of preoperative embolization therapy?

Highly vascular tumors, especially those that are anatomically difficult to access, present a high risk for substantial intraoperative bleeding. In addition to the systemic risks associated with gross blood loss, peritumor bleeding can severely compromise surgical exposure and exacerbate neuronal and neurovascular inflammation.

To reduce this risk, patients often undergo embolization of the vessels feeding the tumor in the days immediately before surgery. An arterial catheter is inserted, usually in the femoral artery, and guided under fluoroscopy until it rests in any of the vessels that have evolved to supply only the tumor and not normal brain. Low-dose systemic heparinization to achieve activated clotting times of 200 to 300 seconds is required to prevent the formation of microthrombi. At this point, an embolic agent is slowly delivered to occlude the vessel, reducing its vascular supply and thus the degree of bleeding during the operative resection. Currently, the embolic agents available can be considered as two groups: particulate (using a variety of substances such as coils, gelatin sponges, fibrin glue, and polyvinyl alcohol) and liquid (ethylene vinyl alcohol, hyperosmolar mannitol). The choice of agent is determined by angiographic anatomy, tumor vascularity, and tumor histology. Because of collateralization and reestablishment of blood supply, embolization is effective for only a short period and is usually performed within 48 hours of the intracranial resection.

Tumor embolization comes with its own risks and challenges: Vascular anatomy might not always permit embolization, and the embolization itself can precipitate peri-tumor edema and hyperemic changes in blood flow dynamics. These changes are particularly relevant in this patient with a posterior fossa tumor proximate to the brainstem. Deposition of embolic agent into vessels supplying normal brain amounts to an embolic stroke and can have catastrophic consequences. Catheter-related complications including vessel dissection and rupture, and access site hematomas are well described. Further, embolizations

often require general anesthesia and thus assume all of the associated general and neurospecific risks. Current literature reports embolization-related complication rates for meningiomas at between 2.9% and 4.6% but with significant decreases in intraoperative blood loss.

Ashour R, Aziz-Sultan A. Preoperative tumor embolization. *Neurosurg Clin N Am*. 2014;25(3):607-617.

Carli DF, Sluzewski M, Beute GN, et al. Complications of particle embolization of meningiomas: frequency, risk factors, and outcome. *AJNR Am J Neuroradiol*. 2010;31:152-154.

Raper DM, Starke RM, Henderson F Jr, et al. Preoperative embolization of intracranial meningiomas: efficacy, technical considerations, and complications. *Am J Neuroradiol*. 2014;35(9):1798-1804.

Young WL. Anesthesia for endovascular neurosurgery and interventional neuroradiology. *Anesthesiol Clin*. 2007;25:391-412.

B. Preoperative Evaluation and Preparation

B.1. What are the special considerations in preoperative evaluation of the patient scheduled for posterior fossa craniotomy?

In addition to the routine thorough preoperative evaluation, the evaluation of the patient for craniotomy should answer

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several questions that critically influence anesthesia management:

- What is the ICP? If ICP is still in the normal range, how much intracranial compliance reserve is likely to exist?
- How is autoregulation likely to be affected by the pathology and chronic changes in blood pressure? What range of arterial pressures will be required to preserve adequate CPP and CBF?
- Does the patient have any of the electrolyte and endocrine abnormalities associated with intracranial pathology or treatment, such as neurogenic diabetes insipidus, or hypernatremia resulting from hypertonic saline therapy?
- Is the lesion highly vascular, difficult to access, or situated proximate to one of the large draining veins—all of which increase the probability of significant bleeding?
- What is the likely positioning, and does it incur a risk of VAE, obstruction of jugular venous outflow, or neck hyperextension? Are there preoperative patient conditions that would significantly increase the risk of, or preclude certain positions, such as patent foramen ovale and right to left intracardiac shunts?
- Is the tumor located in a position close to the brainstem such that severe autonomic dynamics are likely?
- Will the baseline neurologic status affect the ability to extubate or to establish an early neurologic assessment after general anesthesia?
- Will the anesthetic technique need to accommodate specific monitoring requirements, such as electroencephalography (EEG), electrocorticography, brainstem auditory evoked responses (BAERs), or SSEPs?

Fischer SP. Preoperative evaluation of the adult neurosurgical patient. *Int Anesthesiol Clin*. 1996;34:21-32.

Jellish WS, Murdoch J, Leonetti JP. Perioperative management of complex skull base surgery: the anesthesiologist's point of view. *Neurosurg Focus*. 2002;12:E5.

Lieb K, Selim M. Preoperative evaluation of patients with neurological disease. *Semin Neurol*. 2008;28:603-610.

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B.2. In a patient who presents with intracranial hypertension, what management might have already been initiated preoperatively, and what are the implications for anesthetic management?

A patient with evidence of intracranial hypertension will be aggressively monitored and treated preoperatively; it is likely that the preoperative assessment will occur in an intensive care setting. The anesthesiologist must be familiar with the management of intracranial hypertension. These therapies will likely need to be initiated or continued in the operating room. Further,

the anesthesiologist must be mindful of potential sequelae that can arise from various perioperative therapies and interventions such as:

- *Corticosteroids*. Treatment can lead to hyperglycemia, which should be aggressively treated to maintain plasma glucose less than 150 to 180 mg per dL while taking care to avoid hypoglycemia.
- *Head elevation*. Care should be taken to maintain 30-degree head elevation, where possible, and to avoid rapidly lowering the head during transport.
- *Diuretics (mannitol, furosemide)*. These can result in electrolyte or acid-base abnormalities. Decreased preload can increase the risk of hypotension in the peri-induction period.
- *Isotonic or hypertonic saline therapy*. This can result in hypernatremia or a hyperchloremic, non-anion gap metabolic acidosis.
- *Intubation and institution of hyperventilation*. If prolonged, the CBF response to CO_2 can become diminished or absent, with a risk for dangerous increases in CBF and ICP if hyperventilation is rapidly ceased. It can also lead to a compensatory loss of bicarbonate and other basic metabolic buffers leading to the development of acidosis if

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ventilation was normalized. Care should be taken to avoid hypoventilation during transport.

- *Ventriculostomy*. This is usually clamped during transport to or from the ICU, as the level of the drain relative to the head is critical, and accidental changes in position can result in excessive draining of CSF. It should be attended to on arrival to the operating room because even relatively short periods of clamping can result in elevations of ICP.
- *Manipulation of systemic pressures to optimize CPP*. Care should be taken to ensure drug infusions are maintained during transport to avoid rebound hypertension or hypotension.
- *Drug-induced cerebral vasoconstriction and coma*. Propofol infusion and pentobarbital are the typical agents currently used in the United States, following the decline in the availability of thiopental. This signifies a critical neurologic status. The therapy is often continued as the primary anesthetic.
- *Deliberate hypothermia*. This signifies a critical neurologic status and requires discussion of intraoperative temperature management goals with the neurosurgeon and neurointensivist because the neuroprotective benefits may be countered by hypothermia-induced coagulopathy.

Li LM, Timofeev I, Czosnyka M, et al. Review article: the surgical approach to the management of increased intracranial pressure after traumatic brain injury. *Anesth Analg*. 2010;111:736-748.

Perez-Barcena J, Llompart-Pou JA, O'Phelan KH. Intracranial pressure monitoring and management of intracranial hypertension. *Crit Care Clin*. 2014;30(4):735-750.

Stevens RD, Bhardwaj A. Evolving paradigms in the management of severe traumatic brain injury. *Crit Care Med*. 2005;33:2415-2417.

Vincent JL, Berré J. Primer on medical management of severe brain injury. *Crit Care Med*. 2005;33:1392-1399.

B.3. What are the types of intraoperative neurophysiologic monitoring (IOM) that would likely be used for this procedure, and how will they affect the anesthetic management plan?

IOM uses a combination of stimulators and sensing electrodes to detect the functional integrity of sensory, motor, and cranial nerves and their associated nerve tracts and/or muscles. The primary monitoring modalities are EMG, evoked potentials (EPs), and EEG. EEG is rarely used for craniotomies for tumor resection and will not be considered in detail in this chapter.

EMG records the electrical activity within muscle in response to the stimulation of its innervating cranial or peripheral nerve. The most common EMG monitoring during posterior fossa surgery is for cranial nerve VII, although monitoring of V, IX, X, and XI is frequently encountered. Usually, the surgeon will deliver a very low current to a structure he or she believes could be the cranial nerve of interest, and muscular activity is monitored in the distribution of the nerve. Mechanical manipulation of a nerve will often also cause muscular activity, which may herald potential inadvertent injury. EMG is relatively unaffected by volatile and intravenous anesthetic agents but requires intact functioning of the neuromuscular

junction. Therefore, neuromuscular blockers cannot be used for EMG monitoring beyond anesthetic induction. Some anesthesiologists advocate the use of succinylcholine for intubation; nevertheless, a low intubating dose of a medium-duration nondepolarizing agent such as rocuronium, vecuronium, or cisatracurium typically allows adequate return of muscular function by the time monitoring is relevant and avoids the potential problems associated with succinylcholine.

EPs measure electrical activity generated within the nervous system in response to a stimulus. The most common EP monitoring encountered during resection of posterior fossa tumors is the BAER, which monitors cranial nerve VIII and auditory pathway function (including portions of the brainstem, midbrain, and the primary auditory cortex) in response to sounds generated in the auditory canal. SSEPs can also be used to monitor dorsal column-medial lemniscus tract integrity, which is useful for posterior fossa surgery given the superficial location of the medial lemniscus in the brainstem and pons. These are elicited via electrical stimulation of peripheral sensory nerves (most commonly median and posterior tibial nerves) and recorded via scalp needle electrodes directed over the somatosensory cortex. Similarly, motor evoked potentials (MEPs) are obtained through transcranial stimulation of cortical pyramidal cells and recorded distally along the spinal cord, motor nerves, and muscle.

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EPs are recorded as positive and negative deflections from baseline. The time delay from stimulus to first recorded deflection is termed the latency, and the maximal deflection from baseline is the amplitude. A significant increase in latency or decrease in amplitude of EPs can reflect injury along the nerve tract, or dysfunction due to physiologic or pharmacologic factors. Anesthetic agents can dramatically alter EPs in the absence of other abnormalities (Table 17.4). Although BAERs are reasonably robust, MEPs (and SSEPs to a lesser but still significant degree) are exquisitely sensitive to volatile anesthetics, which cause decreases in amplitude and increases in latency in a dose-dependent manner. Further, neuromuscular blockers cannot be used if MEPs are proposed. Volatile agents should be kept at less than 0.5 MAC, and nitrous oxide should not be used. The anesthetic plan will often rely heavily on opioids; propofol and dexmedetomidine infusions are also often incorporated, the latter of which may also offer improvements in overall hemodynamic stability. Perhaps more important than the specific anesthetic regimen is that a maintenance equilibrium is established for the baseline neurophysiology measurements and is then kept constant throughout the procedure. Pseudo-equilibrated steady-state continuous infusions are key to this strategy.

TABLE 17.4 Anesthetic Effects on Intraoperative Neuromonitoring

	AFFECTED BY	RESISTANT TO
SSEP	Volatile agents (goal <0.5 MAC) Nitrous oxide Intravenous agents	Muscle relaxants Opioids
BAEP		Volatile agents Nitrous oxide Muscle relaxants Intravenous agents Opioids
MEP	Muscle relaxants Volatile agents (avoid; use TIVA)	Opioids
EMG	Muscle relaxants	Volatile agents Propofol Nitrous oxide Opioids

BAEP, brainstem auditory evoked potential; EMG, electromyography; MAC, minimum alveolar concentration; MEP, motor evoked potential; SSEP, somatosensory evoked potential; TIVA, total intravenous anesthesia.

TABLE 17.5 Physiologic Effects on Intraoperative Neuromonitoring

	EFFECTS
Temperature	• Progressive hypothermia predictably increases latency in SSEPs but has variable effects on amplitude (can increase in mild hypothermia and decreases with moderate hypothermia). • Visual evoked potentials are completely lost at 25°C-27°C. • BAEPs are more resistant to hypothermia, but changes reflect those of SSEPs at lower temperature thresholds.

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	• Hyperthermia to 40°C decreases latency but with further increases slowing occurs, likely reflecting neuronal injury.
Hematocrit	• Changes similar to ischemia in SSEPs and VEPs are seen with acute isovolemic hemodilution to hematocrit of 10%-15% in animals, with resolution when hematocrit was increased to 20%-22%.
Oxygen	• Mild hypoxemia has minimal effects on SSEPs and BAEPs. • Severe ischemia increases latency and decreases amplitude of SSEPs, with cortical responses being more sensitive than spinal responses. BAEPs are similarly affected.
Carbon dioxide	• Hypocarbia ($PaCO_2$ 20-25 mm Hg) decreases latency in SSEPs. • Hypercarbia (to $PaCO_2$ 55 mm Hg) has minimal effects on SSEPs.

BAEPs, brainstem auditory evoked potentials; SSEPs, somatosensory evoked potentials; VEPs, visually evoked potentials.

Although anesthetic agents are major influences on the accuracy of IOM, it should be remembered that physiologic factors such as hypothermia, acidosis, and excessive hemodilution and hypotension can also influence EPs as well as neuronal integrity and should be avoided (Table 17.5).

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Deiner S. Highlights of anesthetic considerations for intraoperative neuromonitoring. *Semin Cardiothorac Vasc Anesth*. 2010;14:51-53.

Harper CM. Intraoperative cranial nerve monitoring. *Muscle Nerve*. 2004;29:339-351.

Lotto ML, Banoub M, Schubert A. Effects of anesthetic agents and physiologic changes on intraoperative motor evoked potentials. *J Neurosurg Anesthesiol*. 2004;16:32-42.

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B.4. What are the options for patient positioning during posterior fossa surgery?

- *Sitting position*. Although used far less often now than two decades ago, it is critically important for the anesthesiologist to understand the sitting position: partly because it could still have specific surgical advantages in some situations and partly because it provides the archetype for the risks and management of VAE. The patient is in a reclined sitting posture such that the feet are at or near the level of the heart. The head is held in a flexed position with a skull fixation device, and the arms are crossed over the chest.
- *Modified sitting position*. Due to concerns about the sitting position, a modified sitting position has been described. This involves the same reclining position as described earlier but with careful position of the hips and legs so that the feet and knees are above the level of the heart. The head is anteriorly flexed and held in place with a fixation device, and the arms are padded and placed on arm boards by the patient's side.

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- *Prone position*. This is especially suitable for lesions in the midline but can be adapted for more lateral approaches by having the head slightly rotated. Depending on body habitus, supporting rolls are placed horizontally across the chest and hips or in parallel along the longitudinal axis of the body. The head is held with a skull fixation device with the neck in a neutral to flexed position.

- *Lateral decubitus position*. This position is suited to cerebellopontine angle tumors and cerebellar hemispheric lesions.
- *Park bench (semiprone) position*. The patient is turned toward a more prone position, moving the upper shoulder out of the surgeon's view and permitting better access to midline lesions.
- *Supine position*. This can sometimes be used with the patient's head rotated. To reduce the amount of rotation of the neck, which can obstruct venous outflow, a supporting roll can be placed under the ipsilateral shoulder and the whole bed rotated away from the surgeon.

Jadik S, Wissing H, Friedrich K, et al. A standardized protocol for the prevention of clinically relevant venous air embolism during neurosurgical interventions in the semisitting position. *Neurosurgery*. 2009;64(3):533-538.

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Rozet I, Vavilala MS. Risks and benefits of patient positioning during neurosurgical care. *Anesthesiol Clin*. 2007;25(3):631-653.

B.5. What are the principal disadvantages associated with the common posterior fossa craniotomy positions?

The greatest concern for the sitting position is the increased risk of VAE. In this position, the head is elevated above the right atrium and beyond the height of the central venous fluid column. This will reduce venous bleeding; it will also enable large volumes of air to be entrained into the central venous circulation, especially through the large dural sinuses, which are tented open. When propagated to the right heart and pulmonary circulation, VAE can range in severity from subclinical to severe, precipitating acute hemodynamic collapse and death. In a patient with a patent foramen ovale—which is present in 25% of the general population and is often undetected—air can traverse to the arterial circulation, causing embolic strokes. Although VAE can occur with other positions, the risk and severity are substantially higher in the sitting position, with recent reported incidences detected by precordial Doppler as high as 50% for minor and major VAE, and significant VAE causing hypotension at 2% to 6% (other literature using transesophageal echocardiography for detection have reported higher rates). Further, the sitting position complicates the effective treatment of VAE, as it is difficult to rapidly lower the patient's head below heart level, and precludes easy access for airway manipulation and cardiopulmonary resuscitation maneuvers when required. The sitting position is also associated with a greater degree of hypotension (thus compromising CPP), an increased risk of pneumocephalus causing postoperative drowsiness, and compression of vulnerable structures including cervical spinal cord from neck flexion causing quadriplegia, oropharyngeal structures causing macroglossia and peripheral nerves causing nerve palsies and pressure areas.

In the prone position, the head is usually slightly elevated above the heart; therefore, the risk of VAE remains ever-present, although the risk of massive entrainment is reduced. Prone positioning can cause a significant decrease in pulmonary compliance and will increase ventilation/perfusion mismatch, leading to atelectasis, venous admixture, and shunting. Virtually no access is available to the airway, chest, or limbs, and in the event of an airway, pulmonary, or cardiovascular emergency, the prone position places the anesthesiologist in a substantially compromised position.

The supine position alleviates many of these issues. Nevertheless, to access even the lateral posterior fossa from the supine position usually requires substantial rotation of the neck. This can cause obstruction of jugular venous outflow, leading to cerebral venous engorgement, with potentially undesirable effects on ICP, CPP, surgical exposure, and bleeding. The neck rotation can also cause brachial plexus injury as well as significant pressure on laryngeal structures with potential vocal cord injury. Placing supports to elevate the ipsilateral shoulder can reduce rotation at the neck.

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Feigl GC, Decker K, Wurms M, et al. Neurosurgical procedures in the semisitting position: evaluation of the risk of paradoxical venous air embolism in patients with a patent foramen ovale. *World Neurosurg*. 2014;81:159-164.

Ganslandt O, Merkel A, Schmitt H, et al. The sitting position in neurosurgery: indications, complications and results. A single institution experience of 600 cases. *Acta Neurochir*. 2013;155:1887-1893.

Lindroos AC, Niiya T, Silvasti-Lundell M, et al. Stroke volume-directed administration of hydroxyethyl starch or Ringer's acetate in sitting position during craniotomy. *Acta Anaesthesiol Scand*. 2013;57(6):729-736.

Rath GP, Bithal PK, Chaturvedi A, et al. Complications related to positioning in posterior fossa craniectomy. *J Clin Neurosci*. 2007;14:520-525.

B.6. How does the sitting position affect your preoperative assessment and planning?

In addition to the standard, meticulous preanesthetic and neurologic assessment, preoperative evaluation should be focused on the following:

- *Presence of intracardiac shunts*. The presence of a patent foramen ovale, right-to-left intracardiac shunts, and pulmonary arteriovenous malformations are generally considered absolute contraindications to the sitting position due to the risk of VAE and subsequent paradoxical air embolism (PAE), which can have disastrous clinical consequences. In the era of increasing litigation, preoperative contrast echocardiography with Valsalva has become part of routine workup for those considered for elective sitting position craniotomy. However, there is a significant drop-off between the incidences of diagnosed VAE, PAE, and subsequent neurologic sequelae. Therefore, in the rare patient with a demonstrated shunt that still requires sitting position craniotomy, it is not routine to proceed to percutaneous shunt closure. Rather, it serves to heighten the surgeon's awareness for absolute, meticulous control of venous bleeding because it is the presence of open entraining vessels that ultimately determines the risk of VAE.
- *Other complications of the sitting position and their impact on the patient* . General anesthesia in the sitting position is associated with a greater degree of hypotension compared with other positions. This is in large part due to venous pooling in the dependent portions of the body causing a fall in preload, coupled with anesthetic depressant effects on systemic vascular resistance and inotropy. This results in a fall in stroke volume and cardiac output, which is compensated in otherwise healthy patients with increases in heart rate and vasoconstriction. Conditions that exaggerate this fall in MAP include hypovolemia and preoperative diuresis, cachexia, advanced age, and therapeutic β-blockade, all of which can blunt compensatory autonomic responses. The concern with aggressive fluid loading intraoperatively is that it could run counter to the therapeutic goals of diuresis and ICP reduction, and the subsequent redistribution when returned to the supine position can cause an exaggerated increase in cardiac filling pressures. Further, the use of vasoconstrictors to maintain adequate MAP in the face of a preload deficit increases the risk of end-organ hypoperfusion and dysfunction, particularly the kidneys. This is particularly relevant if electrolyte derangements coexist because they may worsen with perioperative renal injury.

The additional hydrostatic gradient between the heart and cerebral vasculature in the sitting position places the brain at a greater risk of hypoperfusion, particularly in patients who have underlying carotid or vertebrobasilar atherosclerosis. This history should be actively sought because these patients may require higher MAPs intraoperatively to maintain adequate CPP, and intraoperative MAP measurements should be made at the level of the circle of Willis. There is also a hydrostatic gradient in lung perfusion when under positive pressure ventilation, with the lung apices being susceptible to hypoperfusion. Functionally termed West Zone 1, after the physician and physiologist John West, this area becomes alveolar dead space. A hallmark of increasing alveolar dead space is a broadening arterial-$ETCO_2$ gap, which places the patient at risk of hypercarbia and increased ICP if $ETCO_2$ is used as a surrogate for $PaCO_2$ monitoring. Increases in alveolar dead space also place a greater ventilatory burden on the rest of the lung, which may be of particular concern in patients with obstructive airway disease, despite the gains in functional residual capacity and ventilation/perfusion matching in the dependent portions of the lung in the upright position.

Patients with cervical spinal stenosis and occult atlantoaxial instability are at an increased risk of cervical spinal cord

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ischemia from compression in the anterior flexed neck position and cord hypoperfusion for the reasons discussed earlier. Quadriplegia is a rare

but well-documented complication of the sitting position. The patient should be carefully examined for motion that elicits neurologic symptoms, and these findings discussed with the neurosurgeon. Similarly, patients with macroglossia and obstructive sleep apnea should be identified because they are at risk of further airway swelling and potential obstruction postextubation due to direct compression and potential decrease in venous drainage. Finally, the presence of pressure sores and preexisting peripheral neuropathies should be evaluated because these can potentially worsen even with careful padding in the sitting position.

- *Invasive monitoring*. This involves planning for the detection and management of potential VAE as well as routine invasive arterial pressure monitoring. Patients with neck pathology, scarring from prior central access or irradiation, and morbid obesity can increase the difficulties of central venous or right atrial catheter placement and render emergency placement impossible. This may influence the decision to place a central line preoperatively under radiologic guidance. Collateral flow for arterial catheterization should also be assessed, and the patient interviewed for contraindications for transesophageal echocardiography if it is a part of the management plan.

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Gracia I, Fabregas N. Craniotomy in sitting position: anesthesiology management. *Curr Opin Anaesthesiol*. 2014;27(5):474-483.

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Stendel R, Gramm HJ, Schröder K, et al. Transcranial Doppler ultrasonography as a screening technique for detection of a patent foramen ovale before surgery in the sitting position. *Anesthesiology*. 2000;93:971-975.

B.7. How should the patient position ultimately be determined?

This requires careful patient evaluation and clear communication between the surgeon and anesthesiologist. Surgical exposure should be a primary determinant for patient positioning; however, the vigilant anesthesiologist should be aware of specific patient conditions that may preclude certain positions, anticipate any physiologic insult that may result, and ensure adequate access to treat these insults. If there are significant safety concerns, the anesthesiologist is obliged to discuss these with the neurosurgeon and advocate for alternative positioning if appropriate. One such safety concern is the presence of patent foramen ovale or right-to-left intracardiac shunt. Other conditions may be amenable to a trial of positioning prior to anesthetic induction or surgery. For example, a patient with cervical spinal canal stenosis should be evaluated for neck and shoulder positions that precipitate neurologic symptoms. A patient with compromised pulmonary compliance or reserve can be positioned prone and monitored during other preparations, with alternative positioning sought if the trial fails.

It bears repeating that the risk of VAE is such that we are very reluctant to use the sitting position except where the surgical exposure considerations are overwhelming.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2199.

B.8. Should this patient receive premedication?

Although preoperative anxiety is common among neurosurgical patients, pharmacologic premedication in patients with intracranial mass lesions presents risks that can result in neurologic decompensation, outweighing any benefit in reducing the sympathetic stress response and increasing patient satisfaction. It is prudent, therefore, to avoid sedation premedication outside of the operating room in these patients. Emphasis should instead be placed on nonpharmacologic methods to address anxiety, including a professional, empathetic preoperative visit from the neuroanesthesiologist. Psychoactive medications can unmask subclinical neurologic symptoms and can have a lingering effect at the end of surgery, which at best confuses the postoperative neurologic examination, and at worse can contribute to a failure to

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emerge from anesthesia. Opioids can cause sedation, partial upper-airway obstruction, and

hypoventilation, all of which leads to hypercarbia and increases in intracranial blood volume. In patients with limited intracranial compliance reserve, this small degree of hypoventilation can lead to dangerous increases in ICP. For these reasons, it is imperative that sedating premedication only be administered in a fully monitored setting and under the direct supervision of an anesthesiologist who is able to rapidly intervene and take over ventilation. Once the patient is transferred to the operating room and monitored, we would then administer small doses of short-acting agents to facilitate placement of invasive monitors prior to induction.

Oral dosing of gabapentin and clonidine will attenuate the hemodynamic instability resulting from laryngoscopy and head pinning when given before anesthetic induction and potentially decrease postoperative pain and nausea. The effects of clonidine can likely be mimicked by starting an infusion of dexmedetomidine—also an α_2-adrenergic agonist—as soon as the patient arrives in the operating room.

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Misra S, Koshy T, Unnikrishnan KP, et al. Gabapentin premedication decreases the hemodynamic response to skull pin insertion in patients undergoing craniotomy. *J Neurosurg Anesthesiol*. 2011;23(2):110-117.

Misra S, Parthasarathi G, Vilanilam GC. The effect of gabapentin premedication on postoperative nausea, vomiting, and pain in patients on preoperative dexamethasone undergoing craniotomy for intracranial tumors. *J Neurosurg Anesthesiol*. 2013;25(4):386-391.

C. Intraoperative Management

C.1. What are the anesthetic goals for craniotomy?

Clearly the anesthetic goals for craniotomy include the basic principles of physiologic stability that are common to all anesthetic management. Craniotomy incurs several specific goals that follow from the effects—both helpful and unhelpful—of anesthetic drugs on the brain. Stated succinctly, the anesthetic goals specific to craniotomy are to protect the brain from injury resulting from mechanical or physiologic insult during the perioperative period. *Direct* protection (often referred to simply as *neuroprotection*) can be conceptualized as actions that facilitate the ability of neural tissue to withstand ischemic episodes without inflammation or activation of the apoptotic cascade leading to infarction. Less discrete is the concept of *indirect* protection, which aims to minimize the anteceding ischemic episodes. The principal elements are as follows:

- Management of CBF and CPP
- Management of ICP while the skull is intact
- The provision of a “relaxed” brain. This optimizes surgical exposure, which is critically important in many cases because the field of view available to the surgeon in many craniotomy approaches can be extremely narrow. Further, relaxation reduces the parenchymal pressure—resulting in ischemia exerted by the retraction devices on underlying brain tissue.
- Implementation and timing of pharmacologic measures specifically intended to effect direct neuroprotection, traditionally involving anesthetic-induced induction of a burstsuppression pattern on the EEG (although experimental data suggest that anesthetics can be protective without burst suppression)
- Strict management of physiologic parameters that may contribute to brain injury, such as serum glucose, osmolarity, and acid-base balance
- Minimize the effect of anesthetic pharmacology, cerebral perfusion, and temperature on neurophysiologic monitoring, such as EEG, BAERs, or SSEPs.
- Facilitate early neurologic assessment.

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Bhagat H, Dash HH, Bithal PK, et al. Planning for early emergence in neurosurgical patients: a randomized prospective trial of low-dose anesthetics. *Anesth Analg*. 2008;107:1348-1355.

Chui J, Mariappan R, Mehta J, et al. Comparison of propofol and volatile agents for maintenance of anesthesia during elective craniotomy procedures: systematic review and meta-analysis. *Can J Anesth*. 2014;61(4):347-356.

Citerio G, Franzosi MG, Latini R, et al. Anaesthesiological strategies in elective craniotomy: randomized, equivalence, open trial—the NeuroMorfeo trial. *Trials*. 2009;10:19.

Mantz J, Degos V, Laigle C. Recent advances in pharmacologic neuroprotection. *Eur J Anaesthesiol*. 2010;27:6-10.

Miura Y, Kamiya K, Kanazawa K, et al. Superior recovery profiles of propofol-based regimen as compared to isoflurane-based regimen in patients undergoing craniotomy for primary brain tumor excision: a retrospective study. *J Anesth*. 2012;26:721-727.

Pasternak JJ, Lanier WL. Neuroanesthesiology update. *J Neurosurg Anesthesiol*. 2010;22:86-109.

Schifilliti D, Grasso G, Conti A, et al. Anaesthetic-related neuroprotection: intravenous or inhalational agents? *CNS Drugs*. 2010;24(11):893-907.

C.2. What monitors should be used during craniotomy?

In addition to electrocardiography (ECG), noninvasive blood pressure, pulse oximetry, temperature, and capnography monitoring, an arterial line is considered mandatory for all except the most superficial and nonvascular supratentorial tumors, even in those without significant comorbidity. The real-time dynamic assessment of arterial pressure is of paramount importance in patients with intracranial pathology and impaired autoregulation, as CPP and CBF become entirely dependent on MAP. There are multiple occasions of high hemodynamic stress that require rapid measurement and management of blood pressure—namely, induction, intubation, head pinning, epinephrine infiltration of scalp, and emergence, intraoperative emergencies notwithstanding. It also allows for repeated arterial blood monitoring of CO_2, glucose, acid-base physiology, hematocrit, and electrolytes, all of which critically affect patient management. A key concept in neuroanesthesia practice is to ensure the measured arterial blood pressure reflects cerebral inflow pressure. In the prone or sitting position, the head may be significantly higher than the level of the heart, so care must be taken to position the arterial pressure transducer at the level of the circle of Willis, which corresponds approximately to the level of the tragus.

The use of central venous and right heart catheters is less common in craniotomies, except in cases where the sitting position is planned, or where preexisting comorbidity or therapies require it. A central venous catheter allows the safe infusion of hypertonic saline and allows for air aspiration in the event of VAE, although its performance is variable. Beyond these reasons, there is little additional advantage in patient management. Because of this and the potential for complications in its placement, the placement of central lines is not routine in our practice.

Depth of anesthesia monitors, if surgical access allows, are commonly used in some institutions to allow for titration of anesthetic agent and for possible induction of burst suppression. It is rarely used in our practice, mostly because of our frequent use of intraoperative neuromonitoring, which provides similar useful data from the cortical tracing on SSEPs. The use of neurophysiology monitoring such as EEG, EMG, BAERs, or SSEPs is determined by the location of the tumor; although these methods are often performed by neurophysiologists, the anesthesiologist must understand the principles behind them and be aware of the effects of anesthetics, other drugs, and physiologic variables on their integrity.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2199.

C.3. Would you monitor for venous air embolism (VAE)? What are the monitoring options?

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VAE can potentially occur whenever there is an open venous channel beyond the venous fluid column to the heart. The sitting position confers the highest risk of VAE, although it is also been described in prone and lateral position craniotomies where the head is typically slightly elevated above the heart. An additional consideration is that the posterior fossa contains several major dural venous sinuses and their confluences, which are noncollapsible, drain into the internal jugular vein. For these reasons, any posterior fossa craniotomy, regardless of position, should be considered for VAE monitoring.

- *Transesophageal echocardiography* (TEE) is the most sensitive monitor for VAE and PAE, able to detect volumes of 0.02 mL per kg in both the right and left heart, but is invasive and requires expertise in interpretation. Further, it requires constant vigilance and can divide attention from other essential monitoring.

- *Precordial Doppler ultrasound* is noninvasive, highly sensitive (able to detect air volumes of 0.05 mL per kg), and is a part of our routine monitoring for posterior fossa craniotomies. It provides audible feedback, thereby minimizing distraction from other monitoring. However, the requirement for precise placement of the Doppler probe over the right heart becomes challenging when the variety of surgical positioning is considered and is particularly difficult in the prone position. This limits its sensitivity when applied in realworld scenarios. We find that rapid intravenous injection of 5 to 10 mL of saline is useful to ensure adequate detection of turbulent flow, which causes a characteristic coarse change in the basal “swishing” sound of normal pulsatile blood flow.
- *Pulmonary artery catheters* are a less sensitive detector of VAE (0.25 mL per kg air), and invasiveness generally limits use in patents with no other indication for right heart monitoring. Characteristically, a sudden increase in pulmonary artery pressures occurs with VAE, first from reflex pulmonary vasoconstriction and later from the air lock formed by the embolus at right-ventricular outflow tract.
- *End-tidal N_2 monitoring* is not routinely available on anesthesia gas monitors but is noninvasive and highly specific for air embolism. It is superior to $ETCO_2$ despite the latter's ubiquity, being more sensitive, specific and rapidly responsive to air in the pulmonary circulation, but can be difficult to interpret when using air-oxygen carrier gas mixtures. Both end-tidal N_2 and CO_2 can be affected by pulmonary hypoperfusion.
- *Esophageal stethoscope* is discussed here for its historical interest in producing a characteristic mill wheel murmur but is too low in sensitivity (1.7 mL per kg air) and of limited use in detecting late, large VAE.

In our experience, the combination of precordial Doppler, $ETCO_2$, and arterial pressure monitoring is minimally invasive and extremely effective at detecting clinically significant VAE.

The use of a right atrial catheter as a means to aspirate air should be considered in any situation when the risk of VAE is high. Catheter tip position, type, and size have been extensively studied over the years, but consensus on the ideal approach remains disputed. Large-bore (14 gauge), single-lumen, multiorifice catheters have performed best in animal and human studies. Traditionally, the ideal catheter tip position is 2 cm distal to the superior vena canal-right atrial junction. This can be established through TEE, radiographic or intravascular ECG guidance. In the last method, the patient is attached to standard three-lead ECG and the catheter inserted in the usual manner. The lumen is then flushed with $NaHCO_3$ to reduce electrical impedance along the catheter, and the right-arm ECG lead is attached to a conductive connector placed on the line. The catheter should then be advanced into the right ventricle, which can be detected by transducing the pressure waveform. It should then be drawn back until the P wave on the catheter lead is biphasic (midatrium) and then back further to the point at which the P wave and QRS complex are of equal amplitude. The catheter is then pulled back another centimeter and secured. The right atrial catheter can confirm the presence of VAE through the aspiration of air, but its principal utility is therapeutic: It enables significant volumes of air to be rapidly extracted from the right atrium, thus breaking the “air lock” that causes the loss of cardiac output. Nonetheless, even under controlled conditions using ideal equipment, the success rate of air aspiration is 30% to 60% at best, and the catheter is liable to migrate as patient position is changed.

Jadik S, Wissing H, Friedrich K, et al. A standardized protocol for the prevention of clinically relevant venous air embolism during neurosurgical interventions in the semisitting position. *Neurosurgery*. 2009;64(3):533-538.

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Schubert A, Deogaonkar A, Drummond JC. Precordial Doppler probe placement for optimal detection of venous air embolism during craniotomy. *Anesth Analg*. 2006;102:1543-1547.

C.4. What specific risks are associated with induction of anesthesia?

The key considerations for anesthetic induction in the patient with marginal intracranial reserve include the onset of apnea and the hemodynamic effects of anesthetic agents and intubation. With prolonged apnea and hypercarbia, CBV and CBF increase, worsening ICP.

Hypoxemia also has similar effects on ICP, although unless it is in the extremes, hypoxemia causes more deleterious effects by impacting oxygen delivery to the brain.

Hypotension from induction agents compromises CPP, whereas hypertension with laryngoscopy and coughing from inadequate neuromuscular blockade abruptly increases CBF and CBV further. The end point of all these events is a tendency to increase ICP and reduce CPP, leading to decreased cerebral oxygen delivery, ischemia, and potentially herniation in a patient with minimal intracranial compliance.

Lanier WL, Albrecht RF II, Laizzo PA. Divergence of intracranial and central venous pressures in lightly anesthetized, tracheally intubated dogs that move in response to a noxious stimulus. *Anesthesiology*. 1996;84:605-613.

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Sharma D, Brown MJ, Curry P, et al. Prevalence and risk factors for intraoperative hypotension during craniotomy for traumatic brain injury. *J Neurosurg Anesthesiol*. 2012;24(3):178-184.

C.5. How would you induce anesthesia?

In the absence of potential airway difficulty, the most common choice of anesthetic agents will involve an opioid, induction agent, and neuromuscular blocker. Benzodiazepines are not recommended due to their prolonged elimination and disinhibiting effects, especially in the elderly, and can delay awakening and cloud the postoperative neurologic examination. If preinduction anxiolysis is required, dexmedetomidine can be given as a preinduction infusion in the operating room during monitor placement and invasive access. It has advantages over benzodiazepines including preservation of respiratory effort, minimal disinhibition, and reduced interference with EP monitoring. The infusion can be continued through the case, with the additional benefits of MAC reduction and improved intraoperative hemodynamic stability.

A common induction technique is to coadminister large doses of opioid. This reduces the ED50 of intravenous anesthetic dosing (thereby limiting postinduction hypotension), blunts the responses to intubation, and prevents the hypertensive spike seen with head pinning. Fentanyl (slowly titrated to a total dose of 5 to 10 μg per kg), remifentanil bolus and infusion (1 μg per kg bolus, followed by infusion at 0.1μg/kg/min or a target effect site concentration of 3 ng per mL), and alfentanil (30 μg/kg bolus) are all effective regimens. Fentanyl has the advantage of achieving these characteristics without the inconvenience and technical risks of a continuous infusion but at the expense of titratability. All contribute to a relatively cardio-stable induction (especially with an appropriately decreased dose of the intravenous anesthetic agent) and steady maintenance levels, thereby extending MAC-and ED50-sparing effects through the procedure. If volatile agents are used, this allows us to run at less than 1 MAC (and typically at 0.5 to 0.6 MAC) with greater confidence in adequate anesthesia while limiting deleterious effects on ICP. Despite these advantages, high-dose opioids can cause significant sympatholysis, particularly in patients with a dominant sympathetic tone (such as the elderly), necessitating small doses of phenylephrine (40 to 120 μg) or ephedrine (5 to 10 mg) to support the cardiac output. All opioids given in high dose, particularly the more potent drugs such as remifentanil and alfentanil, can precipitate chest wall rigidity, which can compromise ventilation and increase ICP. Finally, it should be reiterated that this technique is only safe if there is certainty that immediate control of ventilation can be achieved.

Propofol is the induction agent of choice, given its favorable effects on CBF, $CMRO_2$, and ICP. However, its vasodilating and negative inotropic effects can cause significant hypotension even in the dose-sparing presence of opioids. With the loss of thiopental from our regular armamentarium, etomidate should be considered in patients where the

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cardiodepressant effects of propofol are considered dangerous. Ketamine is inappropriate at induction doses in patients with marginal intracranial compliance due to increases in CBF, $CMRO_2$, and ICP, despite promising data of its protective effects in neurotrauma literature. An alternative is to add lidocaine 1.5 mg per kg to a high-dose opioid induction, which can further reduce the ED50 of the induction agent further.

Although succinylcholine is not contraindicated in patients with increased ICP, the risks and benefit should be assessed prior to its use. It is preferred in situations where a rapid sequence induction is required and IOM is proposed because an equivalent dose of rocuronium may lead to prolonged paralysis and interfere with baseline recordings. However, because fasciculations can transiently increase ICP, it is recommended to administer a small precurarizing dose of nondepolarizing agent or lidocaine 1.5 mg per kg prior to the administration of succinylcholine. In most other situations, the use of nondepolarizing neuromuscular blockers is generally preferred.

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Bozeman WP, Idris AH. Intracranial pressure changes during rapid sequence intubation: a swine model. *J Trauma*. 2005;58:278-283.

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C.6. What are the effects of anesthetics on cerebral metabolic rate of oxygen ($CMRO_2$), CBF, and ICP? With this in mind, how would you maintain anesthesia?

Volatile Anesthetics

Volatile anesthetics have the characteristic of being direct cerebral vasodilators while reducing $CMRO_2$ in a dose-related fashion. This has been described as an “uncoupling” the flowmetabolism relationship; however, autoregulation remains largely intact at doses of up to 1 MAC. It is more accurate to say that it is a balance between the reductions in $CMRO_2$ with the concomitant decrease in CBF, and the direct vasodilator effect, which causes an increase in CBF. At 1 MAC or greater, autoregulation is lost and the vasodilating effect becomes dominant. In most patients, this increased CBF would be potentially beneficial to the extent that it improves the supply-demand balance (termed *luxury perfusion*), with minor, compensated effects on ICP. In patients with intracranial pathology, however, this increase in CBF causes an increase in CBV and can potentially elevate ICP while the cranial bone is intact, or impede surgical exposure once the bone plate is removed. At doses below 1 MAC in the normal brain, this increase in CBV and ICP can be fully reversed by hypocapnia, as cerebrovascular CO_2 reactivity is preserved. However, as previously discussed, this is impaired or absent in pathologic states.

At equivalent doses, isoflurane causes the greatest decrease in $CMRO_2$, which mitigates some of its direct cerebral vasodilator effect leading to a proportionately modest increase in CBF and ICP. Desflurane has effects similar to isoflurane but appears to cause greater increases in ICP on normocapnic patients and in those with intracranial mass lesions. Sevoflurane causes minimal or slight changes in CBF and ICP despite dose-related decreases in $CMRO_2$ and appears to have the most favorable characteristics in patients with raised ICP.

Additionally, all volatile anesthetics appear to exert neuroprotective effects. And although isoflurane has best been described in animal and human studies, sevoflurane appears to have a similar effect at clinical doses (Table 17.6).

Nitrous Oxide

Despite conflicting studies, nitrous oxide (N_2O) is generally agreed to increase CBF, $CMRO_2$, and ICP. The difficulty with interpreting data on the cerebrovascular effects of N_2O is the heterogeneity of existing literature, with large variations in

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the anesthetic regimens. When given as a sole agent or with minimal adjuvant anesthesia, N_2O markedly increases global CBF, $CMRO_2$, and ICP. This effect is preserved when N_2O is given together with volatile anesthetics, but attenuated with intravenous anesthetics are administered. As an *N*-methyl-D-aspartic acid (NMDA) antagonist, both neuroprotective and neurotoxic effects have been attributed to N_2O through its modulation of glutamate excitotoxicity. N_2O has also been shown to induce neuronal apoptosis via its effects on homocysteine and the formation of reactive oxygen

species. At best, N_2O offers no neuroprotection, and at worst, its effects might be neurotoxic and counterproductive to surgical exposure. When considered together with its other detrimental effects, including the increased risk of vascular thrombosis, postoperative nausea and vomiting, and the potential expansion of air in the cranium and vasculature, the use of N_2O should be limited in craniotomies.

TABLE 17.6 The Effects of Anesthetic Agents on Cerebral Blood Flow, Metabolism, and Intracranial Pressure

	CBF	$CMRO_2$	ICP
Nitrous oxide	↑↑	↑ or =	↑↑
Halothane (1 MAC)	↑↑↑	↓↓	↑↑
Isoflurane (1 MAC)	↑ or =	↓↓↓	↑ or =
Sevoflurane (1 MAC)	↓ or =	↓↓	↑ or =
Desflurane (1 MAC)	↑	↓↓	↑
Propofol	↓↓↓	↓↓	↓↓
Thiopental	↓↓↓	↓↓↓	↓↓
Ketamine	↑↑	=	↑ or =
Etomidate	↓↓	↓↓	↓
Fentanyl	= or ↓	= or ↓	=
Lidocaine	↓↓	↓↓	
Dexmedetomidine	= or ↓	= or ↓	=

CBF, cerebral blood flow; $CMRO_2$, cerebral metabolic rate of oxygen; ICP, intracranial pressure; MAC, minimum alveolar concentration.

Intravenous Anesthetics

The intravenous anesthetics that act through GABAergic mechanisms (e.g., barbiturates, propofol, etomidate) cause a dose-dependent reduction in $CMRO_2$, CBF, CBV, and ICP. In contrast to volatile anesthetics, CBF-$CMRO_2$ coupling is preserved in the basal state, with no added vasodilatory effect. Thus, the direct effect of a drug such as propofol is to

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cause a reduction in $CMRO_2$, and the decreases in CBF, CBV, and ICP follow from intact normal physiologic responses. CO_2 reactivity is preserved. $CMRO_2$ can be reduced to as low as 40% of resting values in the presence of an isoelectric EEG. The preservation of CBF-$CMRO_2$ coupling affords many benefits but also carries an underappreciated risk: If hyperventilation is instituted, it will have an additive effect on the decreases in CBF caused by an intravenous anesthetic. The result is an appreciable risk of inadequate CBF and hypoperfusion ischemia. It must be remembered that the mantra of "craniotomy → hyperventilation" owes its legacy to a time when most neuroanesthetics involved the use of MAC equivalents of vasodilating volatile agents. Etomidate impairs collateral perfusion of ischemic brain in animal experiments through inhibition of nitric oxide synthase and is thus relatively contraindicated in cerebral ischemia.

The NMDA-antagonist ketamine can increase $CMRO_2$, CBF, and ICP, although in small doses concerns about these effects are probably overstated. Indeed, while ketamine may change the oxygen supply-demand relationship in an adverse way, recent studies suggest that ketamine possesses direct neuroprotective effects, especially when combined with GABAergic agents. There is no definitive evaluation of its clinical use; nevertheless, judicious use of ketamine can probably be justified where there are appropriate indications.

Opioids

Broadly speaking, synthetic opioids such as fentanyl, alfentanil, and remifentanil have minimal effects or slightly decrease $CMRO_2$, CBF, and ICP. In human and animal studies, opioids appear to complement the cerebrovascular effects of the background anesthetic, displaying

vasoconstrictor effects in the presence of vasodilating agents and minimal effects when used with vasoconstricting anesthetics. In the spontaneously breathing patient, however, it must be remembered that opioids cause hypoventilation and hypercarbia, leading to increases in CBF, CBV, and ICP.

Many neuroanesthesiologists favor a maintenance strategy of total intravenous anesthesia (TIVA) in an oxygen and air mixture, which is difficult to fault provided that hyperventilation is not excessive. A TIVA approach maximizes the ability to reduce $CMRO_2$ without impairing surgical exposure through increased CBF or causing cerebral steal, but it incurs the disadvantage of complex pharmacokinetics. Other neuroanesthesiologists (including the authors) favor a mixed volatile-intravenous regimen as a primary strategy in most patients. We typically use 0.3 to 0.5 MAC equivalent of a volatile agent, with propofol titrated to the EEG as an end point. Dexmedetomidine and (usually high-dose) opioids are added to blunt hemodynamic responses and confer hemodynamic stability. This strategy causes a reduction in $CMRO_2$ but with minimal impairment of surgical exposure. Unless precluded by monitoring, a nondepolarizing muscle relaxant is added to ensure that the patient does not move while the head is fixed. We revert to TIVA if there is inadequate brain relaxation or if monitoring dictates.

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C.7. How would you manage ventilation and maintain arterial carbon dioxide?

A reduction of $PaCO_2$ decreases CBF and CBV within minutes. Therefore, hyperventilation is a rapidly effective measure that can be instituted to decrease ICP and undoubtedly can improve surgical exposure. Nevertheless, hyperventilation has substantial limitations. At $PaCO_2$ values less than 25 mm Hg, cerebral ischemia can result from a critical reduction in CBF combined with impaired oxygen unloading caused by a large left shift of the oxyhemoglobin dissociation curve due to respiratory alkalosis. Prolonged hyperventilation results in a compensatory loss of serum bicarbonate and can result in rebound acidosis if hyperventilation is rapidly terminated. Further, hyperventilation-induced alkalosis decreases in ionized Ca^{2+}, leading to hemodynamic difficulties and prolonged emergence from effects on synaptic function.

It is important to remember that the difference between $PaCO_2$ and $ETCO_2$ can vary greatly. Therefore, arterial blood gas analysis should be performed as soon as possible after induction to establish the arterial-end-tidal gradient in CO_2 partial pressure. A $PaCO_2$ of approximately 35 mm Hg is reasonable unless ICP is elevated. If, once the bone plate is removed, the surgeons determine that exposure is suboptimal, hyperventilation to a $PaCO_2$ of 30 mm Hg for a limited period is helpful for temporizing while other methods to improve brain relaxation are implemented. Further hyperventilation is reserved for situations in which establishing adequate exposure is extremely difficult. To avoid postoperative acid-base instability,

hyperventilation can be gradually reduced throughout the closure, permitting reestablishment of bicarbonate and Ca^{2+} equilibrium.

Brian JE Jr. Carbon dioxide and the cerebral circulation. *Anesthesiology*. 1998;88:1365-1386.

Curley G, Kavanagh BP, Laffey JG. Hypocapnia and the injured brain: more harm than benefit. *Crit Care Med*. 2010;38:1348-1359.

Gelb AW, Craen RA, Rao GS, et al. Does hyperventilation improve operating condition during supratentorial craniotomy? A multicenter randomized crossover trial. *Anesth Analg*. 2008;106:585-594.

Meyer MJ, Megyesi J, Meythaler J, et al. Acute management of acquired brain injury part I: an evidence-based review of non-pharmacological interventions. *Brain Inj*. 2010;24:694-705.

C.8. How would you approach diuretic therapy?

The purpose of diuretic therapy in intracranial procedures is to dehydrate the brain, thereby leading to a reduction in the volume of the fluid compartment. This facilitates surgical exposure and reduces the requirement for brain retraction. Through the same principle, mannitol is used as therapy for elevated ICP states when the cranium is closed.

Mannitol is an osmotic diuretic that is usually prepared in a 20% solution (20 g per 100 mL). It should initially be given in a dose of 0.5 to 1 g per kg; the total dose can be increased to 1.5 g per kg if initial efforts are ineffective. Higher doses have been reported to lead to cardiac arrest from disruption of cardiac cellular function. Because mannitol initially draws water into the vascular space before it is excreted, rapid dosing can cause a transient increase in ICP, so it should be infused over 20 to 30 minutes. If there is very little intracranial compliance reserve, aggressive dosing should be synchronized with the removal of the bone plate.

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If mannitol does not provide adequate surgical conditions, the loop diuretic furosemide can be used. In a naive adult patient, a dose as low as 5 mg might be adequate. Furosemide does not have the problem of an initial increase in vascular volume and so is preferred in patients with marginal cardiac function who can develop congestive heart failure with a large mannitol load. The combination of mannitol and furosemide can cause electrolyte abnormalities and severe systemic dehydration, placing the patient at risk for hemodynamic instability and cardiac arrhythmias. The use of point of care testing for electrolyte derangements is extremely useful in correcting acute changes in serum sodium and potassium. Because mannitol therapy alone is often adequate, we do not administer furosemide routinely, instead reserving its use for situations when surgical exposure is suboptimal. There is evidence in the neurocritical care setting that substituting loop diuretics with an aldosterone antagonist (which is potassium-sparing) may reduce the severity of potassium flux and arrhythmias; however, this is infrequently used in the perioperative arena.

In cases of extreme cerebral edema, hypertonic saline in concentrations of up to 20% can be used—although the most common concentrations used are 2% or 3%. This can be effective in refractory intracranial hypertension and might even be superior to mannitol for routine diuresis, particularly in patients with preexisting hypovolemia. Its use requires caution because of the risk of severe hypernatremia, and central access is required. Patients who are already receiving hypertonic saline should usually have the infusion maintained during the operative period.

Bebawy JF, Ramaiah VK, Zeeni C, et al. The effect of furosemide on intravascular volume status and electrolytes in patients receiving mannitol: an intraoperative safety analysis. *J Neurosurg Anesthesiol*. 2013; 25:51-54.

Bilotta F, Giovannini F, Aghilone F, et al. Potassium sparing diuretics as an adjunct to mannitol therapy in neurocritical care patients with cerebral edema: effects on potassium homeostasis and cardiac arrhythmias. *Neurocrit Care*. 2012;16:280-285.

Rozet I, Tontisirin N, Muangman S, et al. Effect of equiosmolar solutions of mannitol versus hypertonic saline on intraoperative brain relaxation and electrolyte balance. *Anesthesiology*. 2007;107:697-704.

Thenuwara K, Todd MM, Brian JE Jr. Effect of mannitol and furosemide on plasma osmolality and brain water. *Anesthesiology*. 2002;96:416-421.

Wu CT, Chen LC, Kuo CP, et al. A comparison of 3% hypertonic saline and mannitol for brain relaxation during elective supratentorial brain tumor surgery. *Anesth Analg*. 2010;110:903-907.

C.9. How would you manage serum glucose?

Serum glucose control and its impact on critical care outcomes have been exhaustively studied in the last decade. There is, however, a paucity of literature specific to neurosurgical patients, and fewer yet focus on the influence of intraoperative glucose control on morbidity and mortality. To date, no study has definitively recommended one strategy over another for neurosurgical patients—much of the neuroanesthesiologist's practice is guided by the medical and general surgical critical care experience.

The relationship between glucose control and morbidity can be described as a U-shaped curve, with worsened outcomes seen with both hypo- and hyperglycemia. Hyperglycemia in neuroanesthesia is common, due to the surgical stress response and perioperative administration of steroids. It is associated with increased rates of infection and sepsis, renal insufficiency, and longer duration of intensive care admission. Conversely, hypoglycemia is particularly detrimental to the brain, which is reliant on glucose as a major metabolic substrate.

The two dominant treatment strategies are intensive insulin therapy (IIT) to maintain serum glucose between 80 and 100 mg per dL, and standard therapy (ST) to maintain serum glucose below 180 mg per dL. Neurologic subgroup analyses of the landmark study by Van Den Berghe et al. suggested that IIT was associated with a reduction in ICP, seizures, critical illness polyneuropathy, and diabetes insipidus. More recent data from The Normoglycemia in Intensive Care Evaluation-Surviving Using Glucose Algorithm Regulation (NICE-SUGAR) study investigators, however, did not demonstrate benefit in IIT over ST and actually suggested IIT might be harmful due to higher rates of severe hypoglycemia. This is supported by microdialysis studies in traumatic brain injury patients showing that IIT can cause precipitous neuroglycopenia and increase neuronal injury. For these reasons, it would be prudent to aim for serum glucose levels between 110 and 180 mg per dL in the intraoperative setting while taking meticulous care to avoid hypoglycemia.

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Finfer S, Chittock DR, Su SY, et al; for NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med*. 2009;360:1283-1297.

Kramer AH, Roberts DJ, Zygun DA. Optimal glycemic control in neurocritical care patients: a systematic review and meta-analysis. *Crit Care*. 2012;16:R203.

Lipshutz AK, Gropper MA. Perioperative glycemic control: an evidence-based review. *Anesthesiology*. 2009;110:408-421.

Rice MJ, Pitkin AD, Coursin DB. Review article: glucose measurement in the operating room: more complicated than it seems. *Anesth Analg*. 2010;110:1056-1065.

Rovlias A, Kotsou S. The influence of hyperglycemia on neurological outcome in patients with severe head injury. *Neurosurgery*. 2000;46:335-342.

Van den Berghe G, Schoonheydt K, Becx P, et al. Insulin therapy protects the central and peripheral nervous system of intensive care patients. *Neurology*. 2005;64:1348-1353.

Vespa P, Boonyaputthikul R, McArthur DL, et al. Intensive insulin therapy reduces microdialysis glucose values without altering glucose utilization or improving the lactate/pyruvate ratio after traumatic brain injury. *Crit Care Med*. 2006;34:850-856.

Zetterling M, Hillered L, Englad P, et al. Relation between brain interstitial and systemic glucose concentrations after subarachnoid hemorrhage. *J Neurosurg*. 2011;115:66-74.

C.10. How would you approach fluid management?

If the blood-brain barrier (BBB) is intact, the principal determinant of brain tissue water is the osmotic gradient across the BBB. It is this importance of osmotic gradient that guides the use of hypertonic solutions such as mannitol or hypertonic saline to reduce interstitial water and reduce ICP or to optimize surgical exposure. By the same principle, hypotonic solutions are rarely used because they favor the transport of water into the brain interstitium, thereby promoting the development of edema.

In regions where the BBB is not intact because of pathology and surgical tissue injury, osmotic particles can cross from the capillaries into the interstitial tissue. Therefore, the benefits of hypertonic solutions are lost in these areas. It follows that the benefit obtained from the use of hypertonic solutions is because of an *overall* effect on the brain, not from a *specific* effect in localized regions of brain injury.

These considerations favor the use of isotonic fluids as maintenance fluid in craniotomies. Conventionally, normal saline has been the preferred crystalloid solution; however, concerns

over the risk of developing a non-anion gap, hyperchloremic metabolic acidosis has led to the use of other isotonic crystalloids such as PlasmaLyte (Table 17.7). More controversial is the approach to volume management. Historically, craniotomy patients have been kept deliberately hypovolemic in the belief that this will increase the passage of free water from the brain in situations involving a disrupted BBB. Relatively recent evidence suggests that there is in fact very little reduction in interstitial water and that it comes at the price of significant systemic hypoperfusion and hypotension. Therefore, the favored approach to fluid management is now maintenance of isovolemia with isotonic fluids. Dextrose-containing solutions should never be used except to treat hypoglycemia. Colloids such as 5% albumin can be used when volume expansion is a requirement. Albumin has a plasma half-life of 16 hours, and little is known about how the passage of albumin across a damaged BBB influences interstitial water movement over this time period. Therefore, its routine use is not recommended.

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TABLE 17.7 The Osmolarity and Composition of Commonly Used Crystalloid Solutions

	OSMOLARITY (mOsm/L)	SODIUM CONCENTRATION (mmol/L)	CHLORIDE CONCENTRATION (mmol/L)
Plasma	280-300	140	100
0.9% Saline	308	154	154
Lactated Ringer's	273	130	109
PlasmaLyte	294	140	98
5% Albumin	290	145	0

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2199.

Tommasino C. Fluids and the neurosurgical patient. *Anesthesiol Clin North America*. 2002;20:329-346.

C.11. Once the bone plate is removed and the dura retracted, the surgeon reports that the brain is still "tight." What would be your response?

In almost all cases, the most effective initial response is to transiently increase hyperventilation to a $PaCO_2$ of approximately 27 to 30 mm Hg. If mannitol 1 g per kg has already been administered, small doses of intravenous furosemide can be given until a diuresis is established. If a volatile agent is being used, this should be discontinued and the maintenance strategy converted to TIVA. If the patient has a CSF drain, this can be opened and CSF removed in no greater than 10- to 20-mL aliquots, with reassessment in between. Hypertension should be addressed and treated, and the patient should be well anesthetized to attenuate CBF responses to surgical stimulation. Positioning should be reassessed to eliminate any obstruction to jugular venous outflow. Deliberate hypotension can reduce swelling but incurs the risk of inadequate CPP and hypoperfusion ischemia and is thus instituted sparingly.

C.12. If deliberate hypotension is indicated, how will you achieve it?

Although sodium nitroprusside and volatile anesthetics are historically the most commonly used drugs to achieve sustained decreases in blood pressure, both are very far from ideal. Nitroprusside is highly effective and titratable over extremely short periods, but because it causes cerebral vasodilation, it can actually increase vascular engorgement. Nitroglycerin is also a potent cerebral venous vasodilator, and so it has the same limitation. Similarly, high levels of volatile anesthetic have direct cerebral vasodilatory effects. Further, the uncoupled cerebral vasodilation caused by nitrates and volatile anesthetics can theoretically produce cerebral steal.

In most cases, the required level of blood pressure reduction can be achieved with the use of high-dose remifentanil (or other opioid) and propofol, possibly with the addition of

a β-adrenergic blocker. Remifentanil enables a profound but rapidly reversible opioid level without unfavorable effects on CBF or vasodilation. Similarly, propofol can produce hypotension through systemic vasodilation but does not cause cerebral vasodilation and is rapidly reversible. The mixed adrenergic receptor blocker labetalol is often effective as an adjunctive agent. However, the calcium channel blocker nicardipine is probably the most versatile drug for blood pressure control: It is titratable over relatively short periods and is an excellent choice if hypotension is required in situations in which opioids and anesthetic agents are not appropriate—such as during emergence or in the ICU—although it might impair

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autoregulation. Esmolol infusions can be utilized for a rapidly titratable β_1-adrenergic blockade but are not especially effective if the problem is refractory hypertension. With the advent of these newer drugs, the ganglionic blocker trimethaphan is now rarely used.

Degoute CS. Controlled hypotension: a guide to drug choice. *Drugs*. 2007;67:1053-1076.

Hoffman WE, Edelman G, Ripper R, et al. Sodium nitroprusside compared with isoflurane-induced hypotension: the effects on brain oxygenation and arteriovenous shunting. *Anesth Analg*. 2001;93:166-170.

Narotam PK, Puri V, Roberts JM, et al. Management of hypertensive emergencies in acute brain disease: evaluation of the treatment effects of intravenous nicardipine on cerebral oxygenation. *J Neurosurg*. 2008;109:1065-1074.

C.13. While the surgeon is resecting tumor from near the brainstem, the patient's heart rate suddenly drops to 20 beats per minute. What is your assessment and management?

Surgery near the brainstem nuclei can result in dramatic autonomic disturbances. Profound vagal reflexes can be alarming, sometimes resulting in asystole. These are often followed by a compensatory parasympatholytic-sympathetic reflex. Under such circumstances, the hemodynamics can shift from extreme bradycardia and hypotension to tachycardia and hypertension in a matter of seconds.

The first step is to alert the surgeon to stop operating, which almost always alleviates the problem. Once the hemodynamic status has stabilized, an “autonomic blunting” prophylactic regimen can be given. Glycopyrrolate should be titrated until a 15% to 20% increase in heart rate is observed; if sympathetic reflexes are also involved, β-adrenergic blockade can be added. This approach is usually effective in attenuating the reflexes. In surgery in which an elevated risk of autonomic instability is present, the institution of parasympatholytic prophylaxis should be strongly considered from the outset.

The sudden development of bradycardia should always alert the anesthesiologist to the possibility of a sudden increase in ICP, leading to the Cushing reflex. In this case, hypertension will be seen and the surgeon should be immediately notified.

Koerbel A, Gharabaghi A, Samii A, et al. Trigeminocardiac reflex during skull base surgery: mechanism and management. *Acta Neurochir (Wien)*. 2005;147:727-733.

Schaller B, Probst R, Strebel S, et al. Trigeminocardiac reflex during surgery in the cerebellopontine angle. *J Neurosurg*. 1999;90:215-220.

C.14. Are there any measures you can take to prevent VAE?

Prevention is the cornerstone to the management of VAE because current treatment methods of established VAE are limited in their efficacy. The best prevention of VAE is the neurosurgeon's meticulous control of venous bleeding and the tolerance of lower head positions. Extra vigilance on the part of the neuroanesthesiologist also plays an important role—observing a lack of bleeding on the cut edge of bone during removal of the craniotomy bone flap is an early sign of negative venous pressure and an increased likelihood of VAE. Other measures to reduce VAE include raising the venous fluid column by ensuring adequate hydration, and minimizing venous capacitance through the use of pneumatic calf compression devices and avoidance of venodilators such as nitroglycerin. The use of positive end-expiratory pressure (PEEP) is controversial: PEEP increases cerebral venous pressure and can reduce the risk of entrainment, but it also increases surgical bleeding and can potentially impede CPP. It promotes right-to-left intracardiac shunting, which increases the risk of PAE in susceptible patients, and sudden releases of PEEP (such a ventilator adjustment, or a recruitment

maneuver performed during craniotomy) can increase air entrainment as well as the propagation of PAE. We recommend a limitation of PEEP to <5 cm H_2O and only as a means to optimize patient oxygenation. The use of nitrous oxide has clear theoretical disadvantages in posterior fossa craniotomy, not only in the risk of expanding subclinical intravascular air but also in postoperative tension pneumocephalus. Although there is no clear clinical data to demonstrate these associations, its additional adverse effects on CBF and metabolism, ICP and neurotoxicity makes it difficult to justify its

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use, particularly with the easy availability of excellent alternatives in neuroanesthesia.

Giebler R, Kollenberg B, Pohlen G, et al. Effect of positive end-expiratory pressure on the incidence of venous air embolism and on the cardiovascular response to the sitting position during neurosurgery. *Br J Anaesth*. 1998;80:30-35.

Pasternak JJ, Lanier WL. Is nitrous oxide use appropriate in neurosurgical and neurologically at-risk patients? *Curr Opin Anaesthesiol*. 2010;23:544-550.

Schmitt HJ, Hemmerling TM. Venous air emboli occur during release of positive end-expiratory pressure and repositioning after sitting position surgery. *Anesth Analg*. 2002;94:400-403.

C.15. During the procedure, the precordial Doppler becomes loud and turbulent. The end-tidal CO_2 ($ETCO_2$) drops from 31 mm Hg to 13 mm Hg, and the systemic pressure from 121/63 mm Hg to 64/32 mm Hg. What is your assessment and management plan?

This is a classic presentation of VAE. Immediately inform the surgeon, institute 100% oxygen, and call for skilled assistance. The surgeon should flood the field with saline and urgently prepare the field for lowering the head (e.g., placement of a protective drape over the operative site, adjusting the head fixation device to allow for position change). Where possible, an assistant should reach under the drapes and apply pressure to the jugular veins to prevent further entrainment (but not enough to occlude carotid flow), although this should be only a transient measure. If a right atrial catheter is in place, an attempt should be made to aspirate air with a large syringe (enough to accommodate 15 to 20 mL air). Intravenous fluids should be opened to full flow, and inotropes and vasopressors should be titrated to support the altered hemodynamics. The head should then be lowered to a level below the heart, or as much as possible. The left lateral decubitus position has been advocated but is probably of little benefit.

If the VAE is detected early, the episode will usually resolve. It is almost always appropriate to resume and complete the surgery, although placement of additional monitors before resumption might be warranted. Undetected, massive, or prolonged entrainment of air can lead to cardiac arrest. If cardiac arrest is present or imminent, and the patient is in a prone or semiprone position, the anesthesiologist must prepare the surgeon and others in the room for an emergent move to the supine position to enable resuscitation. For this reason, a stretcher must always be available outside the operating room when patients are in the prone position.

Kerr RH, Applegate RL II. Accurate placement of the right atrial air aspiration catheter: a descriptive study and prospective trial of intravascular electrocardiography. *Anesth Analg*. 2006;103:435-438.

Mirski MA, Lele AV, Fitzsimmons L, et al. Diagnosis and treatment of vascular air embolism. *Anesthesiology*. 2007;106:164-177.

C.16. What is your approach to emergence? What if the patient does not wake up?

Providing an early neurologic assessment is one of the most valuable contributions of the anesthesiologist to outcome in neurosurgical patients. Therefore, it is imperative to have patients emerge quickly, even when surgery has been prolonged. At the same time, the emergence from anesthesia incurs substantial changes in pressure, $PaCO_2$, CBF, and autonomic activity and therefore must be carefully planned. Transitioning from hyperventilation should be gradual in order to prevent rebound acidosis. Adrenergic blocking agents should be administered to attenuate the sympathetic effects often seen during and following emergence in these patients. Nicardipine or labetalol can be considered if the patient exhibits refractory hypertension or hyperreactivity. Reversal of neuromuscular block should be carefully titrated to avoid autonomic instability, with care taken to ensure that the patient does not

move while the head is fixed in pins. Antiemetic therapy should be aggressive because the elevation in ICP caused by retching and vomiting are particularly undesirable in craniotomy patients.

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Coughing or “bucking” during emergence causes dramatic spikes in ICP and must be avoided. Several approaches can be used to avoid this, including the use of intravenous lidocaine, an opioid-based anesthetic, or a deep extubation. In the case of a deep extubation, it must be kept in mind that there is always a risk that an intraoperative neurologic event might cause delayed or failed emergence. A strategy of converting the final phase of the anesthetic to a high-dose remifentanil 0.3 to 0.4 μg/kg/min infusion can be highly effective and enables the volatile agent to be eliminated without the patient reacting. After return of ventilation and cognition, remifentanil infusion is stopped and the patient is extubated.

A failure to emerge can represent a neurologic event resulting from the surgery (such as an intracranial bleed, vessel occlusion, embolic event, or seizure), metabolic derangements, or a pharmacologic effect. In such cases, the time to diagnosis is a critical determinant of outcome. The anesthesiologist must be able to state with confidence that the delayed emergence is unlikely to be pharmacologic. A rapid assessment can be made in the operating room to exclude nonneurologic causes of failure to emerge (Table 17.8); unless there is a clear cause found, a CT scan should immediately be performed. Should this be necessary, the operating room should be left available in the event that an emergent return is required.

In some posterior fossa procedures—especially when near the brainstem—postoperative edema can lead to an anticipated worsening of neurologic status before subsequent improvement on the first or second postoperative day, thereby necessitating prolonged intubation. In these cases, the patient can be awakened at the conclusion of the surgery and once a

neurologic assessment is obtained, resedated for transport to the ICU. A remifentanil infusion of approximately 0.1 μg/kg/min usually enables an intubated patient to perform a cognitive examination and tolerate the presence of the endotracheal tube.

TABLE 17.8 Rapid Assessment of Persistent Coma Immediately Postcraniotomy

INTERVENTION	ASSESS CAUSE OF COMA
Pupillary exam	• New anisocoria suggesting herniation • Pinpoint pupils suggesting narcotic overdose • Dilated reactive pupils suggesting central anticholinergic syndrome
Arterial blood gas with electrolyte and glucose analysis	• Hypoxia • Hypercarbia • Acidosis • Hypoglycemia/hyperglycemia • Hyponatremia/hypernatremia
Processed electroencephalogram (e.g., BIS monitor, IOM)	• Assess depth of anesthesia • Seizure activity
Nerve stimulator	• Deep neuromuscular blockade
Core temperature	• Hypothermia
Review medication syringes, infusions, vaporizer	• Inadvertent overdose • Medication swap • Consider reversal agents:

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	- Naloxone in 40 μg aliquots, up to 400 μg - Flumazenil 200 μg aliquots, up to 1 μg - Physostigmine 1.25 mg, if centrally acting anticholinergics administered
CT scan	• Hemorrhage • Thrombosis (consider basilar artery thrombosis) • Pneumocephalus • Cerebral edema
Other considerations	• Hypothyroidism • Addisonian crisis

BIS, bispectral index; CT, computed tomography; IOM, intraoperative neurophysiologic monitoring.

Bilotta F, Lam AM, Doronzio A, et al. Esmolol blunts postoperative hemodynamic changes after propofol-remifentanil total intravenous fast-track neuroanesthesia for intracranial surgery. *J Clin Anesth*. 2008;20:426-430.

Lauta E, Abbinante C, Del Gaudio A, et al. Emergence times are similar with sevoflurane and total intravenous anesthesia: results of a multicenter RCT of patients scheduled for elective supratentorial craniotomy. *J Neurosurg Anesthesiol*. 2010;22:110-118.

D. Postoperative Management

D.1. What postoperative complications are of greatest concern? What level of monitoring is required?

Part of the neurologic assessment conducted immediately on emergence should be an evaluation of the lower cranial nerves. Damage to the nerves or to nuclei can result in difficulty swallowing and protecting the airway. The principal concern is the development of edema or hematoma causing compression of the brainstem or midbrain structures. The brainstem sits in an anatomic location with very low compliance; even small degrees of edema that would be well tolerated following supratentorial procedures can lead to catastrophic neurologic compromise. It is critical to appreciate that edema and hematoma can develop over the course of several hours following the procedure; a patient who had a satisfactory emergence might deteriorate neurologically in the middle of the night. In certain circumstances, the risk of postoperative edema is so high that the patient is left intubated prophylactically, as discussed earlier. Deterioration cannot always be anticipated, and these patients should be initially monitored in an intensive care setting in all cases.

Dubey A, Sung WS, Shaya M, et al. Complications of posterior cranial fossa surgery: an institutional experience of 500 patients. *Surg Neurol*. 2009;72:369-375.

Sughrue ME, Rutkowski MJ, Shangari G, et al. Risk factors for the development of serious medical complications after resection of meningiomas. Clinical article. *J Neurosurg*. 2011;114(3):697-704.

Wong JM, Panchmatia JR, Ziewacz JE, et al. Patterns in neurosurgical adverse events: intracranial neoplasm surgery. *Neurosurg Focus*. 2012;33(5):E16.

D.2. What is your approach to postoperative pain control?

Optimal pain control after craniotomy has traditionally been hampered by several challenges. First is the misconception that craniotomy and tumor resection causes minimal pain, despite the rich nociceptive afferents to the meninges, dura, falx, and calvarial periosteum. Using traditional analgesic approaches, nearly 70% of postcraniotomy patients experience moderate to severe pain on the first postoperative day, and just under half continue to do so on the second postoperative

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day.

Another dogma that persists to this day is that most analgesics are dangerous for the postcraniotomy patient and should be dosed sparingly. Concern remains that opioids have the potential to cause sedation and respiratory depression in the neurologically vulnerable patient. Despite this, patient-controlled analgesia (PCA) opioid regimens have been used safely in supra- and infratentorial postcraniotomy patients, improving both pain control and patient satisfaction.

In addition to opioid PCAs, we suggest a multimodal approach to minimize opioid use and their side effects. Acetaminophen is nonsedating and safe in recommended doses in the absence of liver disease. Neurosurgeons have traditionally avoided nonsteroidal anti-inflammatory drugs (NSAIDs) in the perioperative period due to risk of postoperative hematoma, although what little evidence exists is not robust. Nonetheless, it behooves the neuroanesthesiologist to discuss the use of NSAIDs with the surgeon before prescribing. Scalp blocks or scalp infiltration performed at the end of surgery have little morbidity and improve pain control in the early postoperative period. Although this effect is not sustained beyond the first postoperative day, there is evidence to suggest this technique reduces the

development of chronic postcraniotomy pain. Preinduction gabapentin, in addition to its beneficial effects on minimizing the hemodynamic response to laryngoscopy and head pinning, also decreases postoperative pain and opioid requirements, although it may result in greater sedation and slow extubation times. Tramadol has been used successfully for postcraniotomy pain; however, due to its increased risk of nausea and vomiting, and the lowering of the seizure threshold, we do not recommend it as part of a first-line analgesic regimen.

Gottschalk A, Berkow LC, Stevens RD, et al. Prospective evaluation of pain and analgesic use following major elective intracranial surgery. *J Neurosurg*. 2007;106:210-216.

Hansen MS, Brennum J, Moltke FB, et al. Pain treatment after craniotomy: where is the (procedure-specific) evidence? A qualitative systematic review. *Eur J Anaesthesiol*. 2011;28:821-829.

Morad A, Winters B, Stevens R, et al. The efficacy of intravenous patient-controlled analgesia after intracranial surgery of the posterior fossa: a prospective, randomized controlled trial. *Anesth Analg*. 2012;114:416-423.

Rahimi SY, Alleyne CH, Vernier E, et al. Postoperative pain management with tramadol after craniotomy: evaluation and cost analysis. *J Neurosurg*. 2010;112(2):268-272.

Türe H, Sayin M, Karlikaya G, et al. The analgesic effect of gabapentin as a prophylactic anticonvulsant drug on postcraniotomy pain: a prospective randomized study. *Anesth Analg*. 2009;109(5):1625-1631.

Umamaheswara Rao GSU, Gelb AW. To use or not to use: the dilemma of NSAIDs and craniotomy. *Eur J Anaesthesiol*. 2009;26(8):625-626.

Williams DL, Pemberton E, Leslie K. Effect of intravenous parecoxib on post-craniotomy pain. *Br J Anaesth*. 2011;107:398-403.

D.3. In the ICU, the patient's neurologic status deteriorates and ICP monitoring is instituted. What are the different methods of monitoring ICP, and what are their limitations?

ICP monitoring is commonly used in neurosurgical critical care as a marker of intracranial compliance and to allow a more objective calculation of CPP. Typically, an ICP monitor is placed at a discrete anatomic point of measurement, and data from this monitor is extrapolated to the whole brain. It is important to remember, however, that significant differences in regional ICP can exist, particularly in patients where there is a pathologic disruption of normal CSF circulation. In the case of this patient, for instance, an ICP monitor positioned in the supratentorial region may not accurately represent the pressure in the posterior fossa.

There are many methods of ICP monitoring available, differing on the basis of invasiveness, site of measurement, and degree of validation. An external ventricular drain (EVD) is considered the gold standard and allows for both ICP measurement and CSF drainage to treat intracranial hypertension (although not simultaneously). The catheter tip is

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introduced into one of the lateral ventricles via a blind technique or with imaging guidance and connected to a fluid column with a pressure transducer and drainage system. It is the most invasive method of ICP monitoring and is associated with significant rates of intracranial infection and bleeding during placement. Other limitations of the EVD include difficult placement in patients with midline shift, catheter malfunction, and potential CSF overdrainage. An alternate method of measuring ICP is through the use of microtransducers. These devices transduce an external force (e.g., applied by edematous brain tissue) to an alteration in electrical or light signal. Fiberoptic devices transmit light to a flexible reflective tip that is displaced by an external force, and the change in light reflection is extrapolated into a change in ICP. Similarly, electronic strain gauge devices are deformed by external pressure thereby inducing a change in electrical resistance. These devices are miniaturized to the extent that their placement into brain parenchyma would cause little damage and are typically secured to the skull with a bone bolt. Depending on manufacturer, microtransducers may also be introduced into the subarachnoid, epidural, or subdural spaces, with some attrition in accuracy. The primary advantages of microtransducers are the decreased rate of intracranial infection, the absence of catheter-related malfunction, and the stability of the fixation bolt. However, these devices are prone to zero drift over time (between 1 mm Hg per 1 to 5 days) and cannot be re-zeroed without removing the device entirely. Further limitations include local sampling of parenchymal pressure and significantly higher cost compared to catheter systems.

More recently, the use of transcranial Doppler (TCD) has been proposed as an alternate, noninvasive method of ICP and CPP measurement. This method analyzes middle cerebral

artery flow characteristics for degree of pulsatility. This pulsatility index (PI) has been used as a surrogate measurement of a variety of neurovascular parameters, including cerebrovascular resistance, vasospasm, and CPP. Although initial reports showed good correlation between TCD-PI and ICP, subsequent studies have revealed wide discrepancies in predicted ICP and measured ICP with a catheter-based system. Further investigations are needed before TCD can be considered an acceptable alternative to invasive methods of ICP measurement.

Raboel PH, Bartek J Jr, Andresen M, et al. Intracranial pressure monitoring: invasive versus non-invasive methods—a review. *Crit Care Res Pract*. 2012;2012:950393.

Steiner LA, Andrews PJD. Monitoring the injured brain: ICP and CBF. *Br J Anaesth*. 2006;97(1):26-38.

Zweifel C, Czosnyka M, Carrera E, et al. Reliability of the blood flow velocity pulsatility index for assessment of intracranial and cerebral perfusion pressures in head-injured patients. *Neurosurgery*. 2012;7:853-861.

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Chapter 18
Carotid Endarterectomy

Christine Lennon

An 85-year-old woman is scheduled for a left carotid endarterectomy (CEA) for asymptomatic left carotid stenosis. She has 90% occlusion of her left carotid artery and 60% occlusion of the right carotid artery. Her past medical history is remarkable for hypertension, insulin-dependent diabetes mellitus, and coronary artery disease. She had coronary artery bypass surgery 4 years ago. Her blood pressure is 170/80 mm Hg, and her pulse is 59 beats per minute and regular.

A. Medical Disease and Differential Diagnosis

1. What are the presenting symptoms of carotid stenosis?
2. What is the prevalence of carotid artery disease?
3. What is the natural course of carotid artery disease?
4. Discuss diabetes mellitus as a risk factor for CEA.
5. What are the indications for surgical intervention in the management of carotid atherosclerotic disease?
6. Discuss the anatomy of the cerebral vasculature, including the carotid artery and the circle of Willis.
7. Discuss cerebral perfusion in the presence of carotid artery disease.
8. Discuss the different surgical approaches to carotid revascularization.
9. What is normal cerebral blood flow (CBF)?
10. What is critically low CBF as measured by the electroencephalogram (EEG)?
11. What is cerebral autoregulation?
12. How does $PaCO_2$ affect CBF?
13. What are the principal determinants of CBF?
14. What is meant by the term *luxury perfusion*?
15. What is meant by the term *intracerebral steal*?
16. What is “inverse steal” or the “Robin Hood” syndrome?

B. Preoperative Evaluation and Preparation

1. What will you be looking for in your preoperative evaluation of this patient?
2. Is this patient's blood pressure too high for elective surgery?
3. What laboratory data are required preoperatively?
4. Will you premedicate this patient?

C. Intraoperative Management

1. How will you monitor this patient?
2. How will you know that the patient's cerebral perfusion is adequate during surgery?
3. Discuss the differences and relative advantages and disadvantages of the unprocessed EEG and the processed EEG.

4. How will you measure CBF intraoperatively? What are the relative advantages and disadvantages of each technique?

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How much CBF is considered adequate?

5. Does internal carotid stump pressure accurately reflect cerebral perfusion?
6. Discuss somatosensory evoked potentials (SSEPs) as a monitor of CBF during CEA.
7. Describe the role of the transcranial Doppler as a monitor of cerebral perfusion during CEA.
8. What type of anesthesia will you choose for this patient?
9. How will you induce and maintain general anesthesia in this patient?
10. How would you proceed if the patient were to receive regional anesthesia?
11. Discuss the effects of anesthetics on CBF.
12. Discuss the protective effects of anesthetic agents on cerebral function.
13. How will you manage this patient's ventilation under general anesthesia?
14. How will you manage this patient's blood pressure intraoperatively?
15. Discuss reperfusion injury following CEA and carotid artery stenting (CAS).
16. What intravenous fluids will you give this patient intraoperatively?

D. Postoperative Management

1. The patient does not “wake up” from general anesthesia. Why?
2. Postoperatively, the patient's blood pressure is 170/96 mm Hg. Will you treat this?
3. What immediate postoperative complications might you expect?
4. Discuss postoperative neurocognitive dysfunction following uncomplicated CEA.

A. Medical Disease and Differential Diagnosis

A.1. What are the presenting symptoms of carotid stenosis?

Carotid disease may manifest as only an asymptomatic bruit. It can also present, though, with amaurosis fugax, a transient ischemic attack (TIA), or a cerebrovascular accident. Amaurosis fugax is a temporary monocular blindness caused by a TIA of the retina. It is an indication of an evolving arterial thrombus in the internal carotid artery, which is the main blood supply to the optic nerve and retina through the ophthalmic artery. The symptoms of amaurosis fugax, which have been described as a shade descending over one eye, often last less than 10 minutes, and are ipsilateral to the evolving and symptomatic vascular disease.

Other manifestations of symptomatic carotid artery disease include episodes of paresthesias, clumsiness, or difficulties with speech that resolve spontaneously over a short period.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2014.

Longo DL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012.

A.2. What is the prevalence of carotid artery disease?

Carotid artery disease is a manifestation of generalized arteriosclerosis. The reported prevalence of asymptomatic carotid stenosis varies with differences in demographic factors, screening methods, and cut-off points used to identify stenosis. In a meta-analysis of 40 studies reviewing the prevalence of carotid stenosis in asymptomatic patients, the pooled prevalence of moderate (≥50%) stenosis was 4.2%, and the pooled prevalence of severe (≥70%) stenosis was 1.7%. Both advanced age and male gender were found to be associated with increased prevalence of disease.

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Symptomatic carotid stenosis may be defined as focal neurologic symptoms that are sudden in onset and referable to the appropriate carotid artery distribution, including one or more TIAs or nondisabling strokes. A population-based study in Rochester, Minnesota, found the incidence rate of TIAs from the years 1985 to 1989 to

be 68 per 100,000. Another population-based study in Italy found the incidence rate of TIAs between the years 2007 and 2009 to be 52 per 100,000. Cerebrovascular disease is the fourth leading cause of death in the United States, after heart disease, cancer, and chronic lower respiratory disease.

Brown RD Jr, Petty GW, O'Fallon WM, et al. Incidence of transient ischemic attack in Rochester, Minnesota, 1985-1989. *Stroke*. 1998;29(10):2109-2113.

Cancelli I, Janes F, Gigli GL, et al. Incidence of transient ischemic attack and early stroke risk: validation of the ABCD2 score in an Italian population-based study. *Stroke*. 2011;42(10):2751-2757.

de Weerd M, Greving JP, de Jong AW, et al. Prevalence of asymptomatic carotid artery stenosis according to age and sex: systematic review and metaregression analysis. *Stroke*. 2009;40(4):1105-1113.

Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulation*. 2014;129(3):e28-e292.

A.3. What is the natural course of carotid artery disease?

The risk factors for the development of carotid artery bifurcation disease are similar to those causing atherosclerotic occlusive disease in other vascular beds, namely, increasing age, male gender, hypertension, tobacco smoking, diabetes mellitus, homocysteinemia, and hyperlipidemia. In carotid artery disease, atherosclerotic plaques develop at the lateral aspect of the bifurcation of the carotid artery. Thrombus may become superimposed on the atheroma; this most likely occurs where the plaque narrows the lumen to the greatest degree. The mechanism of resultant TIA or stroke may be embolism of the thrombotic material or low flow due to the stenosis with inadequate collateral compensation. Severe carotid stenosis is a strong predictor for stroke, and a prior history of neurologic symptoms such as TIA or stroke is a predictor for recurrent ipsilateral stroke.

Approximately 15% of all strokes are preceded by a TIA. Meta-analyses have shown that the short-term risk of stroke following a TIA is approximately 3% to 10% at 2 days and 9% to 17% at 90 days. Mortality within the first year following a TIA is approximately 12%. The incidence and fatality rates associated with stroke have been declining over the past several decades, which has mainly been attributed to cardiovascular risk control interventions.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2014.

Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulation*. 2014;129(3):e28-e292.

A.4. Discuss diabetes mellitus as a risk factor for CEA.

Diabetes is a major risk factor for stroke. When matched for associated risk factors, symptomatic cerebrovascular disease is more common in patients who have diabetes mellitus than in those who do not have diabetes. The relative risk conferred is greatest in patients younger than 65 years of age; in a population-based study in the Greater Cincinnati/Northern Kentucky region in 2005, risk ratio for ischemic strokes in Blacks younger than 65 years of age with diabetes was 5.2, compared with a risk ratio of 12.0 for Whites younger than 65 years of age with diabetes. Additionally, mortality and the severity of stroke are greater in patients with diabetes.

In a study from 1992 to 1995, 732 CEAs were performed in diabetic and nondiabetic patients. Patients with diabetes

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were younger at presentation than nondiabetic patients and were more likely to have history of coronary artery disease. This may contribute to the higher incidence of postoperative cardiac morbidity in diabetic patients. However, diabetes mellitus by itself is not a risk factor for postoperative cardiac morbidity in patients who undergo carotid surgery.

Diabetes mellitus and obesity are considered independent risk factors for neurocognitive decline after CEA.

Akbari CM, Pomposelli FB Jr, Gibbons GW, et al. Diabetes mellitus: a risk factor for carotid endarterectomy? *J Vasc Surg*. 1997;25:1070-1075.

Khoury JC, Kleindorfer D, Alwell K, et al. Diabetes mellitus: a risk factor for ischemic stroke in a large biracial population. *Stroke*. 2013;44(6):1500-1504.

A.5. What are the indications for surgical intervention in the management of carotid atherosclerotic disease?

Several randomized controlled trials have evaluated the efficacy of CEA for patients with asymptomatic high-grade stenosis. A meta-analysis of these trials found that CEA confers a small absolute risk reduction for stroke compared to medical management. In the two largest trials, the asymptomatic carotid atherosclerosis study (ACAS) and the European asymptomatic carotid surgery trial (ACST-1), the risk reduction was about 3% over 3 years, corresponding to a number needed to treat of approximately 33 to prevent one stroke at 3 years. The role of CAS in asymptomatic patients is also unclear. No randomized controlled trials have been done to evaluate CEA versus CAS in asymptomatic patients. However, a meta-analysis of studies in both symptomatic and asymptomatic patients suggests that in asymptomatic patients, the periprocedural (30-day) rate of stroke or death is higher with CAS than with CEA, although no difference has been shown past 30 days. Thus, recommendations for the treatment of asymptomatic carotid stenosis remain somewhat controversial. Medical management, including treatment of hypertension, hyperlipidemia, diabetes, and smoking coupled with the use of antiplatelet agents, should be considered. Prophylactic CEA may be undertaken in highly selected patients with asymptomatic severe stenosis (60% to 99% according to various guidelines) while taking into account the patient's comorbidities and overall fitness for surgery. The usefulness of CEA versus CAS remains unclear, although guidelines from the Society of Vascular Surgery state that prophylactic CAS should not be undertaken.

Symptomatic carotid disease refers to focal neurologic symptoms, which are acute and referable to the ipsilateral carotid distribution. Optimal medical therapy is recommended in all patients with symptomatic disease. Several large randomized controlled trials have evaluated the efficacy of CEA in symptomatic patients. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) demonstrated that CEA is superior to medical therapy alone in symptomatic patients with >70% stenosis, with a 9% risk of stroke in the CEA group compared to 26% in the medical group, or an absolute risk reduction of 17% over 2 years. These results were largely confirmed by the European Carotid Surgery Trial (ECST). Current guidelines state that revascularization should be undertaken in patients with moderate to severe symptomatic stenosis as long as the perioperative morbidity and mortality risk is estimated to be <6% for the surgeon or center. Many trials have been done in recent years comparing CEA to CAS for symptomatic patients. A meta-analysis of seven trials suggests that long-term outcomes are similar for CEA and CAS groups. However, CEA is associated with a greater risk of periprocedural myocardial infarction, whereas CAS is associated with a greater increase in periprocedural death/stroke. Thus, the decision between CEA and CAS for symptomatic patients depends on a combination of patient-specific factors, including the gender, surgical/anatomic considerations, and the presence of significant comorbidities that would increase surgical risk.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Bonati LH, Lyrer P, Ederle J, et al. Percutaneous transluminal balloon angioplasty and stenting for carotid artery stenosis. *Cochrane Database Syst Rev*. 2012;(9):CD000515.

Brott TG, Halperin JL, Abbara S, et al. 2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease. *Stroke*. 2011;42(8):e464-e540.

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Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2014.

Chambers BR, Donnan GA. Carotid endarterectomy for asymptomatic carotid stenosis. *Cochrane Database Syst Rev*. 2005;(4):CD001923.

Ederle J, Featherstone RL, Brown MM. Randomized controlled trials comparing endarterectomy and endovascular treatment for carotid artery stenosis: a Cochrane systematic review. *Stroke*. 2009;40(4):1373-1380.

Goldstein LB, Bushnell CD, Adams RJ, et al. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2011;42(2):517-584.

Ricotta JJ, Aburahma A, Ascher E, et al. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease: executive summary. *J Vasc Surg*. 2011;54(3):832-836.

A.6. Discuss the anatomy of the cerebral vasculature, including the carotid artery and the circle of Willis.

The common carotid arteries originate in the thorax. The right common carotid artery originates at the bifurcation of the brachiocephalic trunk, and the left originates from the aortic arch. In the neck, the common carotid arteries travel within the carotid sheath. At the level of the thyroid cartilage, each common carotid artery bifurcates into internal and external carotid arteries.

Branches of the external carotid artery include the superior thyroid, lingual, facial, ascending pharyngeal, occipital, and posterior auricular arteries.

The internal carotid artery passes through the neck without branching to enter the middle cranial fossa. It enters the middle cranial fossa through the carotid canal of the temporal bone, adjacent to the sphenoid bone. It supplies the hypophysis cerebri, the orbit, and the major portion of the supratentorial region of the brain. The cerebral arteries are derived from the internal carotid and vertebral arteries. The anastomosis they form at the base of the brain is known as the *circle of Willis*. The two anterior cerebral arteries form the circle anteriorly. They are connected through the anterior communicating artery. The two posterior cerebral arteries form the circle posteriorly, which then ends at the junction of the basilar artery. The posterior cerebral arteries are connected to the internal carotid arteries by the two posterior communicating arteries (Fig. 18.1). The middle cerebral artery primarily supplies the lateral surface of each cerebral hemisphere. The anterior cerebral and posterior cerebral arteries supply the medial and inferior surfaces of the cerebral hemisphere.

Moore KL. *Clinically Oriented Anatomy*. 5th ed. Baltimore: Lippincott Williams & Wilkins; 2006:930-931.

A.7. Discuss cerebral perfusion in the presence of carotid artery disease.

Autoregulation is assumed to be lost in underperfused areas of the brain. Vascular regions subjected to chronic hypoperfusion and relative ischemia are maximally vasodilated and unresponsive to factors that induce vasoconstriction in normally reactive vascular beds. Therefore, in patients with carotid artery disease, blood flow through ischemic regions is passive and dependent on systemic blood pressure. For this reason, hypotension is best avoided in the period before restoration of unobstructed CBF.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

A.8. Discuss the different surgical approaches to carotid revascularization.

CEA involves the removal of atheromatous plaque from the vessel lumen through a fairly standardized surgical procedure.

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This involves occluding the common, external, and internal carotid arteries; isolating the diseased segment; opening the vessel wall; and removing

the plaque. The vessel is then closed. If the remaining intima is too thin, the vessel is closed with a vein graft or a synthetic (Dacron) patch. The use of a shunt during the period of carotid cross-clamping depends on whether evidence of cerebral ischemia becomes apparent with cross-clamping of the carotid artery. Variations in shunt usage exist because there is little evidence that one therapy is superior to the others. Placement of a shunt allows hemispheric CBF to be maintained during cross-clamping and may be especially advantageous when the endarterectomy is expected to be complex and require a long time.

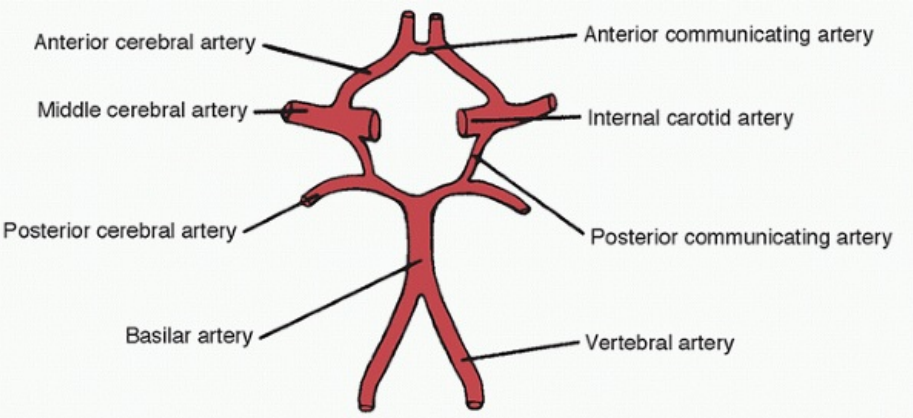


FIGURE 18.1 Arterial circle of Willis.

On the other hand, shunt usage is not without its problems. It may make the surgery technically more difficult. Technical problems with shunts include plaque or air embolism, kinking of the shunt, shunt occlusion on the side of the vessel wall, and injury to the distal internal carotid artery. The use of a shunt does not guarantee adequate CBF nor prevent thromboembolic strokes.

Another intervention to treat carotid stenosis is percutaneous transluminal angioplasty and stenting by interventional radiologists. Advantages to endovascular techniques include avoidance of surgical incision; minimal anesthetic requirements; avoidance of minor complications associated with endarterectomy, including cranial nerve injury and wound infections; shorter duration of induced carotid occlusion by the balloon catheter than with surgical clamping of the carotid artery; and lower hospital costs for shorter hospital and intensive care unit stays.

Clinical trials comparing CEA with angioplasty/stenting have been done. Overall, endovascular treatment is associated with an increased risk of periprocedural stroke or death compared with CEA. This excess risk appears to be limited to older patients. Long-term outcomes do not appear to differ between patients treated with CAS versus CEA.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Bonati LH, Lyrer P, Ederle J, et al. Percutaneous transluminal balloon angioplasty and stenting for carotid artery stenosis. *Cochrane Database Syst Rev*. 2012;(9):CD000515.

Ederle J, Featherstone RL, Brown MM. Randomized controlled trials comparing endarterectomy and endovascular treatment for carotid artery stenosis: a Cochrane systematic review. *Stroke*. 2009;40(4):1373-1380.

A.9. What is normal cerebral blood flow (CBF)?

Normal CBF is approximately 50 mL/100 g/min for the entire brain. Blood flow is approximately four times higher in gray matter than it is in white matter, with the flows being 80 and 20 mL/100 g/min, respectively.

Kety SS, Schmidt CF. The nitrous oxide method for the quantitative determination of cerebral blood flow in man:

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theory, procedure and normal values. *J Clin Invest*. 1948;27:476-483.

Lassen NA, Munck O. The cerebral blood flow in man determined by the use of radioactive krypton. *Acta Physiol Scand*. 1955;33:30-49.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

A.10. What is critically low CBF as measured by the electroencephalogram (EEG)?

Assuming a normal temperature and hematocrit, 100 mL of blood contains approximately 20 mL of oxygen. A normal global CBF of 50 mL/100 g/min delivers oxygen to the brain at a rate of 10 mL/100 g/min. This is in excess of the high metabolic requirements of the brain for oxygen (3 to 5 mL/100 g/min), which affords a relative margin of safety. The CBF at which ischemia becomes apparent in the EEG is approximately 20 mL/100 g/min. Changes on EEG may be delayed for up to 150 seconds following the onset of ischemia. It is impossible to define the specific changes that represent irreversible ischemia. In the setting of an isoelectric EEG, oxygen delivery to the brain may be adequate to keep the neurons alive but may provide insufficient energy for them to function.

The development of cerebral infarction depends on both the degree and duration of ischemia. Jones et al. showed in an animal model of reversible ischemia that with CBF of 18 to 23 mL/100 g/min, animals would recover from impaired neurologic function when blood flow

was returned to normal levels, regardless of the duration of the ischemic period. Infarction development at lower flows depends on both the degree of regional CBF reduction and the duration of ischemia. Neurons that are nonfunctional but will recover fully with restoration of adequate flow are said to be in an ischemic penumbra. Neuronal destruction occurs with CBF less than 10 mL/100 g/min.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Boysen G, Engell HC, Pitolese GR, et al. On the critical level of cerebral blood flow in man with particular reference to carotid surgery. *Circulation*. 1974;49:1023-1025.

Jones TH, Morawetz RB, Crowell RM, et al. Threshold of focal cerebral ischemia in awake monkeys. *J Neurosurg*. 1981;54:773-782.

A.11. What is cerebral autoregulation?

Cerebral autoregulation is the tendency of the brain to match cerebral metabolic oxygen requirements with oxygen delivery in spite of variations in blood pressure. In normotensive individuals, CBF is constant between mean arterial pressures of 50 and 150 mm Hg. What this means is that cerebrovascular resistance increases, through vasoconstriction, as mean arterial pressure increases from 50 to 150 mm Hg. At pressures greater than 150 mm Hg, the cerebral vasculature is maximally vasoconstricted and CBF increases with increasing pressure. At pressures less than 50 mm Hg, cerebral vessels are maximally vasodilated, so that CBF decreases as mean arterial pressure falls.

In hypertensive patients, the upper and lower limits of the autoregulatory curve are shifted to the right, to higher pressures (Fig. 18.2). What this means is that a mean arterial pressure of 60 mm Hg, which would be well-tolerated in a normotensive individual, may actually be below the lower limit of autoregulation in the hypertensive individual, resulting in cerebral hypoperfusion. Conversely, hypertensive patients tolerate marked increases in mean arterial pressure much better than their normotensive counterparts. In treated hypertensive patients, the limits of autoregulation are shifted with time toward normal.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

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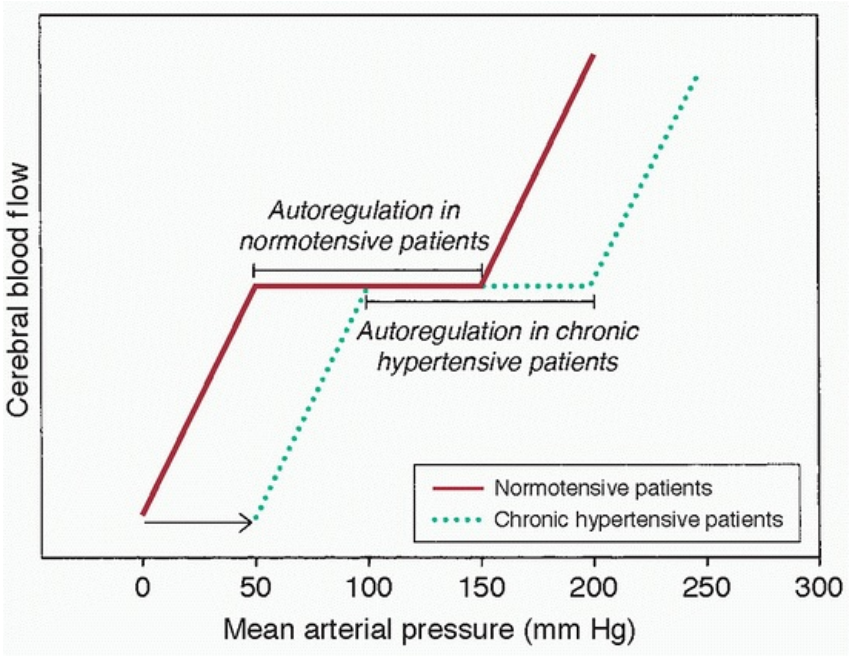


FIGURE 18.2 Cerebral autoregulatory curves in normotensive and chronic hypertensive patients. New autoregulation curve is achieved with chronic hypertension. The curve shifts back to normotensive range once hypertension is well controlled.

A.12. How does $PaCO_2$ affect CBF?

Hypercarbia results in cerebral vasodilation and hypocarbia in cerebral vasoconstriction. CBF changes approximately 4% for each millimeter of mercury increase or decrease in arterial $PaCO_2$ for partial pressures of arterial carbon dioxide between 20 and 80 mm Hg.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

A.13. What are the principal determinants of CBF?

The principal determinants of CBF are nerve cell activity, cerebral perfusion pressure, $PaCO_2$, the pH of the extracellular fluid in the brain, PaO_2, and neurogenic influences.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2010.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

A.14. What is meant by the term luxury perfusion?

Luxury perfusion is blood flow that is in excess of metabolic need (increased CBF relative to cerebral metabolic rate for oxygen). It is most frequently observed in tissues surrounding tumors or areas of infarction. It has also been described in tissues that have been manipulated during surgery.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Elsevier Saunders;

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2010.

Paulson OB. Cerebral apoplexy (stroke): pathogenesis, pathophysiology and therapy as illustrated by regional blood flow measurements in the brain. *Stroke*. 1971;2:327-360.

A.15. What is meant by the term intracerebral steal?

Intracerebral steal is a paradoxical response to carbon dioxide in which hypercapnia decreases the blood flow in an ischemic area. It is the consequence of the vasodilatory effect of carbon dioxide on the normally perfused arterioles at the periphery of an ischemic lesion. Because chronically ischemic vascular beds are maximally vasodilated, they cannot dilate further in response to hypercapnia.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2010.

Paulson OB. Cerebral apoplexy (stroke): pathogenesis, pathophysiology and therapy as illustrated by regional blood flow measurements in the brain. *Stroke*. 1971;2:327-360.

A.16. What is "inverse steal" or the "Robin Hood" syndrome?

Inverse steal is the effect of hypocapnia producing increased blood flow to ischemic regions of the brain. Vasoconstriction occurs in adjacent, normal arterioles, thereby causing a local increase in perfusion pressure and augmenting collateral flow to the ischemic, unreactive, maximally vasodilated area of the brain.

Betz E. Cerebral blood flow: its measurement and regulation. *Physiol Rev*. 1972;52:595-630.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2010.

B. Preoperative Evaluation and Preparation

B.1. What will you be looking for in your preoperative evaluation of this patient?

Once the presence of a carotid lesion amenable to surgical treatment has been documented through Doppler, angiographic, or oculoplethysmographic studies, the anesthesiologist will be asked to evaluate the patient regarding her readiness for surgery. The anesthesiologist should determine whether other manifestations of generalized arteriosclerosis, such as

coronary artery disease, hypertension, and renal disease, are present. Evidence of medical conditions associated with arteriosclerosis, such as obesity, diabetes mellitus, and pulmonary disease secondary to cigarette smoking, should be sought. The patient's neurologic status and airway will need to be evaluated.

Based on the American College of Cardiology/American Heart Association guidelines on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery, CEA is classified as an "elevated risk" procedure. Because 30% to 50% of patients undergoing CEA have coronary artery disease, evidence of heart disease should be sought in the patient's history. Patients should be specifically asked whether they have angina or have had a myocardial infarction or congestive heart failure. An indication of daily activity level should be obtained. A patient unable to ambulate for distances because of claudication may never develop angina or left ventricular failure. Therefore, more invasive evaluation of the patient's cardiac function may be required. Evidence of cardiac disease should also be sought on physical examination. This would include heart rate and rhythm, and presence of jugular venous distention, basilar rales on auscultation of the chest, cardiac enlargement as determined by lateral displacement of the point of maximal impulse, and an S_3 gallop.

Whether the patient has hypertension should be determined. Hypertension is present in 55% to 80% of patients with

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carotid artery disease, and its presence would alter intraoperative blood pressure management. Blood pressure should be measured in both arms with the patient in both the supine and the upright positions. A range of acceptable blood pressures readings, in which the patient is free of symptoms of both cardiac and cerebral ischemia, should be determined. This is done, in part, by reviewing the patient's chart and making note of the highest and lowest blood pressures that were measured. Knowing this range allows the anesthesiologist to determine the range of blood pressures that may be tolerated without treatment in the operating room. Raising the blood pressure excessively to improve cerebral perfusion may exacerbate myocardial ischemia, and lowering the blood pressure to reduce the work of the heart may compromise cerebral perfusion, exacerbating cerebral ischemia.

The presence of other disorders associated with vascular disease, such as obesity, diabetes, and cigarette smoking with their sequelae, should be determined. Evidence of other endorgan effects of vascular disease, such as renal dysfunction, should also be sought.

The patient's neurologic status also needs to be evaluated preoperatively. Although it would be preferable to medically optimize the patient with uncontrolled hypertension or untreated metabolic disease, or if possible, delay surgery in the patient with a recent myocardial infarction, the presence of crescendo TIAs may not allow that option.

The patient's airway needs to be assessed for ease of ventilation and intubation. A patient in whom it is difficult to establish ventilation may become hypercarbic during induction, and the increase in $PaCO_2$ may have adverse effects on regional CBF. As part of the airway evaluation, the range of motion of the patient's neck that is tolerated without evidence of cerebral ischemia needs to be determined so that relative extremes of extension and lateral rotation of the neck during ventilation, intubation, and finally patient positioning can be avoided. Extreme extension and rotation of the neck may occlude the patient's vertebral artery and contribute to postoperative neurologic deficits.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Fleisher LA, Fleischmann KE, Auerbach AD. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol*. 2014;64(22):e77-e137.

B.2. Is this patient's blood pressure too high for elective surgery?

Although hypertension is present in most patients presenting for CEA, its rapid correction is not recommended because this may exacerbate cerebral ischemia. If this patient had evidence of myocardial ischemia at this blood pressure and was stable from a neurologic standpoint, blood pressure could be gradually decreased with antihypertensive medications.

Normal myocardial and cerebral function need to be preserved. These goals are not necessarily at odds with each other. To decrease myocardial oxygen consumption, one would

want to decrease heart rate, blood pressure, and myocardial contractility. In this patient population, decreasing heart rate can decrease myocardial work, whereas cerebral perfusion pressure is maintained with an adequate mean arterial pressure. If a hypertensive patient presents with an unstable neurologic status, it may be necessary to control blood pressure only once the obstruction to CBF has been relieved.

A single blood pressure measurement is of little use in the preoperative assessment of the patient. It is the range of the blood pressures normally tolerated by the patient that will guide perioperative blood pressure management. For example, if a patient's blood pressure is measured at 80/50 mm Hg and at 170/100 mm Hg preoperatively and at these blood pressures she does not develop any new neurologic deficits or myocardial ischemia, the clinician will be inclined to treat blood pressures only beyond these two extremes.

Because this patient is hypertensive, one can expect that wide swings in her blood pressure will occur while she is receiving anesthesia. Variations in blood pressure should be minimized because these have been related to increased cardiac and neurologic morbidity. The anesthesiologist must be prepared for blood pressure variations by having both vasopressors and vasodilators readily available. Total fluid administration should be limited to no more than 10 mL per kg for a typical 2-hour operation in most patients because fluid overload may contribute to postoperative hypertension.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters

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Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Hamilton WK. Do let the blood pressure drop and do use myocardial depressants [editorial]! *Anesthesiology*. 1976;45:273-274.

Smith JS, Roizen MF, Cahalan MK, et al. Does anesthetic technique make a difference? Augmentation of systolic blood pressure during carotid endarterectomy: effects of phenylephrine versus light anesthesia and of isoflurane versus halothane on the incidence of myocardial ischemia. *Anesthesiology*. 1988;69:846-853.

B.3. What laboratory data are required preoperatively?

Laboratory tests should be ordered to determine the patient's baseline cardiac, respiratory, and metabolic status.

Hemoglobin and hematocrit levels should be obtained preoperatively because values may be abnormal in a patient with advanced age or renal or pulmonary disease and because significant blood loss may occur intraoperatively.

A urine analysis and data on blood urea nitrogen and creatinine should be obtained to determine the patient's baseline renal status.

An electrocardiogram (ECG) should be examined preoperatively to look for arrhythmias, evidence of ischemia, previous myocardial infarctions, or left ventricular hypertrophy. Where appropriate, the preoperative ECG should be compared with earlier studies to determine whether interval changes have occurred.

A chest radiograph should be examined to look for cardiomegaly, evidence of pulmonary edema, chronic obstructive pulmonary disease, or pneumonia. If the patient has a history of chronic obstructive pulmonary disease, a preoperative arterial blood gas reading should be obtained to identify the patient's baseline $PaCO_2$. In patients who are chronically hypercarbic, rapid adjustment to normocarbia intraoperatively will be interpreted by the body as relative hypocarbia. CBF will be reduced accordingly. Management of intraoperative ventilation should be aimed at maintaining the patient's normal arterial carbon dioxide level.

Further preoperative evaluation would be based on the presence of concurrent disease.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

B.4. Will you premedicate this patient?

Ideally, the patient should present to the operating room calm and awake. Preoperative anxiety should be alleviated in these patients because it can lead to hypertension, which has been associated with adverse neurologic outcome. Increases in heart rate in the anxious patient lead to increased myocardial oxygen consumption and, potentially, ischemia, ventricular dysfunction, and arrhythmias.

Premedication, however, may lead to ventilatory depression, with resultant hypercarbia and alterations in CBF that can exacerbate cerebral ischemia. Sedation can also interfere with the immediate postoperative neurologic assessment of the patient because it may cause delayed awakening from anesthesia. One of the anesthetic goals for CEA under general anesthesia is to have a patient who promptly emerges from anesthesia and is able to cooperate with a basic neurologic evaluation. A patient who is too sedated at the end of surgery is problematic.

To achieve these goals, a thorough and reassuring preoperative visit alone may provide sufficient anxiolysis. The anesthesiologist should explain the preoperative procedure and what can be expected in the postoperative period, answering any questions that the patient has. If pharmacologic premedication is required, a benzodiazepine (e.g., diazepam 5 mg orally, 1 hour preoperatively; or midazolam 1 to 2 mg intravenously) should provide anxiolysis and minimal respiratory depression.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

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C. Intraoperative Management

C.1. How will you monitor this patient?

Patients who are about to undergo CEA are managed with routine monitoring of cardiovascular, pulmonary, and metabolic function, including ECG leads II and V_5, noninvasive blood pressure monitor, pulse oximetry, end-tidal capnometry, and esophageal temperature.

An intra-arterial catheter should be used to monitor the patient's blood pressure closely. Its presence will permit immediate identification of blood pressure changes and allow for repetitive sampling of arterial blood gases.

Whether a pulmonary artery catheter is required to monitor the patient's cardiac function would be dictated solely by the patient's preoperative cardiac status. CEA is not an operation in which large fluid shifts are anticipated. A pulmonary artery catheter should not be required in the patient with normal left ventricular function.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

C.2. How will you know that the patient's cerebral perfusion is adequate during surgery?

In the awake patient undergoing CEA under local anesthesia, repeated neurologic examinations can be done to assess the adequacy of cerebral perfusion. This is the most sensitive and specific way to detect intraoperative cerebral ischemia.

If the patient receives general anesthesia, neuromonitoring should be employed in order to detect and treat ischemia in a timely fashion. Various neuromonitoring modalities exist, which may be classified in the categories of brain activity monitoring, cerebral perfusion monitoring, and brain oxygen saturation monitoring. These include the EEG, SSEPs, transcranial Doppler, internal carotid stump pressure, jugular venous oxygen saturation, direct xenon CBF measurement, and near-infrared spectroscopy (NIRS). No one monitor is routinely used in all operating rooms, and each modality has its own specific indication as well as its own strengths and weaknesses. Therefore, the simultaneous application of more than one monitoring device is recommended. A recent meta-analysis of 29 studies examined the efficacy of various neuromonitoring modalities for detection of cerebral ischemia during CEA, including EEG, SSEP, transcranial Doppler, stump pressure, cerebral oximetry, jugular venous bulb saturation, and jugular venous lactate levels. A combination of stump pressure and either EEG or transcranial Doppler was found to be the most accurate detector of cerebral ischemia during carotid cross-clamping.

Current interest has considered NIRS, or cerebral oximetry, as a monitor because it is noninvasive, continuous, and easy to use. In recent studies, a relative decrease of 20% or greater in regional cerebral oxygen saturation suggested cerebral ischemia. The monitor, though, has

a low positive predictive value and low specificity. If used exclusively, it would suggest the need for unnecessary shunting and lead to overshunting of patients.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Guay J, Kopp S. Cerebral monitors versus regional anesthesia to detect cerebral ischemia in patients undergoing carotid endarterectomy: a meta-analysis. *Can J Anaesth*. 2013;60(3): 266-279.

Pennekamp CW, Moll FL, de Borst GJ. The potential benefits and the role of cerebral monitoring in carotid endarterectomy. *Curr Opin Anaesthesiol*. 2011;24(6):693-697.

C.3. Discuss the differences and relative advantages and disadvantages of the unprocessed EEG and the processed EEG.

The 16-channel EEG is a sensitive indicator of cerebral ischemia. Intraoperative changes in EEG related to ischemia may be classified as mild, moderate, or severe. Severe EEG changes (>50% decrease in waveform amplitude in a generalized or lateralized distribution) suggest a need for blood pressure augmentation by the anesthesiologist or shunt

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placement by the surgeon. The EEG is neither a measure of CBF nor a way to determine whether irreversible neuronal damage has occurred. Rather, it is an indicator that areas of the brain may be at risk for infarction. Changes that occur in the EEG with hypothermia, hypocarbia, hypoxemia, and deep anesthesia mimic those of ischemia. In patients who have had a cerebrovascular accident, the processed EEG does not predict cerebral ischemia.

Problems associated with intraoperative monitoring of the 16-lead EEG have detracted from its popularity. These include difficulty in obtaining a meaningful recording in the electrically noisy environment of the operating room, the bulk of the equipment required, and the need for specially trained personnel for interpretation.

The processed EEG has eliminated many of the problems associated with the 16-channel EEG. The equipment is generally compact, and the data display allows for ease of interpretation. One commonly used processed encephalogram is the power spectrum analysis. For this analysis, the EEG is studied in short time intervals of 2 to 16 minutes, called *epochs*. Each epoch then is subjected to a fast Fourier transform analysis during which the complex waveform of the unprocessed EEG is broken down into its component sine waves of varying amplitudes and frequencies. The power spectrum is calculated by squaring the amplitude of the individual frequency components. The power spectrum can then be displayed in various graphic forms, two of which are the compressed spectral array and the density modulated spectral array. Data are displayed in these two forms as relative power versus frequency (Fig. 18.3).

It must be remembered that the processed EEG is only as good as the original from which it was obtained. Therefore, meticulous recording techniques are required even when monitoring a processed EEG. During CEA, generally two or four channels of the EEG are monitored to determine right and left symmetry in neuronal activity during interruption of CBF.

The bispectral index (BIS) monitor is another commonly used processed EEG parameter that uses a proprietary methodology to calculate indices of the EEG power spectrum, burst synchronization, and phase coupling. It is primarily used as a monitor to assess depth of anesthesia. Although the BIS may have some utility as a marker of global cerebral ischemia, it has been shown to be unreliable as an indicator of hemispheric cerebral ischemia during carotid cross-clamping.

Deogaonkar A, Vivar R, Bullock RE, et al. Bispectral index monitoring may not reliably indicate cerebral ischaemia during awake carotid endarterectomy. *Br J Anaesth*. 2005;94(6):800-804.

Kearse LA, Martin D, McPeck K, et al. Computer-derived density spectral array in detection of mild analog electroencephalographic ischemic pattern changes during carotid endarterectomy. *J Neurosurg*. 1993;78(6):884-890.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

Rampil IJ, Holzer JA, Quest DO, et al. Prognostic value of computerized EEG analysis during carotid endarterectomy. *Anesth Analg*. 1983;62:186-192.

Sundt TM Jr, Sharbrough FW, Piepgras DG, et al. Correlation of cerebral blood flow and electroencephalographic changes during carotid endarterectomy: with results of surgery and hemodynamics of cerebral ischemia. *Mayo Clin Proc*. 1981;56:533-543.

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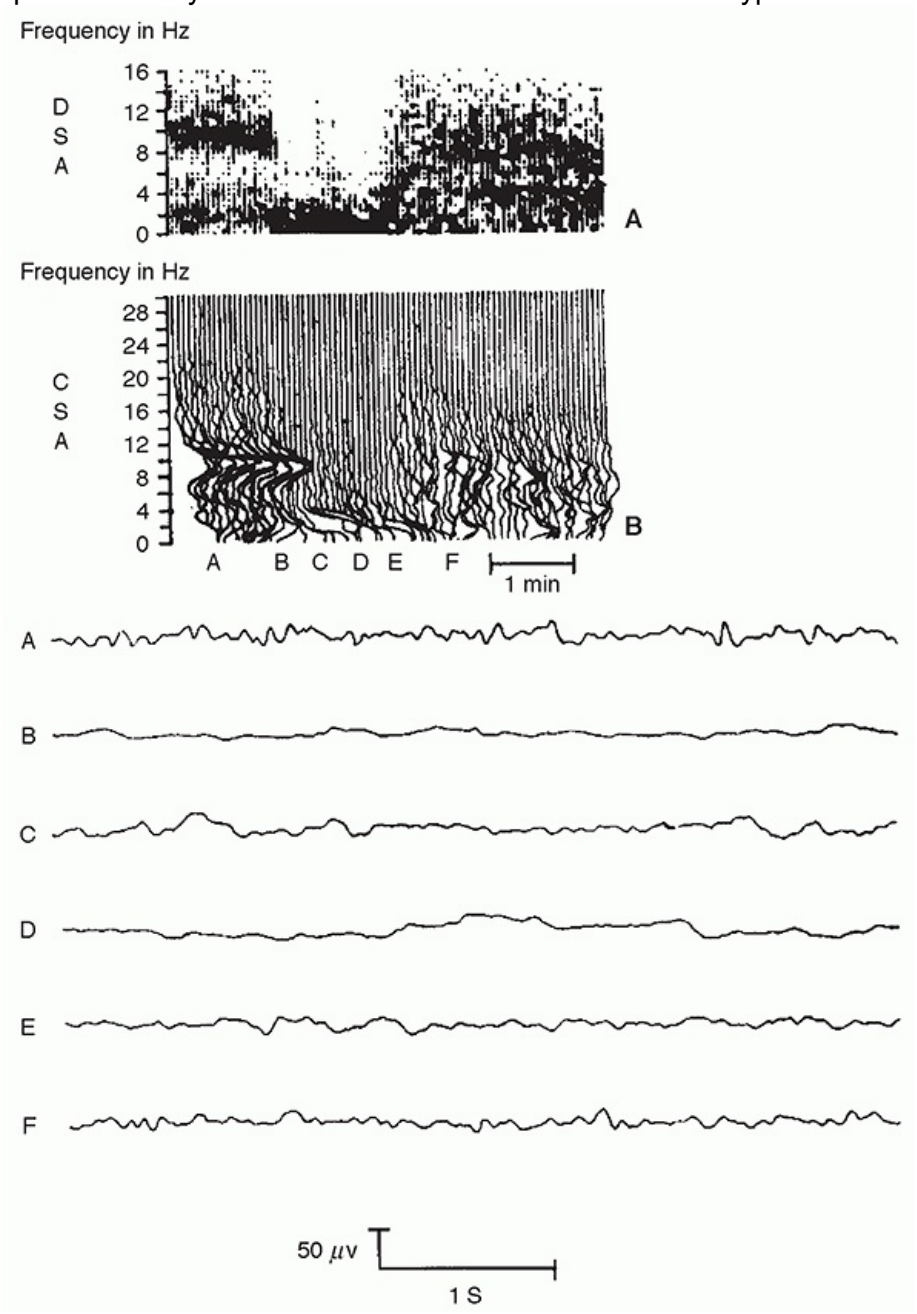


FIGURE 18.3 An example of density spectral analysis **(A)** and the unprocessed electroencephalogram (EEG) **(B)** compressed during a period of marked hypotension during initiation of bypass. Slowing waveform activity in the unprocessed EEG (B to E) is also evident in the density-modulated spectral array (DSA) and compressed spectral array (CSA). (Reprinted with permission from Levy WJ, Shapiro HM, Maruchak G, et al. Automated EEG processing for intraoperative monitoring. *Anesthesiology*. 1980;53:223.)

C.4. How will you measure CBF intraoperatively? What are the relative advantages and disadvantages of each technique? How much CBF is considered adequate?

Measurement of regional CBF is the single best method for detecting decreases in CBF during general anesthesia. Multiple different ways are used to measure this. These include the Kety-Schmidt method and later modifications on this, the intracarotid injection method, and the inhalation and intravenous techniques.

The Kety-Schmidt method, as originally described, involved 10 to 16 minutes of inhalation of 15% nitrous oxide. During this period, equilibration would occur among arterial, venous,

and tissue concentrations of nitrous oxide. Blood samples would intermittently be taken from a peripheral artery and the jugular bulb to determine tracer concentration. The amount of tracer taken up by the brain in a certain period is equivalent

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to the amount delivered to the brain in the arterial blood supply minus that recovered in the cerebral venous blood in the same period. If it is assumed that the brain concentration of the tracer is proportional to the tracer concentrations in the cerebral venous blood, global CBF can be determined with knowledge of the blood brain partition coefficient for the tracer used.

Later modifications of this technique employ the radioactive tracers krypton-85 (^{85}Kr) or xenon-133 (^{133}Xe). CBF, as measured using the Kety-Schmidt method and its modifications, may be overestimated in the case of low perfusion states in which brain and venous blood may not equilibrate. One cannot measure regional CBF using these techniques because jugular venous blood is a mixed venous sample with varying amounts of contamination from the contralateral hemisphere.

In 1961, Lassen and Ingva described the intracarotid injection method of CBF determination. The technique involves injecting a radioactive tracer, ^{85}Kr or ^{133}Xe, as a bolus into the cerebral arterial supply and following the cerebral washout with external scintillation counting. Use of external scintillation counters makes it possible to determine regional CBF, and the sensitivity of the technique is improved by increasing the number of detectors. The tracer is injected directly into either an internal carotid or vertebral artery, minimizing the number of counts obtained from the extracranial circulatory distribution. This method assumes that the tracer mixes completely with brain. Because the tracer is almost completely exhaled on passage through the lungs, it has essentially no recirculation. A typical tracer washout curve in normal brain is the summation of two exponential curves. Two separate flows, fast (gray matter) and slow (white matter), can be calculated using compartmental analysis.

The more noninvasive techniques to determine CBF are the inhalation and intravenous techniques. The inhalation method involves a 1-minute period of inhalation of 133Xe followed by a 10-minute period of washout with external detection. The washout of tracer from the brain is similar to that obtained with intra-arterial injection except that, because of mixing in the heart and the lungs, the input of tracer is not instantaneous. Because the slow component of CBF is contaminated by extracranial clearance of the tracer, the noninvasive methods are suited primarily for determination of gray matter flow. The inhalation and intravenous methods may be less reliable in the presence of pulmonary disease because the end-tidal concentration of tracer may not adequately reflect arterial concentration. With these techniques, extracranial contamination can result in an underestimation of CBF, and under extremely low flow states, they may not give reliable quantitative information.

One thing to bear in mind with all tracer washout techniques is that, in general, they only provide flow information about cortical blood flow and not about deeper structures. Furthermore, with any of these techniques, CBF is a calculated number, and it will vary depending on the specific technique used to measure it. Average global CBF is 50 mL/100 g/min, gray matter flow is 80 mL/100 g/min, and white matter flow is 20 mL/100 g/min. A measured flow intraoperatively of greater than 24 mL/100 g/min is considered to be sufficient and that of less than 18 mL/100 g/min is inadequate. The specific flow differences compatible with ischemia depend on the anesthetic agents used. The expense and expertise required to collect and interpret CBF data have limited its use to only a few centers.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Bell BA. A history of the study of the cerebral circulation and the measurement of cerebral blood flow. *Neurosurgery*. 1984;14:238-246.

Lassen NA, Hoedt-Rasmussen K, Sorensen SC, et al. Regional cerebral blood flow in man determined by krypton 85. *Neurology*. 1963;13:719-727.

C.5. Does internal carotid stump pressure accurately reflect cerebral perfusion?

The internal carotid stump pressure, the pressure in the portion of the internal carotid artery cephalad to the carotid cross-clamp, has been used to determine whether CBF during cross-clamping was adequate to avoid neuronal damage. The stump pressure presumably

reflects pressure transmitted through collateral vessels. Maintaining stump pressures from 25 to 70 mm Hg has been described as necessary to avoid neurologic injury. Nevertheless, this range of stump pressures may not reliably represent the adequacy of collateral CBF because it does not correlate consistently with changes in the EEG, regional CBF, or

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changes in the neurologic status of the awake patient. Furthermore, anesthetic agents can alter carotid stump pressure without changing regional CBF. Inadequate stump pressures have been demonstrated when measured regional CBF was adequate. Therefore, if shunting during CEA were to be done only on the basis of stump pressures, some patients would unnecessarily receive shunts.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Harada RN, Comerota AJ, Good GM, et al. Stump pressure, electroencephalographic changes, and the contralateral carotid artery: another look at selective shunting. *Am J Surg*. 1995;170:148-153.

C.6. Discuss somatosensory evoked potentials (SSEPs) as a monitor of CBF during CEA.

SSEPs are a specialized form of electrophysiologic monitoring that reflects the presence of intact sensory pathways from a stimulated peripheral nerve to the cortex, where electrical activity is monitored. Evidence exists that distortion of certain waveforms is associated with ischemia. These SSEP changes are not consistently associated with changes in the EEG. Questions have been raised regarding whether SSEPs can overpredict the presence of ischemia and the need for shunting. If SSEPs are a useful indicator of ischemia, they may be used when ischemia cannot be detected on an EEG tracing, such as during barbiturate anesthesia. During barbiturate anesthesia, the isoelectric EEG can only indicate that neurons are quiet. It cannot indicate whether these same neurons are ischemic. The SSEP tracing would remain intact with barbiturate anesthesia and, therefore, would potentially be more useful as a clinical monitor. Patients who have had strokes have some asymmetry in baseline SSEP waveforms. This asymmetry does not appear to affect the SSEP as an effective clinical monitor, which may also be a relative advantage over the EEG in patients with prior cerebral vascular accidents.

Manninen PH, Tan TK, Sarjeant RM. Somatosensory evoked potential monitoring during carotid endarterectomy in patients with a stroke. *Anesth Analg*. 2001;93:39-44.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

C.7. Describe the role of the transcranial Doppler as a monitor of cerebral perfusion during CEA.

By allowing for continuous assessment of the velocity of the blood flow in the ipsilateral middle cerebral artery, transcranial Doppler may be useful throughout CEA. It can aid in determining the need for a shunt by detecting a decrease in the middle cerebral artery blood flow velocity with placement of the carotid cross-clamp. It allows for continuous assessment of shunt function. It can be used to assess the adequacy of pharmacologically induced intraoperative hypertensive therapy. Transcranial Doppler also allows for the detection of air or particulate embolization. The disadvantage of transcranial Doppler is that it is technically demanding and not obtainable in approximately 20% of patients.

A good correlation has been shown between intraoperative EEG and transcranial Doppler. Patients who have unchanged EEGs have a middle cerebral artery velocity of 24.1 cm per second during cross-clamping, whereas those with a middle cerebral artery velocity of 14.7 cm per second develop EEG changes. The ratio of the mean velocity while the cross-clamp is in place compared with the mean velocity before placement of the clamp may also be used to predict alteration in neurologic function. A ratio below 0.4 detects 97% of patients with EEG evidence of cerebral ischemia.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Grubhofer G, Plöchl W, Skolka M, et al. Comparing Doppler ultrasonography and cerebral oximetry as indicators for shunting in carotid endarterectomy. *Anesth Analg*. 2000;91:1339-1344.

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C.8. What type of anesthesia will you choose for this patient?

Patients undergoing CEA may have either regional or general anesthesia. Each type of anesthesia has advantages and disadvantages that must be considered when choosing the optimal anesthetic for each patient. Benefits of general anesthesia include a still patient and a quiet operative field; early control of the airway and ventilation; and the ability to "protect" the brain should ischemia, which cannot be eliminated, develop. A disadvantage of general anesthesia is the inability to perform repeated neurologic evaluations during surgery. Therefore, patients receiving general anesthesia should have their CBF or neurologic function monitored as previously discussed.

The primary advantage of a regional anesthetic is that the patient remains awake allowing for repeated neurologic evaluations. Although anecdotal reports support that regional anesthesia allows for greater stability of blood pressure, decreased requirement for vasoactive medications to support blood pressure, and decreased incidence of perioperative myocardial infarction, further outcome studies are warranted. Potential complications associated with regional anesthesia include the following:

- Seizures
- Alteration of mental status with cerebral ischemia
- Loss of patient cooperation associated with cerebral hypoperfusion, inadequate ventilation, and sedation

Early analyses of mainly nonrandomized trials comparing regional and general anesthesia for CEA initially suggested a reduced risk of morbidity and mortality with regional anesthesia. However, subsequent analyses of larger, randomized have generally refuted this finding. The general anesthesia versus local anesthesia for carotid surgery (GALA) trial is a multicenter, randomized controlled trial that included 3,526 patients with symptomatic or asymptomatic carotid stenosis who were randomly assigned to surgery under general anesthesia or regional anesthesia. This study showed no definite differences in the primary study outcome (stroke, myocardial infarction, or death within 30 days), quality of life, or length of hospital stay. However, there was a nonsignificant trend toward a higher rate of myocardial infarction in the regional anesthesia group as well as a nonsignificant trend toward a higher rate of stroke among patients with bilateral carotid disease in the general anesthesia group.

A meta-analysis of 14 randomized trials involving 4,596 procedures (the majority of which came from the GALA study) found that there was no statistically significant difference between general and regional anesthesia groups in the proportion of patients who had a stroke or died within 30 days of surgery. In this meta-analysis, there was a nonsignificant trend toward lower operative mortality with regional anesthetic; however, none of the individual studies or the meta-analysis were adequately powered to reliably detect an effect on mortality. Therefore, evidence suggests that patients and surgeons may choose either anesthetic technique, depending on the clinical situation and individual preference.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Unic-Stojanovic D, Babic S, Neskovic V. General versus regional anesthesia for carotid endarterectomy. *J Cardiothorac Vasc Anesth*. 2013;27(6):1379-1383.

Vaniyapong T, Chongruksut W, Rerkasem K. Local versus general anaesthesia for carotid endarterectomy. *Cochrane Database Syst Rev*. 2013;(12):CD000126.

C.9. How will you induce and maintain general anesthesia in this patient?

Following preoxygenation, all anesthetics should be titrated slowly with special attention to their effect on the patient's blood pressure. Control of the airway should be taken as soon as the patient is no longer able to breathe adequately to maintain normocarbia. While breathing oxygen, the patient is given small doses of fentanyl and reminded to breathe to maintain normocapnia. Opioids are administered until the patient is comfortably sedated. Lidocaine 1 mg per kg is administered intravenously at least 2 minutes before laryngoscopy and intubation to blunt the hyperdynamic response to airway manipulation. Following administration of thiopental, propofol, or etomidate, controlled ventilation is instituted with 100% oxygen to

avoid hypoxia and hypercarbia. A muscle relaxant is administered to facilitate endotracheal intubation. Succinylcholine

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should be avoided in hemiparetic patients because of the possibility of a hyperkalemic response to its administration. Nondepolarizing muscle relaxants with significant hemodynamic effects such as sympathomimetic activity, vagolysis, or histamine release should be avoided. Once the patient is relaxed, an expeditious laryngoscopy and intubation are performed. The time spent intubating the patient's trachea is minimized to decrease the hemodynamic response to airway manipulation.

During the induction and intubation sequence, the patient's blood pressure is kept in her normal range by the use of vasopressors or vasodilators as indicated. Short-acting and easily titratable vasoactive medications should be chosen to facilitate blood pressure control.

Anesthesia can be maintained with a combination of volatile anesthetics and opioids. The addition of opioids to an isoflurane, sevoflurane, or desflurane anesthetic will decrease heart rate, reduce the requirements for volatile anesthetics, and, when properly dosed, allow for a prompt, smooth emergence from general anesthesia. Their use should not be avoided because of anecdotal reports of adverse neurologic outcome after focal ischemia in rodents. Any anesthetic regimen is suitable if it provides hemodynamic stability, does not exacerbate cerebral ischemia, and allows for a prompt emergence from anesthesia at the conclusion of surgery.

Maintenance of a light anesthetic appears to have several advantages over deep anesthesia. It allows ischemic patterns on the EEG to be recognized easily. It also facilitates maintenance of the patient's blood pressure. In addition, administration of a light anesthetic, compared to a deep anesthetic using phenylephrine to maintain blood pressure, results in a lower incidence of perioperative myocardial infarction.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Smith JS, Roizen MF, Cahalan MK, et al. Does anesthetic technique make a difference? Augmentation of systolic blood pressure during carotid endarterectomy: effects of phenylephrine versus light anesthesia and of isoflurane versus halothane on the incidence of myocardial ischemia. *Anesthesiology*. 1988;69:846-853.

C.10. How would you proceed if the patient were to receive regional anesthesia?

Patient cooperation is essential for a regional anesthetic to proceed successfully. For a patient to be adequately anesthetized, a sensory blockade is required in the C2-C4 dermatomes. This can be accomplished with either deep or superficial cervical plexus blocks. In doing the blocks, care must be taken not to excessively palpate the neck because part of the plaque in the carotid artery may dislodge and embolize.

Superficial cervical plexus blocks are performed by infiltrating along with middle third of the posterior border of the sternocleidomastoid muscle with local anesthesia. Deep cervical plexus blocks are performed with three injections along a line drawn from Chassaignac tubercle (C6) to the mastoid process. The C4 nerve root is located at the intersection of that line with one drawn horizontally from the lower border of the mandible. C2 and C3 are located by dividing the distance between the mastoid process and the horizontal line into thirds. Alternatively, a single injection of local anesthetic can be made on the line between the mastoid process and Chassaignac tubercle at the level of C4 with the needle directed medially and slightly caudad.

Patients receiving regional anesthesia must be both cooperative and not oversedated with intravenous medications. If they are unable to cooperate and become obtunded, the primary advantage of regional anesthesia (which is continuous neurologic evaluation) is lost. Intravenous sedation therefore must be given judiciously, if at all, to these patients.

Unic-Stojanovic D, Babic S, Neskovic V. General versus regional anesthesia for carotid endarterectomy. *J Cardiothorac Vasc Anesth*. 2013;27(6):1379-1383.

C.11. Discuss the effects of anesthetics on CBF.

It is important to remember that all general anesthetics affect CBF and cerebral metabolic oxygen consumption. This can be used to the anesthesiologist's advantage when the decrease in oxygen consumption is greater than the decrease in CBF.

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In general, volatile anesthetics are considered to be vasodilators and intravenous anesthetics to be vasoconstrictors. Ketamine is an exception because it will cause increases in both CBF and cerebral metabolic rate. Volatile anesthetics, as vasodilators, produce a dosedependent increase in CBF. The magnitude of vasodilation is dependent on the balance between the anesthetic's intrinsic vasodilatory property and vasoconstriction secondary to its decrease in cerebral metabolic rate.

It has been suggested that anesthetic agents only affect the blood flow in normally perfused areas of the brain. If this is the case, volatile anesthetics will cause a steal phenomenon, in which the blood vessels in normal brain dilate and steal blood flow away from ischemic areas of the brain that are both already maximally vasodilated and unresponsive to the vasodilating effects of the anesthetics.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

C.12. Discuss the protective effects of anesthetic agents on cerebral function.

Although it has not been proved that general anesthetics afford brain protection, agents that cause the greatest decrease in cerebral metabolic oxygen consumption should lessen the risk of cerebral ischemia. Whether a particular anesthetic is optimal for these patients is an area of discussion. Obviously, avoiding or eliminating ischemia is preferable to protecting against it.

Messick et al. examined the effects of volatile anesthetics on critical regional CBF, that is, the regional CBF at which EEG evidence of cerebral ischemia became apparent. He found that critical regional CBF in patients receiving isoflurane was less than 10 mL/100 g/min, and in patients receiving halothane was 18 to 20 mL/100 g/min. This decrease in critical CBF suggests that isoflurane may offer some protective effect. Because of its potential to cause a decrease in blood pressure and reflex increase in heart rate, it probably should not be used at high concentrations as the sole anesthetic. A significant proportion of patients with carotid artery disease also have coronary artery disease and may not tolerate the hypotension and tachycardia associated with the use of high-dose isoflurane. By using this anesthetic in low concentrations in combination with other anesthetic agents, one can better maintain hemodynamic stability while perhaps providing for an increased tolerance of cerebral hypoperfusion. Other evidence suggests that isoflurane may not offer protection during regional cerebral ischemia.

The newer agents, sevoflurane and desflurane, have been investigated for their possible role in neuroanesthesia. Compared to isoflurane, desflurane has no significant difference in its effects on decreasing cerebral glucose utilization, increasing blood flow, and maintaining coupling between local CBF and local cerebral glucose utilization. Although sevoflurane showed no significant difference in its effects on decreasing cerebral glucose utilization, and coupling between local CBF and local cerebral glucose utilization at one minimum alveolar concentration, it did show less of an increase in CBF. This difference between isoflurane and sevoflurane was independent of their effects on systemic blood flow and cardiac output. Hence, desflurane and sevoflurane may have similar neuroprotective effects as isoflurane and, with their lower blood gas solubility coefficients, may promote a more rapid recovery from anesthesia, allowing faster evaluation of neurologic status.

Thiopental affords cerebral protection against focal or incomplete global cerebral ischemia. It is a cerebral vasoconstrictor, as are most other intravenous anesthetics. It will also transiently decrease cerebral metabolism from 40% to 50% of baseline. The combined effect is that cerebral metabolic oxygen consumption is decreased more than oxygen delivery. The reduction in oxygen demand is the result of inhibition of functioning neurons, which can be seen as a quiet or isoelectric EEG. When dosing barbiturates for cerebral protection, the EEG should be monitored and repeated doses given to achieve and then maintain a burst suppression pattern. Once the EEG is isoelectric, indicating lack of neuronal function, further doses of thiopental do not provide additional protection. It is generally not recommended that thiopental be used for cerebral protection during CEA. As mentioned previously, avoidance

of ischemia is preferable to its treatment. If thiopental is used, the EEG, because of its isoelectricity, becomes useless as a monitor of cerebral ischemia. This is especially problematic if selective shunting is to be done. Furthermore, the doses of thiopental required to suppress the EEG may cause hypotension and a delayed emergence from anesthesia.

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Barbiturate use to minimize the possibility of cerebral ischemia has been advocated for the patient undergoing carotid bypass procedures in which temporary occlusion of the recipient vessel is required. Whether treatment of patients with a 3 to 5 mg per kg dose of thiopental affects their outcome in terms of neurologic deficit is not known, although it has been shown to be efficacious in animal models.

Like barbiturates, the intravenous anesthetics propofol and etomidate also decrease brain electrical activity and cellular oxygen requirements while preserving cerebral autoregulation of blood flow. Although the available evidence for the protective effects of etomidate and propofol during CEA is inconclusive, these agents have been demonstrated to reduce brain infarction and prolong tolerable ischemia time in patients undergoing temporary ischemia for intracranial aneurysm clipping. Additionally, animal studies have suggested a degree of neuroprotection with propofol.

Dexmedetomidine is a selective α_2-adrenergic agonist with sedative, analgesic, and anxiolytic properties. It does not cause respiratory depression. In animal studies, dexmedetomidine reduces ischemic damage after transient and permanent ischemia. Its mechanism of neuroprotection is still unclear. One hypothesis suggests that with the onset of cerebral ischemia, one of the initial responses in the central nervous system is the excessive release of norepinephrine and glutamate during energy failure. If the increase in norepinephrine release is a causative component of injury, an α_2-adrenergic agonist may decrease the damage afforded by cerebral ischemia. Dexmedetomidine has been shown to reduce arousal and decrease CBF in volunteers.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Hicks RG, Kerr DR, Horton DA. Thiopentone cerebral protection under EEG control during carotid endarterectomy. *Anaesth Intensive Care*. 1986;14:22-28.

Holzer A, Greher M, Hetz H, et al. Influence of aortic blood flow velocity on changes of middle cerebral artery blood flow velocity during isoflurane and sevoflurane anaesthesia. *Eur J Anaesthesiol*. 2001;18:238-244.

Kuhmonen J, Pokorný J, Miettinen R, et al. Neuroprotective effects of dexmedetomidine in the gerbil hippocampus after transient global ischemia. *Anesthesiology*. 1997;87:371-377.

Matta BF, Heath KJ, Tipping K, et al. Direct cerebral vasodilatory effects of sevoflurane and isoflurane. *Anesthesiology*. 1999;91:677-680.

Messick JM Jr, Casement B, Sharbrough FW, et al. Correlation of regional cerebral blood flow (rCBF) with EEG changes during isoflurane anesthesia for carotid endarterectomy: critical rCBF. *Anesthesiology*. 1987;66:344-349.

Michenfelder JD, Sundt TM, Fode N, et al. Isoflurane when compared to enflurane and halothane decreases the frequency of cerebral ischemia during carotid endarterectomy. *Anesthesiology*. 1987;67:336-340.

Nehls DG, Todd MM, Spetzler RF, et al. A comparison of the cerebral protective effects of isoflurane and barbiturates during temporary focal ischemia in primates. *Anesthesiology*. 1987;66:453-464.

C.13. How will you manage this patient's ventilation under general anesthesia?

Because carbon dioxide is a potent cerebral vasodilator, it was initially recommended that patients undergoing CEA be hypoventilated intraoperatively to achieve hypercarbia and cerebral vasodilation. It is now well accepted that hypercapnia should be avoided in patients with carotid artery disease. Carbon dioxide causes vasodilation in normally reactive, nonischemic, vascular beds. In patients with carotid artery disease, this means that blood flow is diverted away from the already maximally dilated vessels in the territory of the occluded carotid and toward normal areas of the brain. This decrease in regional CBF in ischemic areas of the brain with increased CBF in normal areas of the brain is known as *intracerebral steal*.

Other authors have recommended extreme hypocapnia during CEA, reasoning that this would result in an “inverse steal”

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or “Robin Hood” phenomenon. Hypocapnia will cause constriction of cerebral vessels in normally perfused areas of the brain, possibly diverting blood flow into the maximally vasodilated, unreactive, hypoperfused regions of the brain. Clinical trials have been unable to demonstrate any benefit from hypocapnia, and animal studies have shown that it may, in fact, exacerbate ischemia. This most likely happens not

only because of intense vasoconstriction but also because of a leftward shift of the oxyhemoglobin dissociation curve so that hemoglobin is less able to give its oxygen to tissues.

The general recommendation for patients with cerebrovascular disease is that normocarbia or mild hypocarbia be maintained. After repair of their carotid stenosis, some patients will have a marked hyperemia with CBF of 100 mL/100 g/min. In these patients, decreasing both blood pressure and arterial carbon dioxide tension to decrease their CBF is indicated. Without a decrease in CBF, these patients are at risk for postoperative intracerebral hemorrhage.

Baker WH, Rodman JA, Barnes RW, et al. An evaluation of hypocarbia and hypercarbia during carotid endarterectomy. *Stroke*. 1976;7:451-454.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

C.14. How will you manage this patient's blood pressure intraoperatively?

Various factors need to be considered in the blood pressure management of patients undergoing CEA. In the patient with carotid artery disease, a loss of autoregulation occurs in ischemic areas of the brain. In areas of chronic hypoperfusion, vessels are maximally vasodilated and unresponsive to vasomotor stimuli. Perfusion in these ischemic areas is pressure dependent.

During cerebral arterial occlusion, systemic blood pressure may need to be increased to augment collateral blood flow. The primary collateral pathways include the Willisian channels. If Willisian channels are not available, either because of the patient's anatomy or a therapeutic intervention, secondary collateral channels are available that bridge adjacent major vascular territories. These pathways are known as the *pial-to-pial collateral* or *leptomeningeal* pathways.

Because of the adjustment of the autoregulatory limits in hypertensive patients and because of a lack of autoregulation in ischemic areas of the brain, hypotension should be avoided. The patient's blood pressure should be maintained in its high normal range. During arterial occlusion, the only practical way to increase collateral blood flow may be by increasing the collateral perfusion pressure by raising the systemic blood pressure. The extent to which the blood pressure should be raised depends on the nature of the disease. During deliberate hypertension, the systemic blood pressure is raised by 30% to 40% above the baseline or until ischemic symptoms resolve. Both maintenance of and increases in blood pressure can be accomplished with light anesthesia and, when necessary, infusion of the α-agonist phenylephrine. Phenylephrine has no direct effect on the cerebral vasculature; therefore, cerebral perfusion is increased by an elevation in the cerebral perfusion pressure. Phenylephrine increases blood pressure, cerebral perfusion pressure, stump pressure, and regional CBF. It also increases myocardial oxygen consumption. Because it increases afterload, care must be taken when it is used in patients with coronary artery disease. It may exacerbate myocardial ischemia and congestive heart failure. In patients with coronary artery disease, blood pressure should not be increased above baseline unless evidence of cerebral ischemia develops. Extreme increases in blood pressure can and should be managed with easily titratable intravenous vasodilators such as sodium nitroprusside or nitroglycerin.

After the bifurcation of the carotid artery is exposed, the surgeon often infiltrates the carotid sinus with lidocaine to eliminate the unpredictable hemodynamic response to manipulation of the carotid artery.

Once the stenosis has been relieved and the carotid cross-clamp removed, the patient's blood pressure should be maintained in its low normal range. This lowering of blood pressure offers several advantages. It decreases myocardial oxygen consumption by decreasing the work of the heart, it decreases the amount of stress on the suture line in the carotid artery, and finally, it minimizes the possibility of reperfusion hemorrhage.

Aaslid R, Lindegaard KF, Sorteberg W, et al. Cerebral autoregulation dynamics in humans. *Stroke*. 1989;20:45-52.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

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Smith JS, Roizen MF, Cahalan MK, et al. Does anesthetic technique make a difference? Augmentation of systolic blood pressure during carotid endarterectomy: effects of phenylephrine versus light anesthesia and of isoflurane versus halothane on the incidence of myocardial ischemia. *Anesthesiology*. 1988;69:846-853.

C.15. Discuss reperfusion injury following CEA and carotid artery stenting (CAS).

Reperfusion injury involves cerebral hemorrhage or the development of cerebral edema after obstruction to flow through the carotid artery has been relieved. Although rare, it is an often fatal complication of CEA. Patients with a previous stroke are most likely to suffer reperfusion hemorrhage, but it can occur in otherwise normal brain tissue. Poorly controlled blood pressure after the carotid cross-clamp has been removed contributes to this complication. One proposed mechanism for this injury is that once flow is returned to normal, vascular beds in previously hypoperfused areas of the brain are unable to respond properly with vasoconstriction. They are unable to maintain normal flow with increased perfusion. Because hypoperfusion distal to the carotid stenosis has been long-standing, these vessels have lost their ability to autoregulate. Once the carotid stenosis is eliminated, the perfusion pressure distal to the former site of the stenosis is markedly increased. Because of the lack of autoregulation in this area, CBF increases with increasing perfusion. The patients at highest risk for reperfusion injury have the greatest degree of stenosis and the greatest pressure drop across the carotid lesion. Again, maintaining blood pressure control with antihypertensive medications once the carotid obstruction is eliminated decreases the incidence of reperfusion injury.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Breen JC, Caplan LF, DeWitt LD, et al. Brain edema after carotid surgery. *Neurology*. 1996;46:175-181.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

Solomon RA, Loftus CM, Quest DO, et al. Incidence and etiology of intracerebral hemorrhage following carotid endarterectomy. *J Neurosurg*. 1986;64:29-34.

C.16. What intravenous fluids will you give this patient intraoperatively?

Because moderate hyperglycemia has been shown to worsen neurologic outcome after ischemia, care must be taken to avoid increasing the patient's glucose with exogenously administered dextrose. Intravenous fluids such as normal saline, lactated Ringer's solution, or another buffered crystalloid solution would be appropriate choices for patients undergoing CEA.

These patients should not be vigorously hydrated intraoperatively. It is best to limit their intraoperative fluids to what is required for maintenance, with additional colloid and blood replacement being given as needed. Intraoperative overhydration may lead to some of the frequently observed postoperative hypertension and in patients with myocardial disease may exacerbate congestive heart failure.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Li PA, Siesjö BK. Role of hyperglycaemia-related acidosis in ischaemic brain damage. *Acta Physiol Scand*. 1997;161:567-580.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

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D. Postoperative Management

D.1. The patient does not "wake up" from general anesthesia. Why?

Once other causes of slow emergence from general anesthesia (e.g., hyperglycemia or hypoglycemia, hypothermia, anesthetic overdose, hypercarbia, and hypoxemia) have been ruled out, the possibility of an adverse intraoperative event having occurred needs to be considered. Patency of the carotid artery should be evaluated. This can be done by Doppler studies while the patient is still in the operating room. If no blood flow is seen in the carotid artery, the incision can be reexplored immediately. If Doppler studies are normal, the possibility of a cerebral infarction from prolonged hypoperfusion or from emboli must be considered. The patient should remain intubated while further studies, including a computed tomography (CT) scan

and cerebral angiography, are done as expeditiously as possible. The incidence of new perioperative neurologic deficits is 3% in centers where the operation is done commonly.

Graber JN, Vollman RW, Johnson WC, et al. Stroke after carotid endarterectomy: risk as predicted by preoperative computerized tomography. *Am J Surg*. 1984;147:492-497.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

Paciaroni M, Eliasziw M, Kappelle LJ, et al. Medical complications associated with carotid endarterectomy. *Stroke*. 1999;30:1759-1763.

D.2. Postoperatively, the patient's blood pressure is 170/96 mm Hg. Will you treat this?

This patient's blood pressure needs to be carefully controlled because postoperative hypertension is associated with bleeding at the operative site, myocardial ischemia, arrhythmias, intracerebral hemorrhage, and cerebral edema.

Hypertension is observed more commonly than hypotension after CEA. Causes of hypertension include hypoxemia, hypercarbia, pain, and a full bladder. Obviously, if any or all of these causes are present, they need to be dealt with promptly and appropriately. Another common cause of postoperative hypertension and tachycardia is blunting of the carotid baroreceptor mechanism secondary to carotid sinus dysfunction caused by surgical trauma. If this is the cause of hypertension, therapy with antihypertensive agents should be started.

This patient's blood pressure should be maintained in her low normal range postoperatively. Elevated blood pressure can be treated with hydralazine in 5-mg increments or, if the patient is not bradycardic, labetalol may be used in 10-mg increments. Alternatively, infusions of sodium nitroprusside or nitroglycerin may be used. β-Blockade with metoprolol or an infusion of esmolol may be added to this regimen.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

Wong JH, Findlay JM, Suarez-Almazor ME. Hemodynamic instability after carotid endarterectomy: risk factors and associations with operative complications. *Neurosurgery*. 1997;41:35-41.

D.3. What immediate postoperative complications might you expect?

Immediate postoperative complications include neurologic deficits, hemodynamic instability, and respiratory insufficiency. Evaluation of the NASCET showed that 8.1% of patients had medical complications: 1% with myocardial infarctions, 7.1% with other cardiovascular disorders such as arrhythmias and congestive heart failure, 0.8% with respiratory complications, 0.4% with transient confusion, and 0.7% with other complications. CEA is 1.5 times more likely to be

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associated with complications in patients with a history of cardiac disease or hypertension.

Postoperative neurologic complications are usually embolic in nature, occurring during surgery. Other neurologic complications result from reperfusion injury and intracranial hemorrhage.

Circulatory instability is common after CEA, with either hypotension or hypertension being observed. Hypotension may have any of several causes, as does hypertension, as noted previously. These include hypovolemia, depression of the circulation by residual anesthetics, prolonged effect of intraoperatively administered antihypertensives, dysrhythmias, and myocardial ischemia. Each of these causes needs to be sought and, if present, treated appropriately. Another possible cause of hypotension is an excessive reflex response because of increased sensitivity of the carotid sinus after exposure of the baroreceptor mechanism to a higher pressure with removal of the plaque. If this is the cause, therapy needs to be instituted with fluids and vasopressors.

Postoperative respiratory insufficiency is a rare but potentially life-threatening complication. This can be due to vocal cord paralysis from intraoperative traction on the laryngeal nerves. Should this present with inability to protect the airway, the patient should be reintubated immediately.

A prospective trial found that 12.5% of patients had nerve injuries after CEA, but all were transient, lasting from 1 week to 37 months. No patient had life-threatening respiratory insufficiency from the nerve injuries. The most commonly injured nerves were the hypoglossal, recurrent laryngeal, superior laryngeal, and greater auricular nerves.

Airway obstruction can also occur from hematoma formation at the operative site, from either arterial or venous bleeding. The hematoma needs to be evacuated as quickly as possible, and depending on ventilatory status, the patient may need to be intubated. This is most easily done after evacuation of the hematoma if the clinical condition allows.

Supraglottic edema may also be a rare cause of postoperative upper airway obstruction after CEA. CT analysis of airways postoperatively showed reduction in the volume of the airway in all patients, with a greater reduction seen in intubated patients (63% ± 9%) than in nonintubated patients (32% ± 7%).

Tension pneumothorax can result from air dissecting through the wound and the mediastinum to the pleura. This diagnosis should be considered in all patients after CEA who seem to have respiratory distress and no evidence of upper airway obstruction. Absence of breath sounds over half of the chest and hemodynamic instability would support this diagnosis.

Chemoreceptor function is irreversibly suspended in most patients after CEA for up to 10 months. Lack of chemoreceptor function means that there is a loss of circulatory response to hypoxia and an increase in resting $PaCO_2$ of approximately 6 mm Hg. This complication is potentially very serious, and one needs to be most concerned about its development in patients who have had a previous contralateral CEA, where function may be lost bilaterally. In all patients after CEA, supplemental oxygen should be provided and opioids administered cautiously.

Ballotta E, Da Giau G, Renon L, et al. Cranial and cervical nerve injuries after carotid endarterectomy: a prospective study. *Surgery*. 1999;125:85-91.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013:1123-1128.

Carmichael FJ, McGuire GP, Wong DT, et al. Computed tomographic analysis of airway dimensions after carotid endarterectomy. *Anesth Analg*. 1996;83:12-17.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

Paciaroni M, Eliasziw M, Kappelle LJ, et al. Medical complications associated with carotid endarterectomy. *Stroke*. 1999;30:1759-1763.

Wade JG, Larson CP Jr, Hickey RF, et al. Effects of carotid endarterectomy on carotid chemoreceptor and baroreceptor function in man. *N Engl J Med*. 1970;282:823-829.

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D.4. Discuss postoperative neurocognitive dysfunction following uncomplicated CEA.

CEA will reduce the incidence of stroke in patients with high-grade carotid artery stenosis. Increasing evidence suggests that as many as 28% of surgical patients have significant neuropsychological dysfunction 1 day after carotid artery surgery. Between 9% and 23% of these patients continue to exhibit cognitive decline 1 month after surgery.

The apolipoprotein E (APOE)-*ε*4 allele has been associated with worse outcome following stroke. In a prospective trial, 75 patients undergoing CEA were studied. Of 75 patients, 12 (16%) possessed the APOE-*ε*4 allele. Of the 75 patients, 8 (11%) experienced cognitive dysfunction on postoperative day 30. One month after CEA, APOE-*ε*4-positive patients were more likely to have suffered a neurocognitive injury (42%) than APOE-*ε*4-negative patients (5%).

The presence of the APOE-ε4 allele increases the risk of neurocognitive dysfunction 62-fold 1 month after surgery. Diabetes and obesity also predisposed to injury.

Evidence also indicates cognitive dysfunction in patients with carotid stenosis treated with CAS performed under cerebral embolic protection. In a prospective case control study, 41% of patients undergoing carotid stenting developed moderate to severe cognitive dysfunction compared to a matched control group. The average deficit score was significantly higher in the CAS group at 1 day. These differences were independent of age and history of stroke or TIA. The absence of oral statin medication may increase the probability of cognitive dysfunction.

The influence of regional versus general anesthesia in postoperative subclinical cognitive dysfunction remains unclear. Most concur that multiple factors, including surgical technique, anesthetic technique, and patient status, influence postoperative outcome.

Gaudet JG, Meyers PM, McKinsey JF, et al. Incidence of moderate to severe cognitive dysfunction in patients treated with carotid artery stenting. *Neurosurgery*. 2009;65:325-329.

Heyer EJ, Wilson DA, Sahlein DH, et al. APOE-epsilon4 predisposes to cognitive dysfunction following uncomplicated carotid endarterectomy. *Neurology*. 2005;65:1759-1763.

Mazul-Sunko B, Hromatko I, Tadinac M, et al. Subclinical neurocognitive dysfunction after carotid endarterectomy—the impact of shunting. *J Neurosurg Anesthesiol*. 2010;22:195-201.

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Chapter 19

Awake Craniotomy for Mapping and Surgery in the Eloquent Cortex

Thomas A. Moore II

A 47-year-old right-handed physician presented after two episodes of acute onset of left-sided headache associated with a change in reading comprehension and difficulty with word finding. Each episode lasted several minutes without loss of consciousness or generalized seizure activity. Magnetic resonance imaging (MRI) revealed a 4 cm × 5 cm variably marginated mass in the inferior aspect of the left temporal lobe involving the middle and inferior temporal gyri as well as the occipitotemporal gyrus (Fig. 19.1). He was started on corticosteroids, and his symptoms did not reappear. Diffusion tensor imaging was used to determine that his optic radiations and Meyer loop were not within the lesion. Magnetoencephalography (MEG) was used to determine the location of his primary motor area. He underwent an uncomplicated awake left craniotomy with motor and language area mapping. He was discharged to home the next day. Final pathology revealed an anaplastic astrocytoma World Health Organization grade III.

A. Medical Disease and Differential Diagnosis

1. What is the eloquent cortex?
2. What is the underlying pathology?
3. What determines intracranial pressure (ICP)?
4. How does a space-occupying mass alter ICP?
5. What is autoregulation, and why is it important?
6. How is cerebral blood flow (CBF) regulated?
7. What drug therapies may be associated with this pathology?

B. Preoperative Evaluation and Preparation

1. Why is the craniotomy performed awake?
2. What current symptoms of the patient are important?
3. Are there anesthetic implications from current treatment drugs?
4. What laboratory data are required?
5. What radiology data should be reviewed?
6. How do you prepare the patient for an awake craniotomy?
7. Should this patient receive premedications?
8. What precautions should be made for airway management?

C. Intraoperative Management

1. How should this patient be monitored?
2. Does this patient require invasive monitoring?
3. Can current drug therapy alter eloquent cortex mapping?
4. Why use hypertonic fluids during a craniotomy?

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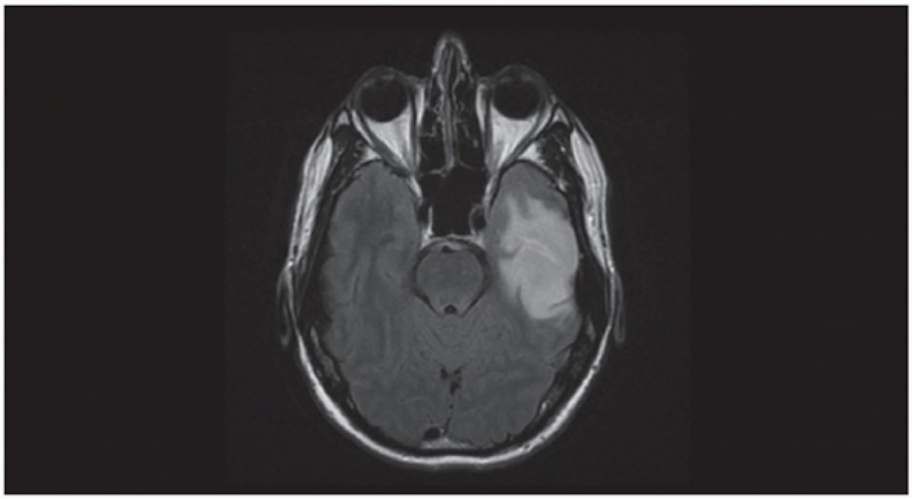


FIGURE 19.1 A 47-year-old man with two episodes of left-sided headaches associated with problems with reading comprehension and difficulty with word finding. He underwent an uneventful left awake craniotomy with motor and language area mapping. Final pathology was a World Health Organization grade III anaplastic oligoastrocytoma.

5. What intravenous fluids (IVFs) are recommended?
6. Would a lumbar drain for cerebrospinal fluid (CSF) removal benefit this patient?
7. Venous air embolism (VAE): Is it a concern in this case?
8. How is the eloquent cortex mapped?
9. How are intraoperative seizures treated?
10. How will you conduct this anesthetic?

D. Postoperative Management

1. What are the major concerns following craniotomy?

A. Medical Disease and Differential Diagnosis

A.1. What is the eloquent cortex?

Eloquent cortex is a term usually used to describe functional areas of the cerebral cortex associated with motor, language, and sensory activity. Traditionally, tumors or epileptic foci within or near these areas have been termed *inoperable* because of the devastation caused to the patient by injury to these neurons.

De Benedictis A, Moritz-Gasser S, Duffau H. Awake mapping optimizes the extent of resection for low-grade gliomas in eloquent areas. *Neurosurgery*. 2010;66(6):1074-1084.

A.2. What is the underlying pathology?

The underlying pathology requiring an awake craniotomy for mapping and resection within the eloquent cortex can be either a space-occupying lesion or epileptic foci. In either case, mapping of the cortical and subcortical structures with an awake and cooperative patient is necessary to minimize neurologic injury and maximize lesion resection. Mapping of the motor cortex is often done under general anesthesia, after reversal of any residual muscle relaxant, because the stimulated area(s) can usually be seen by an observer. Nevertheless,

there are several potential problems. In the case of a space-occupying lesion, the neuronal pathways can become distorted secondary to the expanding mass and mislead the surgeon who is searching not only for the functional area but also a “quiet” area of cortex through which to do the resection. In addition, these patients are frequently in a lateral

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decubitus position, with the side to be observed in the down position. Visualization of the patient can be further obstructed with sheets, blankets, forced warm-air blankets, and other patient-positioning devices. Hence, we tend to map the motor cortex in an awake craniotomy whenever possible.

Supratentorial brain tumors are about 31% gliomas (Fig. 19.1), 15% meningiomas, 12% metastatic lesions, and 8% pituitary tumors. Metastatic lesions are most frequently lung, breast, and gastrointestinal tract tumors. Additional space-occupying lesions include blood and blood vessels, infections, hydrocephalus, cerebral infarctions, radiation necrosis, arachnoid cysts, and cerebral edema.

These space-occupying lesions can present in various manners. The most common presentation of brain tumors is a progressive neurologic deficit (68%), usually motor weakness (45%), headache (54%), and seizures (26%). Others may present from progressive focal deficits resulting from destruction of brain tissue or compression of normal brain structures by the mass itself or peritumoral edema. Additional presentations include nausea or vomiting, vertigo, lethargy, apathy, and changes in mental status as several examples.

In addition to these various presenting signs and symptoms, asymmetric supratentorial tumors can enlarge to the point of causing a midline shift of the intracranial contents, possibly leading to herniation. The brain can be displaced across the midline beneath the falx or compressed through the tentorial incisura into the posterior fossa. As these various areas of the brain are compressed against these dense fibrous structures, stretching and shearing of the penetrating arteries can result in devastating neurologic injuries.

An area of cerebral edema surrounds most intracranial masses secondary to the disruption of the blood-brain barrier (BBB) usually associated with a localized acidosis. Vasogenic edema reflects a shift of fluid from the intravascular to the extravascular space. Cytotoxic edema represents a shift of fluid from the extracellular to the intracellular space. Vasogenic edema responds very well to corticosteroid treatment. Dexamethasone is frequently prescribed for this problem. This area of cerebral edema is known as the penumbral area and represents areas of autoregulatory dysfunction as well as BBB breakdown. The vasculature in this area of the brain is usually maximally vasodilated. Hypercapnia in surrounding normal brain causes vasodilation in the normal vasculature and may result in decreased flow to the ischemic area. Hypocapnia, on the other hand, causes vasoconstriction of the normal adjacent vascular beds, with the resultant redistribution of blood to the ischemic area. This has been referred to as the “Robin Hood” phenomenon. The formation of peritumoral edema increases the overall size of the tumor, which can lead to the same signs and symptoms as noted earlier.

Patients presenting for an awake craniotomy for excision of an epileptic foci have usually had a seizure disorder for many years and have been on numerous antiepileptic drugs (AEDs) in an attempt to control their disorder. Unfortunately, many of these patients develop adverse reactions or cannot tolerate the side effects of the AEDs and become, for practical purposes, medication failures. Table 19.1 lists the more common AEDs and the types of seizure disorder they treat.

Only patients with seizures in whom the foci are localized in an area of eloquent cortex require an awake craniotomy. Temporal lobe, hippocampal-localized foci are usually resected under general endotracheal anesthesia with intraoperative electrocorticography. Most of these patients have had preceding intracranial strips, grids, or electrodes placed to help localize the seizure foci.

Fishman RA. Brain edema. *N Engl J Med*. 1975;293:706-711.

O'Rourke DK, Oldfield EH. Supratentorial masses: surgical considerations. In: Cottrell JE, Smith DS, eds. *Anesthesia and Neurosurgery*. 4th ed. Philadelphia, PA: Mosby; 2001:275-295.

A.3. What determines intracranial pressure (ICP)?

The adult skull is a rigid, bony box with a fixed volume. Neonatal and infant skulls have several noncalcified portions, called fontanels, that allow the skull to deform during passage through the birth canal. These noncalcified areas also allow the volume of the skull to

increase in the presence of increased ICP such as congenital hydrocephalus. Once these areas have calcified, the pediatric skull is also a rigid, fixed volume box.

TABLE 19.1 Commonly Used Drugs in Seizure Control

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TYPE OF SEIZURE	FIRST-LINE DRUG	SECOND-LINE DRUG
Generalized tonic-clonic	Carbamazepine	Clobazam
	Phenytoin	Clonazepam
	Valproate	Lamotrigine
		Phenobarbital
		Vigabatrin
		Felbamate
		Acetazolamide
Generalized absence	Valproate	Clonazepam
	Ethosuximide	Lamotrigine
		Acetazolamide
Tonic, atonic, atypical absences	Valproate	Carbamazepine
	Clobazam	Phenobarbital
	Clonazepam	Felbamate
	Lamotrigine	Acetazolamide
	Phenytoin	
Myoclonic seizures	Valproate	Phenobarbital
	Clonazepam	Acetazolamide
Simple partial, complex partial, secondarily generalized	Carbamazepine	Clobazam
	Valproate	Lamotrigine
	Phenytoin	Gabapentin
		Vigabatrin
		Phenobarbital

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Felbamate

Acetazolamide

From Frost EAM, LaFleur JL. Awake craniotomy for deep brain stimulation. In: Yao FF, Fontes ML, Malhotra V, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:585, with permission.

The intracranial constituents are intravascular blood, CSF, and the brain. As liquids, the blood and CSF are noncompressible. Although water can be extracted from the brain by use of osmotic diuretics and other hypertonic fluids, this does not result in much change in brain volume and its gel-like consistency also makes it virtually noncompressible.

ICP is a relationship of the homeostatic balance of the noncompressible contents within a fixed-volume container, the skull. The normal value is 10 to 15 mm Hg. In the early 19th century, the Monro-Kellie hypothesis was the first attempt to describe this relationship. Although several modifications of this doctrine have been made over the years as more has been learned, the basic principle still holds true: Because the intact skull is unyielding, an increase in volume of any one of the normal contents or the addition of a space-occupying lesion must be accompanied by a reduction in one or more of the normal constituents to maintain normal ICP.

Artru AA. Cerebrospinal fluid. In: Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby; 2010:60-72.

Mokri B. The Monro-Kellie hypothesis: applications in CSF volume depletion. *Neurology*. 2001;56:1746-1748.

A.4. How does a space-occupying mass alter ICP?

There are limits to the balanced relationship described by the Monro-Kellie hypothesis. Figure 19.2 represents an idealized ICP-volume curve and diagrams these limitations.

The flat portion of the curve represents increasing volume with no increase in ICP. Several compensatory mechanisms are at work to keep the ICP steady. The most effective of these mechanisms is the dynamic nature of CSF. The rate of absorption increases or the rate of production decreases in light of an increase in ICP. Cerebral blood volume (CBV) is decreased by a redistribution primarily of the intracranial venous blood volume. These mechanisms work to keep the ICP at its normal value of 10 to 15 mm Hg. As the volume continues to increase, these compensatory mechanisms become exhausted and ICP starts to rise as represented by the “knee” of the graph. It is important to note that at this area of the curve, small increases in volume give rise to a much larger increase in ICP. The sharp rise in the graph demonstrates rapidly increasing ICP with even smaller increases in volume. It is vitally important to understand that as the volume continues to rise and ICP continues to increase, the risk of cerebral herniation also increases. Cerebral perfusion pressure (CPP) is also adversely affected with a rise in ICP. CPP is defined as: CPP = MAP - ICP (CVP), where MAP = mean arterial pressure and CVP = central venous pressure. This equation readily shows that an increase in ICP will lead to a decrease in CPP.

Figure 19.3 shows that CBF remains at 100% for CPPs ranging from 50 to 150 mm Hg. Some have recently advocated that the lower threshold for autoregulation should be shifted more toward 70 mm Hg and the upper threshold shifted more toward 180 mm Hg. In the supine position, ICP in the normal state is effectively zero, making CPP directly related to MAP.

A.5. What is autoregulation, and why is it important?

In its simplest form, autoregulation is a myogenic response of the vascular smooth muscle of the intracranial cerebral arterioles to maintain a nearly constant CBF in the face of changing CPP. Not all of the mechanisms controlling this action are fully understood.

When CPP becomes less than 50 mm Hg or greater than 150 mm Hg, the CBF becomes pressure passive. This response is important to keep in mind when considering the use of deliberate hypotension. A MAP of less than 50 mm Hg could theoretically cause a decrease in CPP and thereby decrease CBF to the point of causing cerebral ischemia. On

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the other side of the spectrum, MAPs greater than 150 mm Hg can cause disruption of the BBB and cause

vasogenic edema throughout the brain, not only in the area of vasogenic edema surrounding the tumor.

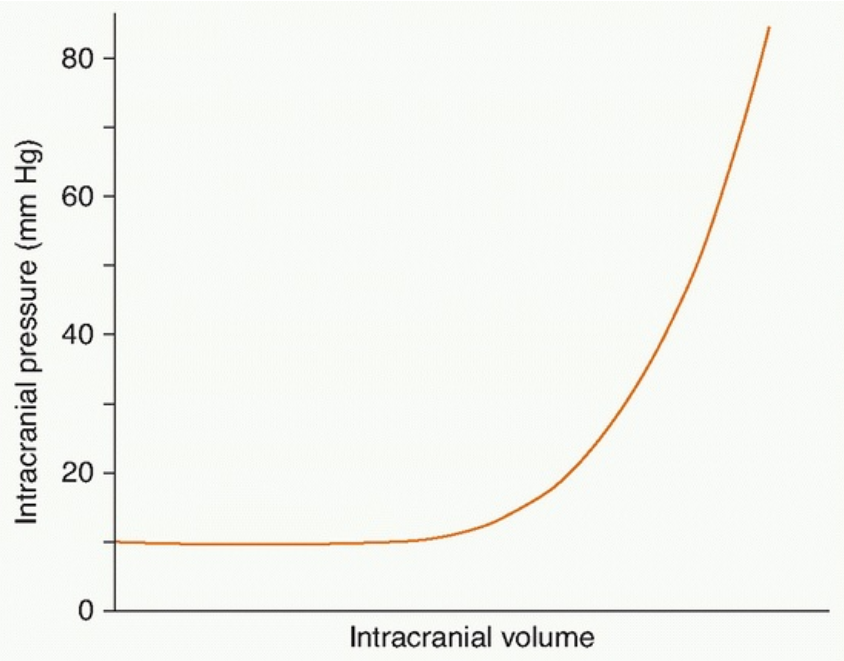


FIGURE 19.2 Idealized intracranial pressure-volume curve. (From Hou YJ, Kass IS. Physiology and metabolism of the brain and spinal cord. In: Newfield P, Cottrell JE, eds. *Handbook of Neuroanesthesia* . 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2012:16, with permission.)

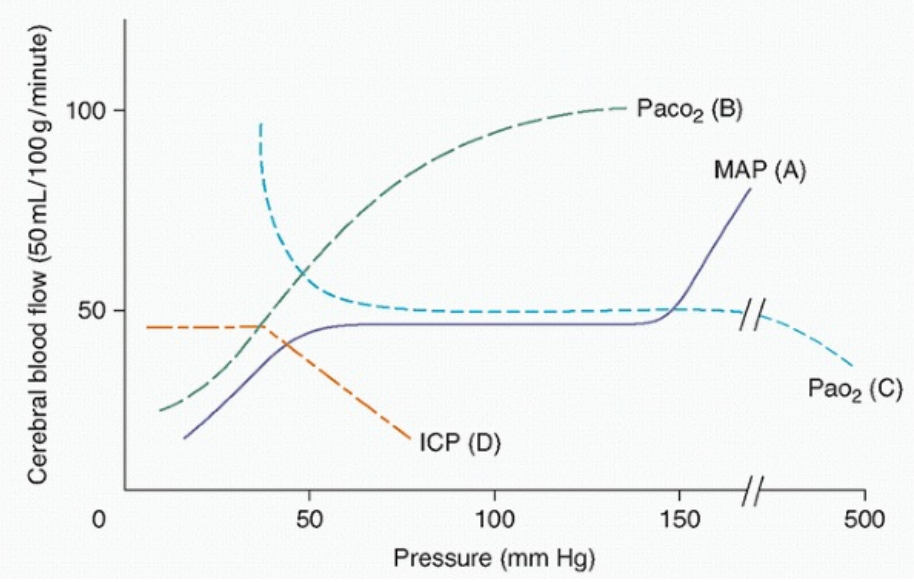


FIGURE 19.3 Pressure-cerebral blood flow relationships. **A.** Cerebral blood flow (CBF) autoregulation. CBF is maintained at 50 mL/100 g/min for mean arterial pressure (MAP)/cerebral perfusion pressure (CPP) = 50 to 150 mm Hg. **B.** Linear relationship between $PaCO_2$ and CBF for $PaCO_2$ = 20 to 80 mm Hg. **C.** PaO_2 and CBF. **D.** Intracranial pressure (ICP) and CBF. (From Hou YJ, Ravussin PA. Anesthesia for supratentorial tumors. In: Newfield P, Cottrell JE, eds. Handbook of Neuroanesthesia. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2012:118, with permission.)

The autoregulation curve is shifted to the right in the presence of chronic uncontrolled hypertension, as shown in Figure

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19.4.

This is important because now the lower threshold for cerebral ischemia is higher than in the normal state. Although there is not a direct correlation between degree of hypertension and rightward shift of the autoregulatory curve, it is possible that where signs of cerebral

ischemia might not have become obvious until the CPP was 30 to 40 mm Hg in the normotensive person, these signs may now occur with the CPP at 80 to 90 mm Hg, a usually normal CPP. Therefore, great care must be taken to keep the MAP near the patient's usual levels in the uncontrolled or poorly controlled hypertensive patient. On the other end of the curve, it is possible that the rightward shift adds some form of cerebral protection against perfusion breakthrough at the higher CPPs. Treatment with antihypertensive drugs modifies this rightward shift back toward the normal range. The degree to which this occurs depends both on the length of time the hypertension has been treated and the resultant decrease in blood pressure.

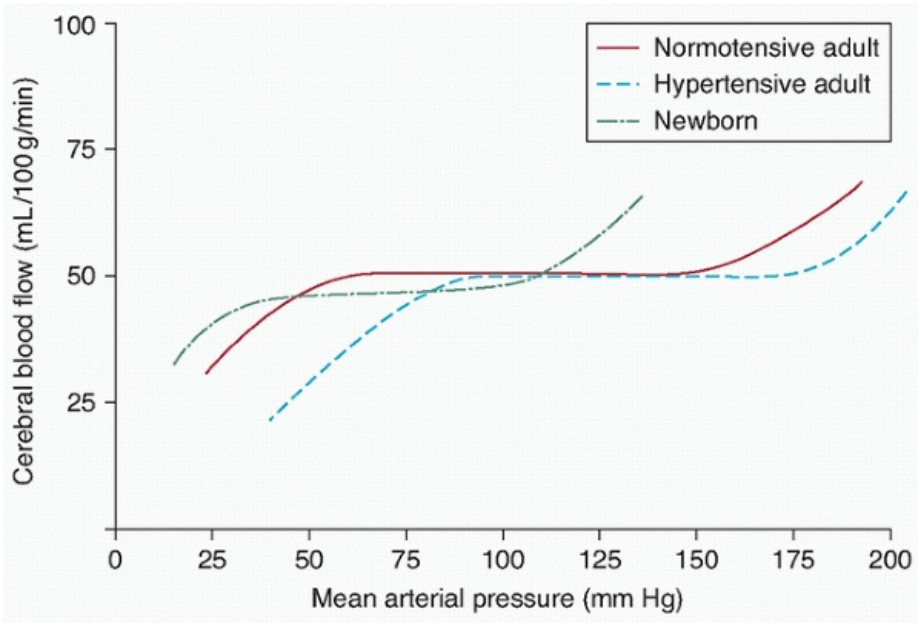


FIGURE 19.4 Autoregulatory curve of the cerebral vasculature in the normotensive adult, the hypertensive adult, and the newborn. (From Hou YJ, Ravussin PA. Anesthesia for supratentorial tumors. In: Newfield P, Cottrell JE, eds. *Handbook of Neuroanesthesia* . 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2012:15, with permission.)

The type of drug used to treat hypertension may also determine the effect on autoregulation. Systemic direct-acting vasodilators without action on cerebrovascular smooth muscle and α-adrenergic and ganglionic blocking drugs should have no effect on cerebrovascular autoregulation. Systemic direct-acting vasodilators that do have an action on the cerebrovascular smooth muscle, such as hydralazine, sodium nitroprusside, nitroglycerin, and calcium channel blockers may influence autoregulation. Treating congestive heart failure may also improve CPP by lowering CVP and thereby decreasing cerebral venous outflow pressure.

Drummond JC. The lower limit of autoregulation: time to revise our thinking? *Anesthesiology*. 1997;86:1431-1433.

Drummond JC, Patel PM. Neurosurgical anesthesia. In: Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2158-2199.

Paulson OB, Strandgaard S, Edvinsson L. Cerebral autoregulation. *Cerebrovasc Brain Metab Rev*. 1990;2:161-192.

A.6. How is cerebral blood flow (CBF) regulated?

CBF also responds to chemical modulation. Figure 19.3 demonstrates these relationships in the arterial carbon dioxide

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partial pressure ($PaCO_2$) and arterial oxygen partial pressure (PaO_2) curves. Carbon dioxide (CO_2) concentration is the most potent modulator of CBF. Insonating the middle cerebral artery of a volunteer by means of transcranial Doppler device and asking the subject to hyperventilate will show an increase in cerebral blood velocity reflecting a decrease in CBF secondary to cerebral vascular constriction, usually within 3 to 4 breaths, a very rapid response. This principle is utilized to treat increased ICP by decreasing CBV secondary to the hyperventilation. However, this mechanism is self-limited after approximately 6 to 10 hours and will no longer provide the decreased ICP.

As shown in Figure 19.3, there is a near linear response in CBF at a $PaCO_2$ between 20 and 80 mm Hg, with CBF increasing about 2% to 4% for each millimeter of mercury change in $PaCO_2$. In general, doubling $PaCO_2$ from 40 to 80 mm Hg doubles CBF and likewise halving $PaCO_2$ from 40 to 20 mm Hg halves CBF. This represents maximal vasodilation at extreme hypercapnia and maximal vasoconstriction at extreme hypocapnia, respectively.

CBF also responds to the oxygen partial pressure. As shown in Figure 19.3, when the PaO_2 reaches approximately 50 mm Hg, a steep increase in CBF occurs as the PaO_2 continues to fall. At normal PaO_2 levels, CBF is not affected. Hyperoxia can actually cause a 10% to 15% decrease in CBF at 1 atm. Temperature can also have an effect on CBF. For each 1°C decrease in body temperature, the cerebral metabolic rate for oxygen consumption ($CMRO_2$) decreases by approximately 7%. The regulation of CBF is known to be closely coupled to the cerebral metabolism and is reflected by a parallel decrease. These changes are not homogeneous with more changes seen in the cerebral and cerebellar cortices; less so in the thalamus and no difference in the hypothalamus and brainstem. During hypothermic cardiopulmonary bypass, lowering the body temperature to 26°C resulted in a 56% calculated reduction in $CMRO_2$ and a 55% reduction in CBF.

The potent inhalational agents can also increase CBF in the presence of decreasing $CMRO_2$, thus uncoupling their relationship. Increasing levels of minimum alveolar concentration can also blunt the CO_2 response or render CBF pressure passive. CO_2 reactivity is preserved during intraoperative use of opioids such as fentanyl and remifentanil.

Govier AV, Reves JG, McKay RD, et al. Factors and their influence on regional cerebral blood flow during nonpulsatile cardiopulmonary bypass. *Ann Thorac Surg*. 1984;38:592-600.

Joshi S, Ornstein E, Young WL. Cerebral and spinal cord blood flow. In: Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby; 2010:17-59.

A.7. What drug therapies may be associated with this pathology?

Patients can present with intracranial pathology at any age. Patients with comorbidities may be taking medications for hypertension, diabetes mellitus, congestive heart failure, or prior myocardial infarction (MI), as examples. It is not uncommon today for many patients to be on some form of antiplatelet drug whether they have suffered an MI or not. The effects of some of these drugs can be reversed with fresh frozen plasma, whereas others are not immediately reversible and need 7 to 10 days before their effect is gone.

Patients with epilepsy may be on several medications in an attempt to control their seizures. These drugs are listed in Table 19.1. Presenting signs and symptoms have been described earlier. AEDs are indicated in 26% of patients presenting with seizures who are later diagnosed with a brain tumor.

Another 20% to 45% of patients with brain tumors will eventually develop a seizure after diagnosis. The current standard (2010) is that prophylactic AEDs should not be started in this group of patients. As a guideline, in patients with brain tumors undergoing craniotomy, prophylactic AEDs may be used, and if there is no seizure activity, they may be tapered, starting 1 week postoperatively.

As previously discussed, most intracranial mass lesions are surrounded by an area of vasogenic edema to varying extents. The use of steroids, in particular dexamethasone, are commonly used to help alleviate the problems associated with this. Dexamethasone is more beneficial, and the effect often much more dramatic in metastatic tumors than primary tumors in reducing the area of edema. The usual dosage in the corticosteroid-naive patient is a loading dose of 10 mg IV and then 6 mg by mouth or IV every 6 hours. Doses of up to 10 mg every 4 hours have been given for severe vasogenic edema. For the patient previously diagnosed and on corticosteroids, the current dose is doubled for acute deterioration.

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Greenburg MS. Tumor. In: Greenburg MS, ed. *Handbook of Neurosurgery* . 7th ed. New York: Thieme; 2010:582-769.

B. Preoperative Evaluation and Preparation

B.1. Why is the craniotomy performed awake?

An awake craniotomy is performed when the pathologic lesion, be it a tumor or an epileptic focus, is in or near an area of eloquent cortex, as defined earlier, in an effort to preserve neurologic function.

The extent of the craniotomy is variable. Some neurosurgeons advocate a carefully planned, limited-exposure craniotomy defined with neuronavigational devices to encompass primarily the area of the lesion and immediate surrounding brain. Others advocate a large craniotomy exposing a wide cortical area for mapping. In either case, the primary goal of the surgical procedure is to obtain the greatest degree of tumor resection with as little damage to the eloquent cortex as possible and hence the least postoperative neurologic deficit.

Even with the cortex exposed, there are many challenges in identifying these areas of eloquent cortex that demand an awake and cooperative patient. As a tumor within or near the eloquent cortex grows and expands, the various neuronal pathways can become distorted from their normal anatomic locations. Ultrasonography may assist the neurosurgeon in identifying the lesion borders so testing can proceed in the surrounding areas of the cortex. Areas that do not elicit a response, respective of the area being tested, are also identified as areas of negative mapping and may serve as an entrance site for both cortical and subcortical resection as needed. Several studies have indicated that surgery through these areas of absolute negative mapping have a significantly lower incidence of both intraoperative and postoperative neurologic deficits. There is also increasing realization that there are more cortical areas that relate to an acceptable quality of life other than the areas of eloquent cortex. Nonlanguage areas that have to do with visual and/or vestibular functions, spatial awareness, cognitive function, understanding and judgment, memory, calculation, and emotion can be

mapped both cortically and subcortically to help prevent postoperative complications that are usually not discussed or described.

De Benedictis A, Moritz-Gasser S, Duffau H. Awake mapping optimizes the extent of resection for low-grade gliomas in eloquent areas. *Neurosurgery*. 2010;66(6):1074-1084.

Duffau H. Awake surgery for nonlanguage mapping. *Neurosurgery*. 2010;66:523-529.

Kim SS, McCutcheon IE, Suki D, et al. Awake craniotomy for brain tumors near eloquent cortex: correlation of intraoperative cortical mapping with neurological outcomes in 309 consecutive patients. *Neurosurgery*. 2009;64:836-846.

B.2. What current symptoms of the patient are important?

In order to successfully complete an awake craniotomy, the patient must be motivated to undergo the demanding procedure and able to effectively communicate with the neurosurgeon, the neurologist, and the neuroanesthesiologist. The patient must also be able to read short phrases, identify various objects, and describe pictures.

A patient who presents with some form of dysphasia may not be able to participate at all. Expressive dysphasia and global dysphasia are extreme examples but not uncommon presentations. At times, a short course of corticosteroids will decrease the penumbral area enough that verbal testing is practical. Some patients will present greatly agitated. Although this is usually their presenting symptom, they cannot cooperate in any fashion, even with minimal commands, and other means are necessary to care for these folks.

Areas of muscular weakness or paralysis, either from the current problem or past injury, must be identified preoperatively to differentiate between postoperative worsening and new neurologic deficits. Rarely will the patient show improvement in the immediate postoperative period; however, preexisting problems can actually be accentuated in the postoperative period.

Overall, patients who cannot communicate effectively or cooperate do not make good candidates for an awake craniotomy.

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B.3. Are there anesthetic implications from current treatment drugs?

Refer to Table 19.1 once again. Many of the AEDs currently available for treating patients with seizure disorders or those secondary to a brain tumor are listed here.

Many of these drugs, such as the benzodiazepines, hydantoins, analogs, and phenytoins, can interfere with drug metabolism in the liver, requiring increased dosages of IV anesthetic agents and narcotics.

In those patients started on dexamethasone, one may encounter several related abnormalities. Potential side effects associated with corticosteroid use include, but are not limited to, increased white blood cell (WBC) count, glucose intolerance, corticosteroid “stress ulcers,” corticosteroid-induced psychosis, hypertension, water and electrolyte imbalance, suppression of the hypothalamic-pituitary-adrenal axis, weight gain, and impaired wound healing.

B.4. What laboratory data are required?

Although the current practice is to minimize the number of preoperative laboratory tests obtained, several are necessary in the patient undergoing a craniotomy, awake or under general anesthesia, for tumor or epileptic foci resection.

Coagulation studies are a must. Although some tumors can have a significant amount of blood loss associated with their pathology (meningiomas), bleeding from an abnormal coagulation system into a tumor bed can pose very serious and at times life-threatening problems. Partial thromboplastin time, prothrombin time, international normalized ratio, and fibrinogen and platelet counts are routinely obtained. In patients who are or have recently taken clopidogrel bisulfate or other antiplatelet, adenosine diphosphate inhibitors, a platelet activity test might prove beneficial. Check with your local laboratory. This test requires specialized equipment and may be done only at certain times of the day; it may require some form of prenotification to the laboratory to ensure that pretesting preparation is completed before the blood sample arrives. Some AEDs may cause thrombocytopenia, but leukopenia is more common.

Electrolyte studies are necessary. This patient population can have imbalances from substances secreted by the tumor, such as atrial natriuretic factor, or secondary to drug effect,

such as hyponatremia or hypokalemia. Blood glucose levels are also included and should be controlled to 120 mg per dL or less, but hypoglycemia (less than 55 mg per dL) should be avoided, although this may differ among patients. Complete blood count with differential will give information about the hematocrit and WBC count. The differential will be normal if the WBC count is elevated from degranulation of the WBCs caused by preoperative corticosteroids. If not, an infection may be present and must be addressed. A routine urinalysis will rule out an asymptomatic urinary tract infection.

Blood type, antibody screen, and crossmatch are also required. In the case of a positive antibody screen, at least 4 units of crossmatched blood are recommended to be available before starting the procedure. Imagine a worst case scenario: a patient with several major antibodies, compatible with 1 in 10,000 blood donors per the blood bank. It could take several days to find the acceptable blood. Two units may be all that is available. Bizarre situations such as this do indeed occur. Transfusion during an awake craniotomy is uncommon because these lesions are usually small. Nevertheless, if it does become necessary, you need that blood immediately, not 30 to 45 minutes from now. For a negative antibody screen, 2 units of blood readily available is acceptable.

Depending on comorbidities, an electrocardiogram (ECG) can be obtained.

B.5. What radiology data should be reviewed?

Reviewing the most recently obtained MRI or computed tomography (CT) scans can give you a great deal of insight about the intracranial pathology. Characteristics of the tumor such as ring enhancement, cystic or lobulated nature, or variously weighted CT studies may give the neuroradiologist and neurosurgeon some insight regarding the diagnosis of the tumor as well as the location of the lesion. The location of the lesion may confirm the presenting symptoms. Vasogenic edema is readily seen, and the progress of resolution with corticosteroids is possible by reviewing a series of CT scans since presentation. Additional information can be gained but is not always present for the smaller lesions usually associated with the awake craniotomy. A midline shift would be evidence of increased ICP, as would loss of sulci and gyri, not to mention the presence of uncal or falcine herniation (Fig. 19.5). The presence of

hydrocephalous from blockage of CSF pathways is also readily seen and could be a source of increased ICP. Previous areas of stroke are usually easily visualized and need to be noted. This is a very rapidly changing field, so there should be no hesitation in calling on the neuroradiologist or neurosurgeon to point out the pathology and their major concerns. A neuroanesthesiologist can never overcommunicate with the neurosurgeon.

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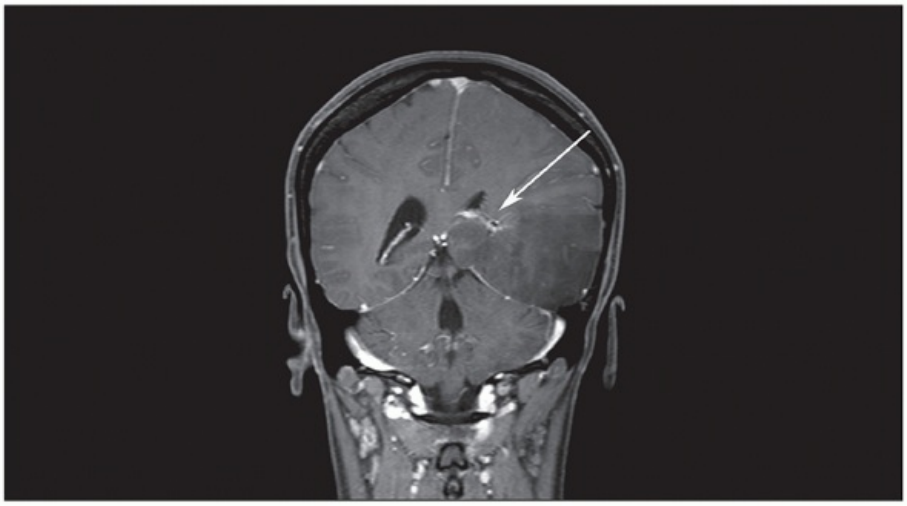


FIGURE 19.5 MRI scan of a 29-year-old female school teacher with a 2-week history of word-finding difficulty and no other symptoms. Note the rather significant uncal herniation *(arrow)*. The patient underwent an uneventful left, awake craniotomy with language area mapping and was discharged to home the next day. Final pathology revealed a World Health Organization grade III anaplastic oligoastrocytoma.

B.6. How do you prepare the patient for an awake craniotomy?

Many things can help prepare the patient for this very demanding procedure. The most important, though, is proper patient selection, which was alluded to earlier. A patient who cannot effectively communicate and cooperate will not do well with this procedure regardless of how precisely everything else is done.

The need for an awake craniotomy is usually first broached by the neurosurgeon during the workup. It is not at all unusual then to have a rather concerned and anxious patient arrive in the preanesthetic clinic. Ideally, the neuroanesthesiologist who will handle the case will conduct the interview, although this is frequently not the case. If not, then the neuroanesthesiologist must make every effort to see the patient well before the time to go to the operating room. In either case, a direct and detailed explanation of what will happen should proceed. Assure the patient, as often as needed, that adequate means will be taken to control any pain. Reassure the patient that he or she can ask for more medications if needed but also discuss limitations secondary to needing the patient awake and cooperative. Discuss additional IV lines, invasive monitors if deemed necessary and why they are used, and when they will be placed.

A discussion about the anesthetic itself is essential. Usually, if patients have a good understanding of the sequence of the procedure and that they may not be exactly fully awake for the entire time they are in the operating room, they are more at ease. Describe everything in detail. This may be the first surgical procedure they have ever had and it is going to be awake.

B.7. Should this patient receive premedications?

Any premedications that might affect the intraoperative ability to adequately map the cortex are contraindicated. This includes medication that might not only cause prolonged sedation, but in the case of epilepsy surgery, interfere with intraoperative intracranial electrocorticography to define the epileptic foci. In particular, benzodiazepines and barbiturates should be avoided for these reasons. Most of the time, the calm and reassuring neuroanesthesiologist is the best “premedication.”

B.8. What precautions should be made for airway management?

Airway evaluation is extremely important in this patient population. The head will most likely be fixed in a three-pronged head-holding device, making the ability to intubate the patient via direct laryngoscopy virtually impossible. Further limitations include the surgical drapes and the instrument table, which often extends over the patient completely. The patient is often positioned in the lateral decubitus position, making moving the patient to a flat position time-consuming, if even possible at all. Patient body habitus can also make this very challenging in the nonsupine position. Obese and morbidly obese patients present exceptionally difficult challenges; edentulous patients have bone erosion of both the axilla and mandible that could make mask ventilation difficult in any position. Patients on phenytoin can have rather impressive

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gingival hypertrophy and associated bleeding that can interfere with intubation if required; teeth can be loose and easily displaced. All of these problems can make placement of an airway or laryngeal mask airway (LMA) difficult at best, impossible at worst. The next section suggests that the use of an LMA or even endotracheal intubation for these cases is for some the preferred method.

Having an airway cart immediately available and prepared for a fiberoptic intubation with an assorted and readily available selection of LMAs is recommended. At baseline, a nasal cannula for oxygen delivery and CO_2 measurement should be placed before starting sedation.

C. Intraoperative Management

C.1. How should this patient be monitored?

Monitoring should be in accordance with the guidelines of the American Society of Anesthesiologists. These include pulse oximetry, electrocardiography, noninvasive blood pressure monitor, capnography, and temperature measurement as a minimum.

American Society of Anesthesiologists. Standards for basic anesthetic monitoring. http://www.asahq.org/~/media/sites/asahq/files/public/resources/standards-guidelines/standards-for-basic-anesthetic-monitoring.pdf. Accessed August 14, 2014.

C.2. Does this patient require invasive monitoring?

In general, for an awake craniotomy, invasive blood pressure monitoring is not a requirement. Nevertheless, some circumstances might be better served with an arterial line. Blood pressure measurement with an oscillometric device can be problematic in patients with atrial fibrillation; it also overestimates both systolic and diastolic blood pressure readings in patients with stiff arteries, such as diabetics. The diabetic patient may also require frequent blood glucose measurements, and the presence of an arterial line facilitates this and avoids multiple venous blood draws in the operating room.

A central venous line (CVL) for pressure measurement is not required in the awake patient. Nevertheless, at times, venous access is so poor that one needs to be placed merely for that purpose.

Remember, the best monitoring system for this case is the awake, cooperative patient.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2158-2199.

van Popele NM, Bos WJ, de Beer NA, et al. Arterial stiffness as underlying mechanism of disagreement between an oscillometric blood pressure monitor and a sphygmomanometer. *Hypertension*. 2000;36:484-488.

C.3. Can current drug therapy alter eloquent cortex mapping?

For mapping of the language areas, any drug that would cause long-lasting, deep sedation, as discussed earlier, would be contraindicated. Patients presenting with new onset of seizures associated with the new diagnosis of brain tumor may have been started on any one or several of the AEDs listed in Table 19.1. These drugs may interfere with mapping of the eloquent cortex. In patients undergoing epilepsy surgery, the surgeon has usually stopped these drugs several days in advance so as not to interfere with intraoperative electrocorticography, the placing of electrodes directly on the surface of the exposed brain. Corticosteroids and opioids would not interfere, but propofol can leave a pattern of high-frequency, high-amplitude beta activity on the electroencephalogram for at least 20 minutes, which can cloud the abnormal activity being sought and should be stopped appropriately.

C.4. Why use hypertonic fluids during a craniotomy?

The intact brain, primarily the BBB, acts as an osmometer. Water will freely cross this semi-permeable membrane in response to various osmotic pressures created by dissolved solutes until there is an equal water pressure across the membrane. This is a function of the number of osmotically active, dissolved solutes (osmoles) present in a solution: The greater the number of osmoles, the greater is the osmolarity or osmotic activity of the solution. At times, this is also called the *osmolality*. This term describes the same principle but does have several differences. *Osmolarity* is defined as

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osmoles per liter of fluid and is a calculated value. Osmolality is one of the four colligative properties of a solution. It is defined as osmoles per kilogram of fluid and is a measured value, usually by a freezing point depression method.

Table 19.2 lists several commonly used IV fluids and compares their osmolarity and osmolality. The osmolality is lower secondary to the presence of undissolved solutes in the solution. When solutes are given IV, the intact BBB prevents the solutes from crossing into the brain, thus sequestering the particles to the intracranial intravascular space and creating a high osmotic pressure. The result is a water concentration in the vessels that is less than that in the brain, with resultant movement of water from the brain into the vascular space. This reduces brain bulk, which may provide better visualization of the tumor by the surgeon and

hopefully decreases the need to apply retractors to the brain surface to enhance visualization. This in turn may help decrease ischemic injury to the brain directly under the retractors. It also decreases ICP in the intact brain. Intravascular proteins create a much smaller oncotic pressure in the intracranial vasculature than do the dissolved solutes, secondary to the intact BBB, and play a lesser role than they do in the systemic circulation, where they are the primary determinant of fluid moving extravascular to intravascular.

TABLE 19.2 Osmotic Values of Common Intravenous Fluids

FLUID	OSMOLARITY (mOsm/L)	OSMOLALITY (mOsm/kg)
Water	0	0
D_5W	252	259
NS	308	282
LR	273	250
3% Saline	1,027	921
6% Hetastarch	310	307
20% Mannitol	1,098	1,280
5% Albumin	290	283
Normosol-R	294	281
D_5W/0.2 NaCl	325	321

D_5W, 5% dextrose in water; D_5W/0.2 NaCl, 5% dextrose and 0.2% sodium chloride; LR, lactated Ringer's solution; NS, normal saline.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:147-160.

Hall JE, eds. *Textbook of Medical Physiology* . 12th ed. Philadelphia, PA: Saunders; 2011:743-752.

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C.5. What intravenous fluids (IVFs) are recommended?

Commonly used IVFs during craniotomy, awake or under general anesthesia, are 0.9% saline, 3% saline, lactated Ringer's solution, 20% mannitol, and 5% albumin.

Normal plasma osmolality is 285 to 295 mOsm per kg. Therefore, any solution with a higher osmolality could act to pull water from the brain. The exception to this is any solution containing 5% dextrose. These solutions have an effective osmolality 259 mOsm less than the measured osmolality because glucose (osmolality 259 mOsm per kg) is rapidly metabolized by the brain. D_5W thus has an effective osmolality of zero and D_5W/0.2 NaCl an effective osmolality of 62 mOsm per kg as examples. These dextrose-containing solutions would present a very high concentration of free water within the intracranial intravascular space and result in water movement into the brain causing an increase in ICP or brain bulk.

It is now well accepted that hyperglycemia before or during an episode of cerebral ischemia worsens outcomes. The mechanism is not clear. One hypothesis is that during a hyperglycemic episode, the increased level of intraparenchymal glucose reacts with substances for lactic acid production during the ischemic period, which is thought to have a negative effect leading to neuronal death. This being said, solutions containing D_5 are not routinely used during intracranial surgery.

Twenty percent mannitol is the most widely used IVF for treatment of elevated ICP. It also acts to decrease CSF production and acts as a scavenger of oxygen free radicals. Mannitol should be given IV over 10 to 15 minutes to prevent a sudden exposure of the cerebral circulation to extreme hyperosmolality (mannitol has an osmolality of 1280 mOsm per kg), which could lead to a vasodilatory effect with resultant increased CBV, possible brain engorgement, and increased ICP. Increased urine output secondary to this diuresis should be replaced with normal saline. The usual mannitol dose is 0.25 to 1 g per kg.

Hypertonic saline comes in a range of concentrations, with 3% probably being the most commonly used during intracranial surgery. A recent study has shown no difference between equiosmolar mannitol and hypertonic saline infusions for providing brain relaxation.

Normal saline has traditionally been the fluid of choice for intracranial procedures and is used to cover fluid requirements and replace blood loss until red blood cells are required. A drawback to its use is that a hyperchloremic, hypokalemic metabolic acidosis can occur when large volumes are given. This can mask any other form of acidosis and cloud the diagnostic picture. Lactated Ringer's solution (osmolality 250 mOsm per kg) would not theoretically, based on the prior discussion, be an ideal replacement for blood loss, insensible loss, or third-space losses. Nevertheless, it is being used in many centers without problems. Some authors have suggested alternating normal saline and lactated Ringer's solution one after the other in the setting of large-volume administration.

The crystalloid versus colloid debate seems to be never ending and is usually centered on head injury. Colloid, in the form of 5% or 25% albumin is rarely, if ever, needed in an awake craniotomy.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2158-2199.

Myburgh J, Cooper J, Finfer S, et al. Saline or albumin for fluid resuscitation in patients with traumatic brain injury. *N Engl J Med*. 2007;357:874-884.

Rozet I, Tontisirin N, Muangmam S, et al. Effect of equiosmolar solutions of mannitol versus hypertonic saline on intraoperative brain relaxation and electrolyte balance. *Anesthesiology*. 2007;107:697-704.

Suarez JI, Shannon I, Zaidat OO, et al. Effect of human albumin administration on clinical outcome and hospital cost in patients with subarachnoid hemorrhage. *J Neurosurgery*. 2004;100:585-590.

C.6. Would a lumbar drain for cerebrospinal fluid (CSF) removal benefit this patient?

The lesions in the eloquent cortex are usually small, so a lumbar drain is not indicated. Historically, neurosurgeons have placed a lumbar drain before the start of the surgery to allow CSF to be drained slowly, usually 10 mL per hour, to decrease brain bulk. This might have been placed in an “open” position when the time came to open the dura, allowing for

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maximal brain relaxation and visualization in addition to preventing any intracranial contents from herniating through the craniotomy site proper.

Bruder N, Ravussin PA. Supratentorial masses: anesthetic considerations. In: Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:184-202.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2158-2199.

C.7. Venous air embolism (VAE): Is it a concern in this case?

VAE is the entrainment of air into open, noncollapsible vascular structures located above the level of the heart. Therefore, the short answer is yes, because the level of the surgical site meets this definition.

VAE is usually associated with posterior fossa craniotomies and cervical spine surgery in the sitting position. Fatal VAE has been described with as little as 3 to 5 cm of surgical site elevation above the heart during lumbar spinal surgery, with the patients supported on a four-poster support device in the prone position.

In this case, the tumors are usually small and within the cortex, and the patient is either supine or in a nearly horizontal lateral decubitus position. Parasagittal and falcine meningiomas encroaching on the posterior portion of the sagittal sinus are the most common situations for VAE development. Fortunately, the eloquent cortical areas are not in this location. Nonetheless, VAE has been reported after pin head-holder placement and after craniotomy but before dural opening. This implies that free air can be entrained through the diploic space of the skull unless adequately sealed during the cranial opening. This is usually done with wax. Therefore, as stated earlier, VAE is a possibility during an awake craniotomy.

Although transesophageal echocardiography is the most sensitive means of detecting VAE, it is impractical in the setting of the awake craniotomy. The precordial Doppler device is the monitor of choice for this particular scenario if the head will be elevated above the level of the heart. When placed in the right or left parasternal region between the third and fourth ribs, Doppler has a high detection rate for VAE. Often, the awake patient may experience an episode of paroxysmal coughing with entrainment of air. The best chance of aspirating a VAE is through a properly placed, multiorificed central line that is positioned 2 cm below the

superior vena caval-atrial junction. This is accomplished by using intravascular ECG. Lead II is observed while the electrode of the CVL is attached to the leg lead. An equibiphasic P wave indicates that the tip of the catheter is in the midatrial position.

Treatment for VAE is supportive. If VAE is suspected, the surgeon must be immediately informed and the surgical field flooded with water to help prevent further air entrainment. Jugular compression and lowering the head are also maneuvers to help stop air entrainment. If it is present, an attempt should be made to aspirate air through the CVL simultaneously with the surgeon addressing the surgical field. Vasopressors or inotropes as needed are given to support hemodynamics, and cardiopulmonary resuscitation initiated if all else fails.

Albin MS, Ritter RR, Pruett CE, et al. Venous air embolism during lumbar laminectomy in the prone position: report of three cases. *Anesth Analg*. 1991;73:346-349.

Jellish WS, Murdoch J, Leonetti JP. Perioperative management of complex skull base surgery: the anesthesiologist's point of view. *Neurosurg Focus*. 2002;12:e5.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2158-2199.

C.8. How is the eloquent cortex mapped?

Before the start of the case, the neurologist will go over the intraoperative testing procedure with the patient. This usually consists of various confrontational type testing in which the patient may be asked to simply count. At other times, the patient may be asked to name items on a card preceded with the phrase “that is a … .” Patients are sometimes asked to do simple math problems. It is important to realize that a patient who speaks multiple languages may need to have each of

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those languages tested separately. Not all learned languages are “laid down” in the same cortical area. This requires extensive preoperative planning to have the needed interpreters available to help with this testing.

Once the craniotomy is completed, the dura opened, and the patient awakened, testing can begin. The tumor surface is often visible and helps guide the surgeon as to where to start the mapping. A handheld wand with two probes, separated by 5 mm, is gently placed on the brain surface about 2 cm from the tumor edge. This is connected to a constant-current, biphasic stimulator. Our neurologists usually stimulate for 2 to 5 seconds with a frequency of 50 Hz and a pulse width of 200 milliseconds. Responses are usually noted with a stimulus power range of 4 to 6 mA. After each test, the surgeon moves the wand freely to other areas of the cortex, repeating this procedure until satisfied that functional areas of the cortex have been localized and marked and that an area of negative mapping has been identified through which the tumor or epileptic foci can be resected.

In the case of seizure focus resection, there are no visible signs to follow. Often, the areas of eloquent cortex in danger will have been mapped out by MEG. This is a noninvasive technique for mapping brain activity by recording the magnetic fields produced by the electrical currents of the brain. These studies can then be “laid over” an MRI study and appear as colored squares representing areas of the eloquent cortex tested and can be used for tumor or epilepsy surgery to help identify the functional areas. Mapping can then start outside of these designated areas looking, again, for a quiet area.

Moore TA II, Markert JM, Knowlton RC. Dexmedetomidine as a rescue drug during awake craniotomy for cortical mapping and tumor resection. *Anesth Analg*. 2006;102:1556-1558.

C.9. How are intraoperative seizures treated?

Intraoperative seizures can be either the baseline type, for which the patient presented, or they can be caused by the cortical surface stimulation used to map the cortex. The surgeon usually will not stimulate the same area more than two consecutive times to avoid this complication. If a seizure should occur, it usually will take the form of the patient no longer answering any questions, but maintaining their airway, and at times maybe a slow moaning sound will be made. This usually responds rapidly to the application of a cold irrigation solution, usually lactated Ringer's solution, to the cortex by the surgeon. If this fails, small doses of propofol, 10 to 20 mg, will usually suffice to stop the seizure.

Schubert A, Lotto M. Awake craniotomy, epilepsy, minimally invasive, and robotic surgery. In: Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:296-316.

C.10. How will you conduct this anesthetic?

The conduct of this type of anesthetic actually begins long before the patient ever enters the operating room. As discussed earlier, the patient must be very motivated for this experience to be successful. The patient must realize fully that this is a lengthy procedure, and 4 to 6 hours is not an unusual expectation for being in the operating room. The patient's family must also be involved and have the same understanding. Most important is a motivated and experienced neurosurgeon and neurologist. Each must realize that time is of the essence and the procedures must be completed as quickly as is safely possible.

The neurosurgeon will be the first person to suggest or inform the patient that this form of surgery is necessary to preserve their language or motor-sensory function.

Ideally, the neurosurgeon and the neuroanesthesiologist have a successful history of performing this procedure. They have developed a technique that has allowed them to have an awake, cooperative patient when the time comes for cortical or subcortical mapping and resection.

In the operating room, before patient arrival, several steps are taken to make the patient as comfortable as possible during this long and demanding procedure. A full-length gel pad is placed on the operating room table under the sheets and the room temperature is set at 70°F or higher. Additional gel pads and foam sheets are available as needed as well as warm blankets.

Following the preoperative visit and IV line placement, the patient is brought to the operating room. As previously discussed, premedications that interfere with the patient's ability to cooperate and follow instructions are contraindicated. Standard intraoperative monitors are placed as described earlier, and a carbon dioxide monitoring nasal oxygen cannula is placed.

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The literature is replete with reports of anesthetic techniques for the awake craniotomy. The common theme is a triphasic "asleep-awake-asleep" technique. The approach is as varied as the number of neuroanesthesiologists who perform these procedures.

Some of these techniques use intubation of the trachea and the use of potent inhalational agents until approximately 20 to 30 minutes before cortex mapping when the anesthetic is discontinued and the patient extubated. Others describe the use of a supraglottic airway in the same fashion. The use of propofol, fentanyl, remifentanil, dexmedetomidine, and various combinations of these drugs have been described as being added to these approaches as a means of transitioning the patient from a general anesthetic to the awake state for mapping and surgery within the eloquent cortex. The use of total intravenous anesthesia using the same drugs has also been described with the airway controlled by a supraglottic airway with controlled or spontaneous breathing or an unprotected airway with spontaneous respirations.

The literature describes cases in which similar, but not identical, approaches for mapping or other tasking has been successful for one group and not for another. This can lead to tremendous frustration in trying to decide how to administer this anesthetic. Many times, the technique is institutionally defined and has worked well for many years.

One of the most important things is to fully understand the pharmacology of the anesthetic regimen chosen.

Our institution uses a triphasic total intravenous anesthesia technique with spontaneous breathing without LMA or tracheal intubation. After standard monitors are placed, two separate infusions are started. Dexmedetomidine is started at 0.35 μg/kg/hr, and propofol is started at 75 μg/kg/min. These drugs are titrated as needed to achieve a sedated yet spontaneously breathing patient. When the patient no longer responds to name call, a Foley catheter, additional IV lines, and an arterial line, as deemed necessary, are placed. Small bolus doses of propofol 10 to 20 mg are given depending on patient response to these procedures.

A loading dose of dexmedetomidine is given at the discretion of the attending neuroanesthesiologist. The recommended administration is 1 μg per kg over 10 minutes, and then the maintenance infusion is started. Several reports have described levels of persistent bradycardia and hypotension with this approach versus starting the infusion without the loading dose. We prefer the dexmedetomidine and propofol combination because it provides good sedation, anxiolysis, and some amnesia without causing respiratory depression.

The anesthesiologist must realize from the beginning that the success of this procedure lies almost entirely with the precision and adequacy of the scalp blocks performed by the anesthesiologist or the neurosurgeon. No amount of sedation will compensate for poorly performed blocks. In our institution, the scalp block addresses the supratrochlear, supraorbital, zygomaticotemporal, auriculotemporal, and greater auricular and the lesser and greater occipital nerves. A combination of equal volumes of 1% lidocaine with epinephrine 1:100,000 and 0.25% bupivacaine with epinephrine 1:200,000 is used as the local anesthetic solution. The mixing of local anesthetic solutions to obtain a solution for injection has been performed in an attempt to obtain an anesthetic solution that will have a rapid onset and longer duration than either of the component solutions separately. In reality, no convincing data support this practice. The use of ropivacaine singularly for the same purpose is described numerous times in the literature. Following the individual nerve blocks, an intradermal ring of the local anesthetic solution is placed around the operative side of the scalp. Each pin site for the pin head-holder device is injected, as is the surgical incision site, by the surgeon, after the patient is prepped and draped.

The dexmedetomidine and propofol infusions are continued as the cranial opening proceeds. When the surgeon has placed the final burr hole, the propofol is turned off and the dexmedetomidine is turned down to 0.2 μg/kg/hr. The cranial opening continues, and approximately 15 to 20 minutes later, the patient is awake and conversant. The neurosurgeon and neurologist begin the mapping process, which can take several hours, but on average, in our institution, this is accomplished in 50 to 60 minutes. The dexmedetomidine is continued at 0.2 μg/kg/hr throughput the mapping process. When satisfied that areas of the eloquent cortex adjacent to the tumor have been localized and an area of negative mapping have been demonstrated, the surgeon proceeds with tumor resection. If the patient is resting comfortably, we do not make any changes in the anesthetic. If they ask to be more sedated, the dexmedetomidine is increased to 0.35 μg/kg/hr; this usually keeps the patient comfortable for the remainder of the procedure. From time to time, the surgeon may ask to remap certain areas. The dexmedetomidine is again lowered to 0.2 μg/kg/hr, if needed, and the remapping with the neurologist commences. The dexmedetomidine is stopped with skin stapling. The pin head-holder is removed, dressings are placed, and preparations are made for leaving the operating room and transferring to the neurosurgery intensive care unit.

A transport monitor capable of providing pulse oximetry, blood pressure measurements, and ECG tracing is attached to the patient, and nasal cannula oxygen is continued during the transport to the neurosurgery intensive care unit.

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Conte V, Magni L, Songa V, et al. Analysis of propofol/remifentanil infusion protocol for tumor surgery with intraoperative brain mapping. *J Neurosurg Anesthesiol*. 2010;22:119-127.

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D. Postoperative Management

D.1. What are the major concerns following craniotomy?

Several problems can occur in the immediate postoperative period following craniotomy. In general, the patient is transported to the neurosurgery intensive care unit and monitored as previously described. The head of the bed is usually elevated 20 to 30 degrees to maximize cerebral venous drainage.

Emergence hypertension is not uncommon in the perioperative period, even after an awake craniotomy. The incidence of postcraniotomy hypertension has been reported to be 57%. In this series of 11,214 craniotomies, perioperative systemic hypertension was associated with postoperative intracranial hematomas with resultant increased mortality and increased length of hospital stay. Other possible causes are pain, hypercapnia, and shivering. Eighty-five percent of postoperative intracranial hematomas become evident within 6 hours of surgery and usually present as a progressive decrease in the level of consciousness. Up to 17% of these hematomas can present at sites remote to the surgical site. Aggressive efforts at controlling this hypertension are required to prevent possible devastating complications such as bleeding into the tumor bed, requiring a second surgical procedure to evacuate that clot.

If not contraindicated, bolus doses of labetalol 5 to 10 mg IV usually control this quite well. Nevertheless, at times, persistent hypertension, without signs of intracranial hypertension, may require additional treatment. Hydralazine 5 to 10 mg IV, an infusion of nicardipine 5 to 15 mg per hour, an infusion of sodium nitroprusside, or nitroglycerin are possible choices. A combination of enalapril and labetalol versus nicardipine alone has been reported, with little difference in the ability to control emergence hypertension.

Acute pain control is essential in the postoperative period. Not only are the patients more comfortable with adequate pain relief, this also helps control postoperative hypertension and decreases the possibility of intracranial hematomas. Pain following craniotomy has probably been vastly understated secondary to concern about respiratory depression and sedation as well as the traditional thought that craniotomies are less painful than other operations. The incidence of postcraniotomy pain may be as high as 70%.

Codeine sulfate has traditionally been the opioid of choice for postcraniotomy pain control because it does not mask pupillary signs and it has a ceiling to its respiratory depressant effects. Nevertheless, it is only about half as potent as morphine sulfate and causes profound hypotension if given IV, leaving the oral, rectal, or intramuscular injection route for administration.

In the immediate postoperative period, almost all pain control medications are given IV. Morphine sulfate patient-controlled analgesia has been reported with good results and without incidence of respiratory depression or need for reintubation. This regimen consists of morphine 1.5 mg with a lockout period of 8 minutes and a total dose not to exceed

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40 mg in 4 hours.

Nonsteroidal anti-inflammatory drugs have been associated with postoperative intracranial hematoma formation. Administration of antiplatelet agents (aspirin and nonsteroidal anti-inflammatory drug) was the most commonly associated risk factor. Therefore, this class of pain control medications should be avoided in the immediate postoperative period.

Postoperative nausea and vomiting is common following craniotomies and can cause hypertension and an increase in ICP. Infratentorial surgery, female gender, and a young age are associated risk factors. Ondansetron 1 to 4 mg IV can provide effective treatment.

Seizures can occur following intracranial tumor resections and can cause serious complications such as secondary intracranial bleeding, hypoxia, and possibly aspiration. An intracranial mass, such as a hematoma (Fig. 19.6), should be suspected if the patient does not regain consciousness within a short period after the seizure has ceased. Small doses of midazolam, 1 to 2 mg, or other benzodiazepines can treat this problem effectively without compromising the airway.

Increased ICP commonly occurs after intracranial surgery, with the most common finding on CT scan being brain edema. Maximum pressures are usually recorded within 16 hours of surgery. Associated risk factors are glioblastoma resection and surgery lasting more than 6 hours. Continuing corticosteroids, dexamethasone 6 to 10 mg every 6 hours, usually controls this problem.

Peripheral nerve injuries are uncommon after awake craniotomy because patient comfort or discomfort can easily be assessed, and minor movements made if needed. We have experienced several episodes of blister formation along the down side of a morbidly obese patient's upper leg after about 5 hours in the lateral decubitus position in spite of the use of gel pads beneath the thigh. Supportive treatment was provided, and this was resolved by the first postoperative follow-up visit.

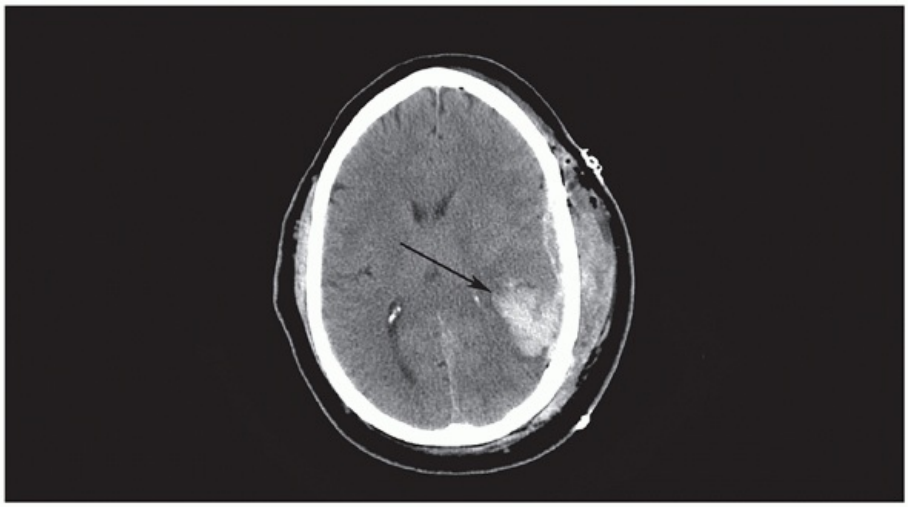


FIGURE 19.6 CT scan of a 73-year-old man who underwent an uneventful left, awake craniotomy with motor and language area mapping. On postoperative day 2, he suffered a generalized tonic-clonic seizure and was extremely slow to awaken. CT scan revealed the presence of a large intracranial hematoma *(arrow)* in the operative site requiring return to the operating room for evacuation. Also note the small epidural and subgaleal hematomas. Coagulation studies were normal. The patient was placed on antiepileptic drugs and was doing well on follow-up visits without further seizure activity. Antiepileptic drugs were successfully weaned over several weeks. Final pathology revealed glioblastoma multiforme.

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Acknowledgments

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Chapter 20
Head Injury

Chris C. Lee

Susan A. Ironstone

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A 52-year-old woman with an unknown past medical history was involved in a highspeed motorcycle collision and was airlifted to the trauma center. On the scene, she was combative, unresponsive, and intubated. At the hospital, she was found to have an open tibial/fibular fracture that was reduced and fixed with regaining of pulses after an initial pulseless left leg, a left small pneumothorax, rib fractures, and a skull fracture extending to the left parietal bone, occipital bone, clivus sphenoid sinus, and temporal bone. On admission, the patient had a Glasgow Coma Scale (GCS) of 7T, and her vital signs were a blood pressure of 69/40 mm Hg, heart rate 150 beats per minute, respiratory rate 20 breaths per minute, and an oxygen saturation 100% on 60% FIO_2. The patient was resuscitated by transfusing packed red blood cells, infusing 0.9% normal saline (NS), and a norepinephrine infusion. Fresh frozen plasma (FFP) and prothrombin complex concentrate were given for correction of her coagulopathy. Her head computed tomography (CT) scans showed bilateral traumatic subarachnoid hemorrhages and subdural hematomas (Fig. 20.1). The patient was GCS 7T; therefore, a right frontal external ventriculostomy drain (EVD) was emergently placed for intracranial pressure (ICP) monitoring and cerebral spinal fluid (CSF) drainage, given that her CT scan showed traumatic subarachnoid hemorrhage and early signs of cerebral swelling. The patient was managed conservatively for her ICPs but required increasing medical treatments, including maximal hyperosmolar therapy, adequate pain control, sedation, and paralysis. Her ICP readings spiked into the 30 mm Hg after initially low ICP readings. The patient was taken to the operating room for a bifrontal craniectomy for emergency decompression secondary to severe bifrontal contusions with malignant cerebral edema (Fig. 20.2).

A. Pathophysiology and Differential Diagnosis

1. What types of intracranial injuries are most likely to have occurred in this patient?
2. What is the difference between primary and secondary injury? What factors contribute to secondary injury?
3. What are the benefits and risks of administering mannitol?
4. What is the effect of hyperglycemia on neurologic outcome following head trauma?
5. What alterations in sodium and potassium balance can occur in patients with head injury?
6. In addition to sodium and potassium, what other electrolyte abnormalities can be present after head trauma?
7. What are the neuroprotective effects of administering magnesium (Mg)?
8. What roles do gender and female sex hormones have in the pathophysiology of traumatic brain injury (TBI)?

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FIGURE 20.1 Initial head CT scan (basal): bilateral traumatic subarachnoid hemorrhage.

9. What is the role of decompressive craniectomy (DC) as a treatment option for ICP control after head injury?
10. Do genetic factors play a role in the outcome after head injury?

B. Preoperative Evaluation and Preparation

1. What is the GCS? What is the significance of a GCS of 7T in this patient?
2. In addition to the GCS, what other assessments can be done to evaluate neurologic function?

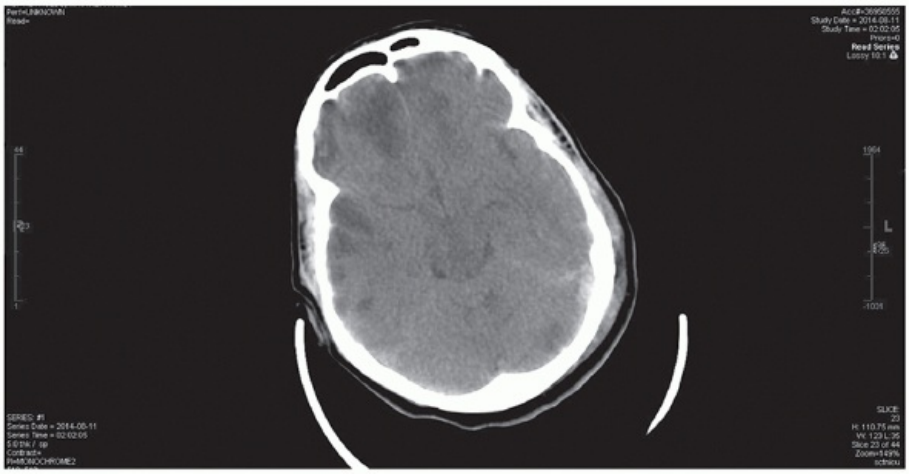


FIGURE 20.2 Follow-up head CT scan: contusions with malignant cerebral edema.

3. What is the role of CT scanning in the initial evaluation of the patient with head injury? What management options can be done in patients whose neurologic condition is deteriorating before obtaining a CT scan?
4. What is the role of ICP monitoring in the management of head injury?
5. How can you clear this patient's cervical spine?
6. What are the advantages of early endotracheal intubation in this patient?
7. What is your plan for airway management in this patient? How would it change if the patient were combative? How would it change if the patient had facial fractures with significant swelling of the head and neck?
8. What are the effects of succinylcholine on ICP? What is the significance of the effect, if any?
9. What coagulation abnormalities are present after TBI? What modalities can be used to provide hemostasis and

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reduce intracranial hematoma expansion?

C. Intraoperative Management

1. What is appropriate hemodynamic monitoring during CT scanning and during craniotomy for evacuation of a subdural hematoma?
2. Should this patient be hyperventilated?
3. What are the implications of arterial hypertension in patients with head injury? How should blood pressure be managed?
4. What should be done about intravenous (IV) fluid replacement? Should corticosteroids be given empirically?
5. Should hypertonic saline (HTS) be administered to this patient? How is HTS administered?
6. The patient underwent a craniectomy for evacuation of a frontal intracerebral hematoma. Which anesthetic agents should be avoided and what agents might be preferred in this situation?
7. Should hypothermia be employed in this patient?

D. Postoperative Management

1. What are the postoperative ventilation concerns in this patient?
2. What specific measures should be used to control the patient's ICP? What type of monitoring devices can be used to measure ICP?
3. What is neurogenic pulmonary edema? Would you avoid positive end-expiratory pressure (PEEP) in a patient with increased ICP?
4. What is the role of antiseizure prophylaxis in the perioperative management of head trauma?
5. How can cerebral oxygenation monitoring be used in the clinical management of TBI?
6. What methods can be used in the neurointensive care unit to prevent hyperthermia?

A. Pathophysiology and Differential Diagnosis

A.1. What types of intracranial injuries are most likely to have occurred in this patient?

The common causes of TBI include falls, motor vehicle accidents, assaults, and gunshot wounds. TBI is a leading cause of death and disability after injury in the United States of America. The following types of intracranial injuries are most likely to have occurred in this patient:

- **Concussion** is the most common type of TBI and the least apparent on imaging. It is often completely invisible to any type of imaging and must be assessed and diagnosed clinically. It is also the most common type of TBI to result in ongoing morbidity, such as decreased job or school performance, and produces lasting cognitive symptoms. This is a very complex type of injury and is a big focus of professional sports team injury experts. Currently, there is a social movement to raise awareness of these injuries, particularly in young athletes.

- **Diffuse axonal injury (DAI)** is difficult to see on CT of the brain (although small punctate hemorrhages in white matter tracts can be seen). Magnetic resonance imaging (MRI), particularly susceptibility weighted imaging, is a more sensitive way to detect it. DAI can produce severe neurologic impairment with a poor prognosis for improvement.
- **Traumatic subarachnoid hemorrhage (tSAH)** is the most common type of posttraumatic intracranial hemorrhage and the least severe indicator of injury. Although this finding often signals the presence of a significant concussion injury, it does not require surgical intervention. tSAH resolves within days and carries far lower risk of the secondary consequences associated with spontaneous aneurysmal subarachnoid hemorrhage (i.e., hydrocephalus and stroke from intracerebral vasospasm). Follow-up CT scans are usually not necessary due to this low risk of secondary neurologic injury.
- **Epidural hematoma** (located between the skull and dura mater) is classically associated with displaced temporal bone skull fractures that cause a laceration of the middle meningeal artery. This arterial hemorrhage results in a rapidly expanding hematoma lateral to the temporal lobe which can lead to death from herniation if not emergently surgically

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evacuated. Injury to large venous structures including the dural sinuses or venous bleeding from fractured bone can lead to a so-called venous epidural hematoma. Because these hemorrhages occur at venous pressure, they are thought to be less likely to expand to a dangerous volume, although sometimes surgical treatment is required. Patients with an acute epidural hematoma often exhibit a lucid interval after the initial impact before deteriorating. The signs of this deterioration can include depressed mental status, an ipsilateral fixed and dilated pupil, contralateral hemiplegia, and imaging demonstrating uncal herniation due to a rapidly expanding hematoma. Arterial epidural hematomas are almost always a true neurosurgical emergency; rapid intervention makes the difference between death and a good prognosis.

- **Subdural hematomas** (located between the brain and dura) arise from a tear in the dural sinuses or bridging veins and may accumulate more insidiously than an epidural hematoma. They are classified as acute (up to 48 hours), subacute (48 hours to 12 days), and chronic (more than 12 days) according to the interval of time between the TBI and the onset of symptoms. Subdural hematomas greater than 1 cm in thickness or causing more than 1 cm of midline shift are generally associated with significant lateralizing neurologic symptoms and often constitute a surgical emergency. Small subdural hematomas can expand in volume as they grow more chronic and can produce delayed onset of significant neurologic signs and symptoms.
- **Intracerebral hematomas and hemorrhages** arise from the tearing of small vessels in the white matter and are due to penetrating head injury or caused by accelerationdeceleration injuries that involve laceration of cortical arteries. These hemorrhages and hematomas can often be managed medically with serial follow-up head CT scans. Surgical evacuation of intracerebral hematomas is rarely indicated due to the deep location of many of these hemorrhages. Although they can be associated with trauma, hypertension, amyloid angiopathy, and/or profound coagulopathy are more common causes.
- **Cerebral contusions** are superficial hemorrhages that occur mainly when the anterior temporal and frontal lobes strike the rough edges of the tentorium (contrecoup contusion). In a patient without focal neurologic deficits, the most probable intracranial injury is a cerebral contusion after ruling out other focal brain injuries. This type of injury is often associated with cerebral edema and can require aggressive management with hyperosmolar therapies or surgical craniectomy for decompression.

Brambrink AM, Kirsch JR, eds. *Essentials of Neurosurgical Anesthesia & Critical Care* . New York: Springer; 2012:93-105.

Faul M, Xu L, Wald MM, et al. *Traumatic Brain Injury in the United States: Emergency Department Visits, Hospitalizations and Deaths, 2002-2006.* Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Injury Prevention and Control; 2010.

Ghajar J. Traumatic brain injury. *Lancet*. 2000;356:923-929.

Jaffe RA, Schmiesing CA, Golianu B. *Anesthesiologist's Manual of Surgical Procedures*. 5th ed. Philadelphia, PA: Wolters Kluwer Health; 2014:37-44.

A.2. What is the difference between primary and secondary injury? What factors contribute to secondary injury?

Primary injury refers to the direct injury of tissue at the moment of head trauma.

Secondary injury occurs minutes, hours, and even days after the initial head trauma and is the consequence of ischemic insults to the brain. The factors contributing to secondary injury include systemic causes (i.e., hypoxia, hypercapnia, and hypotension) and intracranial causes (i.e., intracranial hypertension, or elevated ICP, and herniation). Systemic hypotension and intracranial hypertension are factors related to increased morbidity and mortality in patients with severe TBI. Mental status changes suggest inadequate cerebral perfusion, either from decreased systemic pressure or elevated ICP. Cerebral perfusion pressure equals mean arterial pressure minus either ICP or central venous pressure, whichever is greater (CPP = MAP - ICP or CVP). Therefore, it is critical to maintain adequate oxygenation, cerebral perfusion, and a normal $PaCO_2$ to prevent or decrease the chance of mortality or any deleterious sequelae caused by secondary injury. A general goal is to maintain CPPs greater than 60 mm Hg to ensure adequate brain perfusion and avoid secondary injury.

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Algattas H, Huang JH. Traumatic brain injury pathophysiology and treatments: early, intermediate, and late phases post-injury. *Int J Mol Sci*. 2013;15:309-341.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

A.3. What are the benefits and risks of administering mannitol?

Benefits

Mannitol (20%) 0.25 to 1.0 mg per kg is effective in reducing ICP by increasing serum osmolarity to 300 to 315 mOsm per L to improve CPP, which facilitates surgical exposure and reduces tissue trauma from surgical retraction. The use of hyperosmolar agents is theoretically limited by an upper acceptable osmolarity limit of about 320 mOsm per L. Its osmotic diuretic effect begins in about 5 to 10 minutes and achieves a peak effect in about 30 minutes. Mannitol has been commonly accepted as an acute treatment for cerebral edema for decades.

Risks

- After TBI, the possibility of loss of the blood-brain barrier (BBB) integrity leading to leak of mannitol into cerebral interstitial tissue may actually worsen cerebral edema.
- Osmotic diuresis can cause hypovolemia and consequent hypotension aggravating cerebral ischemia.
- It can transiently cause hypervolemia and result in congestive heart failure in those patients who have borderline cardiac function.
- Electrolyte abnormalities (e.g., hypernatremia) due to diuresis can occur.
- A serum osmolarity above 320 mOsm per L can cause renal failure.
- It could cause rebleeding in patients with expanding hematoma by removing the tamponading effect of the hematoma if mannitol is administered before the dura is opened.

Colton K, Yang S, Hu PF, et al. Responsiveness to therapy for increased intracranial pressure in traumatic brain injury is associated with neurological outcome. *Injury*. 2014;45(12):2084-2088.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

A.4. What is the effect of hyperglycemia on neurologic outcome following head trauma?

Hyperglycemia resulting from the nervous systems response to injury following moderate to severe head trauma has been associated with increased odds ratio for unfavorable neurologic outcome and increased risk for mortality. Additionally, persistent hyperglycemia has been found to be an independent predictor of an unfavorable outcome in patients with severe TBI.

Nevertheless, tight glucose control has been related to elevations in biomarkers for cerebral cellular metabolic distress and to reduced survival at 21 days. This may be a result

of both adverse effects of episodes of severe hypoglycemia as well as increased metabolic requirement of the injured brain.

Currently, moderate glucose control, with a range of 140 to 180 mg per dL is recommended. Glucose levels of less than 100 should be avoided, and hypoglycemia should be treated immediately.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:3103.

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Muehlschlegel S, Carandang R, Ouillette C, et al. Frequency and impact of intensive care unit complications on moderate-severe traumatic brain injury: early results of the Outcome Prognostication in Traumatic Brain Injury (OPTIMISM) Study. *Neurocrit Care*. 2013;18:318-331.

A.5. What alterations in sodium and potassium balance can occur in patients with head injury?

Electrolyte abnormalities such as hyponatremia and hypokalemia are commonly seen following head trauma. Hyponatremia may result via several mechanisms, including hypothalamus-pituitary dysfunction, cerebral salt wasting syndrome, and syndrome of inappropriate antidiuretic hormone. Additionally, sodium loss may be exacerbated by medications used to treat cerebral edema. Severe hypokalemia has been found to be an independent mortality risk factor in patients with TBI and is likely related to trauma and stress-related catecholamine surge. Hypernatremia, resulting from mannitol use, HTS, or diabetes insipidus, is also frequently seen in association with severe TBI.

Wu X, Lu X, Lu X, et al. Prevalence of severe hypokalaemia in patients with traumatic brain injury. *Injury*. 2015;46(1):35-41.

Zhang W, Li S, Visocchi M, et al. Clinical analysis of hyponatremia in acute craniocerebral injury. *J Emerg Med*. 2010;39:151-157.

A.6. In addition to sodium and potassium, what other electrolyte abnormalities can be present after head trauma?

Multiple electrolyte abnormalities, including hypomagnesemia and hypophosphatemia, are often associated with TBI and can be challenging to treat.

Symptoms of hypomagnesemia include ventricular arrhythmias, widened QRS, prolonged PR interval, weakness, and seizures. Symptomatic hypomagnesemia, or Mg level of less than 0.8 mEq per L, should be treated with IV Mg, although oral Mg should be used for asymptomatic patients because most of the IV Mg dose is likely to be renally excreted. Mg repletion may also be required for successful correction of hypokalemia or hypocalcemia.

Hypophosphatemia can present with hypotension, seizures, as well as cardiac or respiratory failure. Treatment of hypophosphatemia can result in severe hypocalcemia. Phosphate replenishment should be considered only for symptomatic patients.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1801-1802.

Wu X, Lu X, Lu X, et al. Prevalence of severe hypokalaemia in patients with traumatic brain injury. *Injury*. 2015;46(1):35-41.

A.7. What are the neuroprotective effects of administering magnesium (Mg)?

N-methyl-D-aspartate (NMDA) receptors are stimulated by excitatory amino acids in the central nervous system, the most abundant of which is glutamate. Once stimulated, the NMDA receptor ion channels (blocked by Mg^{2+} which is relieved by postsynaptic membrane depolarization) will facilitate calcium entry into the cell. In the face of ischemia (TBI), excess glutamate causing excitotoxicity leads to increased intracellular calcium and cell death. Mg, a noncompetitive inhibitor of the NMDA receptor ion channel, will limit the influx of calcium, thereby decreasing cell death. Other effects of Mg include a downregulation of the membrane protein, aquaporin 4, which is known to increase cerebral edema and a decrease in upregulation of the tumor suppressor gene *TP53* which causes apoptosis. The benefits of Mg have been translated into decreased cortical damage noted in the rat brain after brain injury. Furthermore, ionized Mg is decreased in humans after TBI.

Despite encouraging preclinical data of the benefits of Mg as well as established safety studies, human outcome studies

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on the impact of Mg after TBI are varied. Mg administered 12 hours after TBI led to a significant decrease in mortality at 3 months: 13% mortality for patients treated with Mg versus 47% in the placebo group. Of those who survived, good recovery (Glasgow outcome score) was observed in 54% of the patients treated with Mg and 38% of patients treated with placebo. In another study, however, Mg administered to patients within 8 hours of brain injury had no beneficial effect based on mortality, seizures, functional status, or neuropsychological testing at 6 months postinjury. Study design problems, such as missing baseline vital signs, glucose values, concurrent injuries, and neurologic scores at discharge, contributed to the mixed results. Another challenge of translating the benefit of Mg seen in preclinical studies to human research is the notably small, possibly inadequate, increase in ionized Mg in CSF affected by increasing serum Mg levels. This finding may relate to the integrity of the BBB. Finally, the multifactorial etiology of TBI may necessitate research examining combination therapy (e.g., combinations of hypothermia, hyperoxia which restores mitochondrial function, and/or Mg administration) in order to achieve more consistent and favorable outcomes.

Dhandapani SS, Gupta A, Vivekanandhan S, et al. Randomized control trial of magnesium sulphate in severe closed traumatic brain injury. *Indian J Neurotrauma*. 2008;5(1):27-33.

McKee JA, Brewer RP, Macy GE, et al. Analysis of the brain bioavailability of peripherally administered magnesium sulfate: a study in humans with acute brain injury undergoing prolonged induced hypermagnesemia. *Crit Care Med*. 2005;33:661-666.

Sen AP, Gulati A. Use of magnesium in traumatic brain injury. *Neurotherapeutics*. 2010;7(1):91-99.

Temkin NR, Anderson GD, Winn HR, et al. Magnesium sulfate for neuroprotection after traumatic brain injury: a randomised controlled trial. *Lancet Neurol*. 2007;6:29-38.

A.8. What roles do gender and female sex hormones have in the pathophysiology of traumatic brain injury (TBI)?

Approximately 52,000 people in the United States die from TBI per year. Gender is an important consideration in understanding how to improve outcome in TBI as the death rate from this disease is significantly reduced in women. This together with preclinical data suggesting less severe sequelae from TBI in younger women has served as the impetus for exploring how sex hormones may reduce mortality and improve outcome after TBI. Attella et al. demonstrated improved functional outcome in pseudopregnant rats (higher progesterone levels) after TBI compared to normal cycling female rats with similar injuries. Other mechanisms by which progesterone may improve outcome after TBI include an anti-inflammatory action by reducing microglia activation and proinflammatory cytokines and a postinjury remyelination and repair. Estrogen may also be beneficial in cerebral ischemia by stabilizing the BBB and increasing blood flow during and after ischemia as well as improving regeneration and plasticity of new neurons.

Small clinical studies that demonstrated a more favorable outcome with administration of progesterone 8 hours after injury while encouraging did not translate into positive findings in two recently published major progesterone trials. In these two separate randomized controlled trials (SYNAPSE and PROTECT III trial), progesterone administered to TBI patients did not produce a favorable outcome at 6 months as assessed by Glasgow Outcome Score-Extended (includes an assessment of ability to participate in activities of daily living) or other secondary outcomes. At this time, the role of progesterone in TBI is unclear.

Attella MJ, Nattinville A, Stein DG. Hormonal state affects recovery from frontal cortex lesions in adult female rats. *Behav Neural Biol*. 1987;48:352-367.

Coronado VG, Xu L, Basavaraju SV, et al. Surveillance for traumatic brain injury-related deaths—United States, 1997-2007. *MMWR Surveill Summ*. 2011;60(5):1-32.

Herson PS, Koerner IP, Hurn PD. Sex, sex steroids, and brain injury. *Semin Reprod Med*. 2009;27(3):229-239.

Skolnick BE, Maas AI, Narayan RK, et al. A clinical trial of progesterone for severe traumatic brain injury. *N Engl J Med*. 2014;371(26):2467-2476.

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Wright DW, Yeatts SD, Silbergleit R, et al. Very early administration of progesterone for acute traumatic brain injury. *N Engl J Med*. 2014;371(26):2457-2466.

A.9. What is the role of decompressive craniectomy (DC) as a treatment option for ICP control after head injury?

After TBI, DC has historically been reserved for those patients with increasing ICP that is refractory to medical therapy (e.g., sedation, hyperventilation, diuretics, HTS, and ventriculostomy). A skull flap is removed to make room for the expanding traumatized brain thereby affecting a decrease in ICP and improved cerebral blood flow (CBF). However, this procedure is associated with a mortality rate of 26% and is not without risk: contusion expansion, contralateral subdural hematoma or epidural hematoma, CSF leakage, herniation, and infection. Consequently, translating the benefits DC (decreased ICP and increase CBF) into a better neurologic outcome in this patient population has been challenging. Williams et al. found that DC in TBI patients improved the functional outcome in more than 50% of these patients as determined by Glasgow Outcome Scale-Extended. Better functional outcome in young patients was correlated with a decrease in ICP after DC. On the other hand, Cooper et al. found that TBI patients had a significantly worse outcome at 6 months despite a decrease in ICP and an increase in CBF; they attributed this to the aforementioned complications of the procedure. In another study which failed to demonstrate a benefit in DC patients, a decrease in cerebral metabolic rate for oxygen ($CMRO_2$) was noted in patients who had DC; good functional outcome was associated with a higher $CMRO_2$ that was present in medically managed, elevated ICP patients. The authors suggested that the failed benefit of DC may be due to mitochondrial damage with adenosine triphosphate arrest; inactivation of energy-dependent ionic pumps may cause calcium and sodium entry into cells leading to intracellular swelling and cell death. Serious consideration to the need for this procedure in TBI patients with increased ICP unresponsive to medical therapy is in order.

Algattas H, Huang JH. Traumatic brain injury pathophysiology and treatments: early, intermediate, and late phases post-injury. *Int J Mol Sci*. 2013;15:309-341.

Cooper DJ, Rosenfeld JV, Murray L, et al. Decompressive craniectomy in diffuse traumatic brain injury. *N Engl J Med*. 2011;364(16):1493-1502.

Williams RF, Magnotti LJ, Croce MA, et al. Impact of decompressive craniectomy on functional outcome after severe traumatic brain injury *J Trauma*. 2009;66:1570-1576.

A.10. Do genetic factors play a role in the outcome after head injury?

Genetic factors as modulators of neurologic outcome, although far from conclusive, are worthwhile considering in order to elucidate the varied outcomes and to develop more effective treatment strategies.

In the case of excess release of excitatory amino acids, such as glutamate for example, which play a role in secondary brain injury after TBI, glutamate gene polymorphisms (or variations) have been shown to modulate cognition and hypoxic injury. A change from proline to arginine due to a coding polymorphism in the p53 protein (involved in cell death) will facilitate increased apoptosis and poor outcome in TBI patients. Poor neurologic outcome has been associated with a greater rate of individuals homozygous for the arginine allele.

Another genetic polymorphism that may play a role in damage from TBI as well as recovery afterward is the angiotensin-converting enzyme (ACE) gene on chromosome 17. Mutations in this gene are associated with greater levels of ACE and poor cognitive performance after TBI. Vasospasm due to increasing levels of ACE may be responsible for cerebral ischemia affecting poor outcome.

Polymorphism in the proinflammatory cytokine IL-1 has been associated with more hemorrhagic events after TBI.

Genetic variation in the neurotrophin, brain-derived neurotrophic factor (BDNF), which is critical to memory and learning may affect processing speed and suggests an influence of the BDNF gene on cognitive performance after TBI.

Apolipoprotein E facilitates the uptake, transport, and distribution of lipids, neuronal repair, and plasticity after neurotrauma. Chromosome 19 carries a 4-exon gene with three major alleles which codes for this glycolipoprotein. Research has linked the ε4 allele, arginine/arginine, which differs from the other two major alleles, ε2: cysteine/cysteine

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and ε3: cysteine/arginine, to poor outcomes in patients 6 months after brain injury.

McAllister TW. Genetic factors modulating outcome after neurotrauma. *PM R*. 2010;2:S241-S252.

B. Preoperative Evaluation and Preparation

B.1. What is the GCS? What is the significance of a GCS of 7T in this patient?

The GCS is an assessment tool in use since 1974 that uses eye opening, verbal, and motor responses to evaluate neurologic status and severity of TBI (Table 20.1). It was initially developed for evaluation of head trauma patients, and its use has expanded to many other patient populations.

Patients with a GCS score of 13 to 15 are considered to have a mild TBI; moderate TBI is classified by a GCS score of 9 to 12, whereas a GCS score of 8 and below corresponds with severe TBI. *T* indicated the patient was intubated. Compared to patients with other types of traumatic injury, mortality risk is significantly increased with severe TBI. Even with isolated TBI, these patients are also at high risk of failure of nonneurologic organs. Guidelines published for the management of severe head injury by the American Society of Neurological Surgeons (ASNS) and Brain Trauma Foundation (BTF) recommend early therapy directed toward avoiding hypotension and hypoxia as well as ICP monitoring in order to guide therapy for maintenance of cerebral perfusion. Adherence to these guidelines has been associated with improved survival following severe head injury.

Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons, et al. *Guidelines for the Management of Severe Traumatic Brain Injury* . 3rd ed. New York: Brain Trauma Foundation; 2007:S-7-S-13.

Matis G, Birbilis T. The Glasgow Coma Scale—a brief review. Past, present, future. *Acta Neurol Belg*. 2008;108(3):75-89.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2426.

Talving P, Karamanos E, Teixeira PG, et al. Intracranial pressure monitoring in severe head injury: compliance with Brain Trauma Foundation guidelines and effect on outcomes: a prospective study. *J Neurosurg*. 2013;119:1248-1254.

B.2. In addition to the GCS, what other assessments can be done to evaluate neurologic function?

Although the GCS is the most commonly used assessment tool, there are other methods available to assess neurologic function. Abnormalities in pupillary, size, symmetry, and light reflex may reveal conditions requiring immediate intervention such as uncal or cerebellar

herniation. The World Federation of Neurological Surgeons (WFNS) scale is a modified GCS that grades patients according to GCS score and presence or absence of motor deficits. The Hunt and Hess scale is a grading system that predicts mortality in patients with subarachnoid hemorrhage based on clinical presentation and may also be useful for evaluation of TBI patients.

TABLE 20.1 Glasgow Coma Scale

Eye opening:	None	1

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	To pain	2
	To verbal command	3
	Spontaneous	4
Best verbal response:	No verbal response	1
	Incomprehensible sounds	2
	Inappropriate words	3
	Disoriented, conversing	4
	Oriented, conversing	5
Best motor response:	No response (flaccid)	1
	Extension (decerebrate)	2
	Abnormal flexion (decorticate)	3
	Flexion/withdrawal	4
	Localizes to pain	5
	Obeys verbal commands	6

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:3108.

B.3. What is the role of CT scanning in the initial evaluation of the patient with head injury? What management options can be done in patients whose neurologic condition is deteriorating before obtaining a CT scan?

Following head trauma, CT scan can be very useful for revealing acute brain injury. Early CT is indicated for a GCS of 9 to 12 (moderate head injury) as well as severe head injury. Any patient with deterioration of GCS score requires an immediate CT scan.

The Canadian CT Head Rule is a clinical decision-making tool that was developed to guide the use of CT in head injury, as the vast majority of CT scans performed in the context of head trauma are negative for significant brain injury. The rule is used to assess risk level for neurosurgical intervention and brain injury on CT.

The airway should be secured with endotracheal intubation as soon as possible in patients with a deterioration in neurologic function, or those who are likely to have such changes, prior to obtaining a CT scan.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2444.

Stiell IG, Clement CM, Grimshaw JM, et al. A prospective cluster-randomized trial to implement the Canadian CT

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Head Rule in emergency departments. *CMAJ*. 2010;182(14):1527-1532.

B.4. What is the role of ICP monitoring in the management of head injury?

ASNS/BTF guidelines recommend early ICP monitoring and concomitant goal-directed therapy for maintenance of cerebral perfusion in patients with severe head injury. Adherence to these guidelines appears to improve outcome in this patient population, primarily through guiding therapy to minimize secondary insults following the initial injury.

Because of impaired CBF autoregulation in the injured brain, cerebral perfusion is highly dependent on CPP for oxygen delivery and the prevention of cerebral ischemia. Systemic hypotension and intracranial hypertension are factors related to increased morbidity and mortality in severe TBI. Because CPP values of less than 50 mm Hg are correlated with poor outcomes, continuous monitoring of ICP should be used to guide therapy in certain patients with severe TBI. The target range for CPP is 50 to 70 mm Hg according to the most recent ASNS/BTF guideline.

Currently, recommendations for ICP monitoring include (1) patients with GCS 3 to 8 following resuscitation and abnormal CT scan related to the injury (i.e., contusion, swelling, compressed basal cisterns, or hematoma seen on CT) and (2) patients with TBI and age older than 40 years, motor posturing, or systolic blood pressure less than 90 mm Hg, even if the CT scan is normal.

ICP monitoring can be performed using ventricular catheters or intraparenchymal fiberoptic monitors. Ventricular catheters have the advantage of allowing CSF drainage, although they do carry a higher infection risk. In the setting of coagulopathy, placing an ICP monitor is contraindicated.

Griesdale DE, Örtenwall V, Norena M, et al. Adherence to guidelines for management of cerebral perfusion pressure and outcome in patients who have severe traumatic brain injury. *J Crit Care*. 2015;30:111-115.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:3104.

Talving P, Karamanos E, Teixeira PG, et al. Intracranial pressure monitoring in severe head injury: compliance with Brain Trauma Foundation guidelines and effect on outcomes: a prospective study. *J Neurosurg*. 2013;119:1248-1254.

B.5. How can you clear this patient's cervical spine?

The National Emergency X-Radiography Utilization Study (NEXUS) low-risk criteria are commonly used to determine the need for radiographic imaging in the clinical evaluation of cervical spine injury. A patient is considered to be at low risk for a cervical spine injury if they meet all of the following criteria:

a. No posterior midline cervical spine tenderness
b. No evidence of intoxication
c. GCS score of 15—normal level of alertness
d. No focal neurologic deficit
e. No painful distracting injuries

However, there is evidence that patients with clinically significant cervical spine injuries, such as ligamentous injury, cervical spine fracture, or dislocation, may be considered low risk according to the NEXUS criteria, particularly elderly patients. This may be a result of variation in determining the extent or presence of distracting injuries.

The Canadian C-spine Rule is another clinical decision-making tool that may be used in evaluating the need for further imaging in cervical spine injury. The criteria take into account the mechanism of injury, midline neck tenderness, and the ability to rotate the neck more than 45 degrees without pain (if it is safe for the patient to do so). A recent comparison of the Canadian C-spine and NEXUS rules indicated that the Canadian C-spine Rule may have greater reliability.

Nevertheless, CT evaluation is still recommended in the case of major trauma due to the possibility of misdiagnosis in a

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clinically significant cervical spine injury.

Collins NC, McKenzie JV. The NEXUS criteria: do they stand the test of time? *Eur J Emerg Med*. 2013;20:58-60.

Duane TM, Mayglothling J, Wilson SP, et al. National Emergency X-Radiography Utilization Study criteria is inadequate to rule out fracture after significant blunt trauma compared with computed tomography. *J Trauma*. 2011;70:829-831.

Ehrlich F, Wee C, Drongowski R, et al. Canadian C-spine Rule and the National Emergency X-Radiography Utilization Low-Risk Criteria for C-spine radiography in young trauma patients. *J Pediatr Surg*. 2009;44:987-991.

Michaleff ZA, Maher CG, Verhagen AP, et al. Accuracy of the Canadian C-spine rule and NEXUS to screen for clinically important cervical spine injury in blunt trauma: a systematic review. *CMAJ*. 2012;184(16):E867-E876.

B.6. What are the advantages of early endotracheal intubation in this patient?

Endotracheal intubation is indicated in this patient with a severe TBI and a strong probability of further neurologic deterioration. Choosing early endotracheal intubation provides the advantage of securing the airway under more controlled and optimized circumstances as well as providing safer conditions for further evaluation and treatments.

Guidelines published by the Eastern Association for the Surgery of Trauma recommend early endotracheal intubations for all patients with a GCS score of 8 or less (level 1 indication). Other level 1 indications include airway obstruction, persistent hypoxemia, hypoventilation, hemorrhagic shock, and cardiac arrest.

Mayglothling J, Duane TM, Gibbs M, et al. Emergency tracheal intubation immediately following traumatic injury: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg*. 2012;73:S333-S340.

B.7. What is your plan for airway management in this patient? How would it change if the patient were combative? How would it change if the patient had facial fractures with significant swelling of the head and neck?

The practitioner considering airway management in a trauma patient should take into account his or her own skill level and experience with different approaches to intubation. Although fiberoptic intubation could minimize manipulation of the cervical spine, difficulty is increased substantially under emergent conditions, especially in the presence of bleeding or secretions. Additionally, in a combative, uncooperative patient, attempting an awake or lightly sedated fiberoptic intubation would be inadvisable. Rapid sequence induction may provide the best intubating conditions in the trauma patient, who should also be considered a full stomach and at high risk for aspiration of gastric contents.

There is some controversy among practitioners regarding the use of both ventilatory breaths and cricoid pressure during rapid sequence induction of the trauma patient. The risks of oxygen desaturation and hypercarbia for each patient must be taken into consideration when deciding whether ventilation should be used. If ventilatory breaths are necessary, cricoid pressure could limit gastric inflation caused by positive pressure ventilation, although it may also reduce tidal volumes. There is also some evidence that cricoid pressure could degrade the laryngoscopic view in up to 30% of patients and should therefore be discontinued if required to improve intubating conditions and expedite securing the airway.

In-line stabilization (facilitated by removal of the front of the cervical collar if needed) is still recommended in the setting of cervical spine injury. Assistance from one or more individuals will be required in this endeavor, particularly with a combative patient.

Depending on clinician experience, videolaryngoscopy would most likely be highly beneficial under these circumstances to facilitate the intubation while reducing stress on the cervical spine. Difficult airway equipment should also be immediately accessible should the need to follow the difficult airway algorithm arise.

If an extremely difficult airway is anticipated, very cautious use or avoidance of neuromuscular blockading drugs should be

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exercised, and alternative methods for securing an airway, such as cricothyroidotomy, should be considered.

A primary concern in a patient with facial fractures is the ability to provide adequate ventilation and preoxygenation prior to induction. Additionally, there is also a substantial probability that swelling, blood, and secretions will limit visibility and markedly increase the difficulty in securing the airway. Light palpation of the facial bones can help to ascertain the presence of facial fractures.

Oral intubation is highly preferred in trauma situations. Nasal intubation should be avoided in head injury because of the possibility of fractures of the basilar skull and cribriform plate and concerns over entering the cranial vault as well as failed intubation.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2429-2433.

B.8. What are the effects of succinylcholine on ICP? What is the significance of the effect, if any?

The rapid onset and short duration of succinylcholine make it the most suitable of currently available neuromuscular blockading drugs for facilitating intubation in trauma patients. Succinylcholine has been shown to transiently increase ICP. This effect should be weighed against the potential detrimental effects of hypercarbia and hypoxia in patients with severe head injury and is not a contraindication to its use. The rise in ICP may be attenuated by pretreatment with a small dose of a nondepolarizing neuromuscular blocking agent; however, the benefits of this practice have not been proven. In cases where succinylcholine is contraindicated, high-dose rocuronium (1.2 mg per kg) is considered the next best alternative for rapid sequence induction.

Mayglothling J, Duane TM, Gibbs M, et al. Emergency tracheal intubation immediately following traumatic injury: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg*. 2012;73:S333-S340.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2431.

B.9. What coagulation abnormalities are present after TBI? What modalities can be used to provide hemostasis and reduce intracranial hematoma expansion?

Coagulopathy, particularly in the first 24 to 72 hours following severe TBI, is associated with a high risk of mortality and may occur in greater than 60% of these patients. The risk of a poor outcome may be increased by up to 30 times in patients with TBI presenting to the emergency room with an abnormal coagulation profile; the initiation of early coagulation monitoring is recommended.

Both hypo- and hypercoagulable states may be present and include disorders of coagulation enzymes, platelet function, thrombocytopenia, and/or impaired fibrinolysis. Although no specific

mechanism has been established, release of tissue factor, leading to a consumptive coagulopathy as well as hyperfibrinolysis and abnormal activation of the protein C pathway, has been proposed.

Acute coagulopathy following severe head injury is complex and may not be differentiable from a coagulopathy associated with other types of trauma. Treatment should address the primary cause, correct the coagulation abnormality, and focus on controlling bleeding. Although FFP could be useful when there is evidence of coagulopathy, prophylactic early use in head trauma has not proven to be beneficial and is related to adverse events. Similarly, platelet administration may be effective, particularly in reversal of antiplatelet medications. Tranexamic acid has also been investigated and may have some benefit particularly in the first 1 to 3 hours following injury. Recombinant factor VIIa rapidly corrects international normalized ratio and may possibly allow for earlier neurosurgical intervention, but a higher incidence of asymptomatic deep vein thrombosis has also been observed.

de Oliveira Manoel AL, Neto AC, Veigas PV, et al. Traumatic brain injury associated coagulopathy. *Neurocrit Care*.

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2015;22(1):33-44.

Maegele M. Coagulopathy after traumatic brain injury: incidence, pathogenesis, and treatment options. *Transfusion*. 2013;53:28S-37S.

Medzon R, Bracken M, Rathlev NK, et al. Clinically suspected coagulopathy in blunt head trauma. *J Emerg Med*. 2010;39:399-405.

C. Intraoperative Management

C.1. What is appropriate hemodynamic monitoring during CT scanning and during craniotomy for evacuation of a subdural hematoma?

First, the patient should be stabilized prior to CT scanning or any other diagnostic studies. When a patient, who has sustained a TBI, is uncooperative or combative and requires airway control, an urgent tracheal intubation is necessary to facilitate diagnostic procedures such as head CT scan or MRI. The hemodynamic monitoring should include standard monitors as outlined by the American Society of Anesthesiologists (ASA): blood pressure, electrocardiogram, pulse oximetry, and end-tidal carbon dioxide monitoring. Airway patency, adequate ventilation, and stable circulation are initial priorities.

If the patient with TBI shows signs of intracranial hypertension (i.e., a sustained ICP greater than 20 mm Hg), such as headache, nausea/vomiting, papilledema, focal neurologic deficits, altered consciousness, or Cushing triad (i.e., hypertension, bradycardia, and bradypnea), hyperosmolar therapy such as mannitol should be started immediately to lower ICP without direct ICP measurement during CT scanning.

During the craniotomy for evacuation of a subdural hematoma, in addition to the ASA standard monitors earlier, intra-arterial pressure monitoring and urine output monitoring are appropriate in this patient. A CVP line should be considered if the patient has difficulty in peripheral IV access, the injury is extensive or unknown, or the patient is unstable requesting norepinephrine infusions. Furthermore, ICP monitoring is indicated in this patient because she has severe TBI and abnormal findings on her head CT scans. Important objectives in the management of the patient with TBI are to maintain ICP less than 20 mm Hg, prevent or reverse herniation, minimize retractor pressure, and facilitate surgical access. In addition, Doppler monitoring for venous air embolus if the patient's head is elevated above heart, electroencephalogram, bispectral index monitoring, somatosensory evoke potentials, and/or jugular venous oxygen saturation ($SjvO_2$) may be desirable at the anesthesiologist's discretion.

Cooper DJ, Rosenfeld JV, Murray L, et al. Decompressive craniectomy in diffuse traumatic brain injury. *N Engl J Med*. 2011;364(16):1493-1502.

Jaffe RA, Schmiesing CA, Golianu B. *Anesthesiologist's Manual of Surgical Procedures*. 5th ed. Philadelphia, PA: Wolters Kluwer Health; 2014:37-44.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

Smith M. Physiological brain monitoring. *ASA Annual Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2014:119-128.

Warner DS. Anesthesia for craniotomy. *ASA Annual Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2014:156-166.

C.2. Should this patient be hyperventilated?

The BTF guidelines recommend that hyperventilation be avoided during the first 24 hours after TBI when CBF is often critically reduced during the stage of primary brain injury. Thereafter, maintenance of the $PaCO_2$ at 31 to 35 mm Hg is

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usually acceptable. Generally speaking, alteration of $PaCO_2$ within the range of 20 to 80 mm Hg causes changes in CBF accordingly; a decreased $PaCO_2$ results in a decreased CBF. Moderate hyperventilation, $PaCO_2$ 30 to 33 mm Hg, is often very helpful in reducing CBF and normalizing ICP. A modest decrease in $PaCO_2$ counteracts the vasodilating effects of volatile anesthetics. However, excessive hypocapnia with resultant vasoconstriction can cause cerebral ischemia, particularly in a recently injured brain and in a brain beneath retractor. Therefore, the general guideline is that hyperventilation should be employed selectively rather than routinely in the management of patients with TBI. There is no doubt that the hyperventilation is appropriate if herniation is imminent.

Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons, et al. *Guidelines for the Management of Severe Traumatic Brain Injury* . 3rd ed. New York: Brain Trauma Foundation; 2007:S87-S90.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:387, 2163, 2185, 2443-2448.

C.3. What are the implications of arterial hypertension in patients with head injury? How should blood pressure be managed?

Hypertension is common in head injury patients who do not have other injuries associated with massive blood loss. There are three important implications of arterial hypertension in patients with head injury. First, because autoregulation of CBF is usually impaired in areas of brain injury, arterial hypertension can worsen cerebral edema and increase ICP. Intra-arterial blood pressure monitoring is necessary. Next, arterial hypertension may be a reflection of elevated ICP due to compensatory mechanism. Finally, Cushing triad, hypertension, bradycardia, and bradypnea, is associated with an elevated ICP; it is a late and unreliable sign that usually precedes brain herniation.

The etiology of arterial hypertension might be catecholamine-related. In general, CPP (i.e., CPP = MAP - ICP or CVP) should be maintained above 60 mm Hg (at normal to slightly elevated levels) based on the consensus at this time. Hypotension, rarely due to head injury alone, can cause regional cerebral ischemia and should be treated with vasopressors and IV fluids carefully.

Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons, et al. *Guidelines for the Management of Severe Traumatic Brain Injury* . 3rd ed. New York: Brain Trauma Foundation; 2007:S-7-S-13.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

C.4. What should be done about intravenous (IV) fluid replacement? Should corticosteroids be given empirically?

IV fluids are replaced in trauma patients to restore circulation secondary to blood loss and to maintain MAP and CPP. The important principles are that the fluids chosen should be able to prevent decreases in serum osmolarity and colloid oncotic pressure. A mixture of colloids (5% albumin) and crystalloids (0.9% NS) is clinically appropriate. In hypovolemic patients, blood transfusions and/or hydration with a mixture of colloids (5% albumin) and crystalloids (0.9% NS preferred) should be initiated prior to induction.

Corticosteroids should not be given empirically because there are no benefits and may even deleterious effects in the acute head trauma patient. This is unlike the beneficial role that corticosteroids plays in mitigating the vasogenic cerebral edema surrounding brain tumor, subdural hematomas, postoperative swelling, and acute spinal cord injury.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2158-2198.

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C.5. Should hypertonic saline (HTS) be administered to this patient? How is HTS administered?

Even though mannitol is used most commonly intraoperatively because of its rapid onset and its effective ability to decrease in ICP and achieve brain relaxation, HTS can be administered if this patient is refractory to mannitol, or repeated administration of mannitol may result in the adverse effects, such as renal injury or electrolyte disturbances from profound diuresis. More recently, HTS has become increasingly popular, and Kamel et al. found that HTS was more effective than mannitol for the treatment of elevated ICP.

HTS (i.e., 3% saline), like mannitol, creates a hyperosmotic state in the intravascular compartment. It does not cross the intact BBB. As a result of osmotic gradient formed across the BBB, water fluxes from the extravascular into the intravascular compartment. Compared with loop diuretics, hyperosmolar agents are more widely used in neurosurgery to decrease the brain volume.

Three percent HTS is typically administered at a rate of 75 to 150 mL per hour. A bolus of either 250 mL or 500 mL of 3% HTS may also be given to some patients for aggressive therapy at the anesthesiologist's discretion.

Cooper DJ, Myles PS, McDermott FT, et al. Prehospital hypertonic saline resuscitation of patients with hypotension and severe traumatic brain injury: a randomized controlled trail. *JAMA*. 2004;291:1350-1357.

Kamel H, Navi BB, Nakagawa K, et al. Hypertonic saline versus mannitol for the treatment of elevated intracranial pressure: a meta-analysis of randomized clinical trials. *Crit Care Med*. 2011;39(3):554-559.

C.6. The patient underwent a craniectomy for evacuation of a frontal intracerebral hematoma. Which anesthetic agents should be avoided and what agents might be preferred in this situation?

Two important principles in providing anesthesia for craniectomy for the evacuation of an intracerebral hematoma are to control ICP in order to maintain CPP and to provide brain relaxation for surgical access. All of the inhaled anesthetics, the potent volatile anesthetics, and nitrous oxide (N_2O) have some cerebral vasodilatory effect and will increase CBF and ICP; they should all be avoided in this patient. The potent volatile anesthetics uncouple CBF and $CMRO_2$; they produce a dose-dependent increase in CBF but decrease $CMRO_2$. N_2O increases both CBF and $CMRO_2$. Except for ketamine, all of the IV agents, such as propofol, sodium thiopental, and narcotics, are cerebral vasoconstrictors. They decrease both CBF and $CMRO_2$ and would be preferred in this patient such as propofol, sodium thiopental, and narcotics. Like N_2O, ketamine increases both CBF and $CMRO_2$.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:821-863, 2158-2198.

C.7. Should hypothermia be employed in this patient?

Although some early study results seemed promising, recent multicenter studies on the use of mild hypothermia, 32°C to 34°C, after TBI revealed no overall benefit. Currently, there is no established role for hypothermia in patients with TBI.

Clifton GL, Miller ER, Choi SC, et al. Lack of effect of induction of hypothermia after acute brain injury. *N Engl J Med*. 2001;344:556-563.

Clifton GL, Valadka A, Zygun D, et al. Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypotermia II): a randomised trial. *Lancet Neurol*. 2011;10:131-139.

Sahuquillo J, Mena MP, Vilalta A, et al. Moderate hypothermia in the management of severe traumatic brain injury: a good idea proved ineffective? *Curr Pharm Des*. 2004;10:2193-2204.

D. Postoperative Management

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D.1. What are the postoperative ventilation concerns in this patient?

This patient will undoubtedly remain intubated after DC due to a presenting GCS of 7T, acidosis, hyperglycemia, diabetes insipidus, probable lung injury, and pain due to rib fractures. Additional fluid resuscitation may exacerbate respiratory failure in a patient who is still at risk for cardiac dysfunction consequent to neurogenic pulmonary edema. ICP monitoring is

helpful in managing ventilation in the postoperative period because controlling $PaCO_2$ and ensuring adequate oxygenation are necessary to limit secondary brain injury. To maintain a favorable balance between decreasing ICP and minimizing the decrease in CBF, hyperventilation to no lower than a $PaCO_2$ 31 to 35 mm Hg is the goal. Attention to providing physiologic tidal volumes (6 to 8 mL per kg) in order to avoid barotrauma and supplementing with PEEP as needed to maintain adequate oxygenation is important for limiting additional pulmonary damage. Close hemodynamic and ICP monitoring are essential to avoiding increases in ICP and/or decreased venous return with institution of PEEP. Other ventilatory strategies, including high-frequency percussive ventilation and extracorporeal membrane oxygenation, should also be considered if patient oxygenation is a problem.

Ghajar J. Traumatic brain injury. *Lancet*. 2000;256:923-929.

Maas AIR, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. *Lancet Neurol*. 2008;7:728-741.

Mascia L. Acute lung injury in patients with severe brain injury: a double hit model. *Neurocrit Care*. 2009;11:417-426.

Stocchetti N, Maas A. Traumatic intracranial hypertension. *N Engl J Med*. 2014;370:2121-2130.

D.2. What specific measures should be used to control the patient's ICP? What type of monitoring devices can be used to measure ICP?

Controlling ICP is essential to maintaining cerebral perfusion and improving outcome after TBI. Surgery is often required initially in order to evacuate a subdural or epidural hematoma that causes an increased ICP. The neurosurgical service will often place a ventricular drain in the patient in order to drain cerebrospinal fluid. The head of the bed is typically elevated (at least 30 degrees) to promote venous drainage. Keeping the patient sedated and controlling the pain together with the avoidance of hyperthermia will help to ensure decreased brain cerebral metabolic requirements for oxygen. Selective hyperventilation, as mentioned earlier, maybe necessary for controlling ICP; however, this maneuver will also decrease CBF. Assuming that the BBB is intact, hyperosmolar therapy, mannitol, or HTS will help increase serum osmolarity so that fluid is mobilized from the brain; the osmolarity should be no higher than 320 mOsm per L. Electrolyte abnormalities and changes in fluid status require regular blood sampling, close attention to fluid balance, hemodynamic monitoring, and the availability of vasoactive agents. Induction of a barbiturate coma to decrease cerebral metabolism in a patient whose ICP is refractory to treatment will require continued ventilator support, cardiovascular monitors and hemodynamic support, and EEG monitoring. The decrease in ICP affected by mild hypothermia has not translated to improved outcome in TBI patients.

The ventricular catheter or ventriculostomy connected to an external strain gauge is the most accurate, reliable, and low-cost method of monitoring ICP. It can be recalibrated in situ. Fiberoptic or microstrain gauge devices can be used for ICP transduction with a ventricular catheter, but they cost more and are similarly beneficial. Parenchymal ICP monitors, using microstrain pressure transducers, have negligible drift but cannot be recalibrated in situ. Subdural, subarachnoid, and epidural monitors are less accurate.

Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons, et al. *Guidelines for the Management of Severe Traumatic Brain Injury* . 3rd ed. New York: Brain Trauma Foundation; 2007:S-45-S-54.

Maas AIR, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. *Lancet Neurol*. 2008;7:728-741.

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Stocchetti N, Maas A. Traumatic intracranial hypertension. *N Engl J Med*. 2014;370:2121-2130.

D.3. What is neurogenic pulmonary edema? Would you avoid positive end-expiratory pressure (PEEP) in a patient with increased ICP?

Neurogenic pulmonary edema (NPE) occurs suddenly as a consequence of sympathetic nervous system stimulation from the hypothalamus and medulla after severe neurologic injury. Patients are dyspneic and tachypneic with pink frothy sputum. They are often hypoxic, tachycardia, and hypertensive and will have crackles and rales on lung examination. The chest x-ray is often significant for bilateral infiltrates, and the PaO_2/FIO_2 ratio is less than 200.

Theories explaining the pathophysiology of this consequence of TBI are varied. Myocardial injury from the surge in catecholamines causes pulmonary edema due to cardiac dysfunction as in the reversible Takotsubo cardiomyopathy. Neurohemodynamic NPE occurs secondary to an acute rise in systemic and pulmonary pressures leading to left ventricular failure. Fluid then shifts to the low-resistance pulmonary circulation causing pulmonary edema. Damage to the alveolar-capillary membrane from the rise in capillary pressure with a consequent transudative pulmonary edema describes the “blast theory.” This trauma to the pulmonary capillary bed secondary to sympathetic discharge may occur without any systemic changes according to the “pulmonary venule adrenergic hypersensitivity theory.” After ruling out other causes of respiratory distress (i.e., congestive heart failure, aspiration, acute respiratory distress syndrome, sepsis, and/or transfusion overload), treatment is supportive while addressing the underlying neurologic cause.

Adequate oxygenation of the patient is essential to ensuring cerebral perfusion. If ventilator support with an increased FIO_2 is not effective in maintaining a PaO_2 greater than 60 mm Hg, then PEEP may help to improve oxygenation. The unwanted consequences of PEEP may be successfully addressed by regular blood sampling and appropriate monitoring. Avoiding hypercarbia from overdistention of alveoli and increased dead space is essential in managing this patient. Elevation of the head of the bed helps to combat the transient increase in right atrial pressure from PEEP-induced impairment of cerebral venous drainage. Monitoring the central circulation to keep the patient euvolemic and close attention to cardiac function will help avoid decreases in venous return from high PEEP and maintain CPP.

Acosta P, Santisbon E, Varon J. The use of positive end-expiratory pressure in mechanical ventilation. *Crit Care Clin*. 2007;23:251-261.

Davison DL, Terek M, Chawla LS. Neurogenic pulmonary edema. *Critical Care*. 2012;16:212.

D.4. What is the role of antiseizure prophylaxis in the perioperative management of head trauma?

Patients with TBI are at risk for posttraumatic seizures (PTS) in the first 7 days after their trauma (early seizures) and after the 7th day (late seizures). Penetrating trauma carries with it the greatest risk of seizures; however, patients presenting with a GCS less than 8 and subdural or intracerebral hematoma are also at risk for PTS. The risk of increased cerebral metabolism and increased ICP makes seizure prophylaxis a serious consideration. Antiepileptic drugs (AEDs) help prevent seizures in patients with early PTS but have little effect on late PTS. Consequently, prophylactic AED is recommended for the first week after head trauma or surgery. Levetiracetam is beneficial and commonly used for early PTS; it does not require serum concentration monitoring as with phenytoin and has favorable pharmacokinetic properties.

Ghajar J. Traumatic brain injury. *Lancet*. 2000;356:923-929.

Rowe AS, Goodwin H, Brophy GM, et al. Seizure prophylaxis in neurocritical care: a review of evidence-based support. *Pharmacotherapy*. 2014;34(4):396-409.

D.5. How can cerebral oxygenation monitoring be used in the clinical management of TBI?

Brain hypoxia from ischemia due to blood brain barrier disruption and cerebral edema, anemia, hypoxemia, and/or hyperventilation will worsen secondary brain injury. Monitoring cerebral oxygenation can help determine the optimal CPP

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for adequate brain tissue oxygen tension and guide management strategies. Transfusion end points in patients presenting with anemia from trauma may also be determined by cerebral oxygenation monitoring. In most instances, changing FIO_2, increasing PEEP, increasing CPP, and sedation will correct low brain tissue oxygenation. Parenchymal brain oxygen ($PbtO_2$) and $SjvO_2$ monitors are used for assessing brain tissue oxygenation.

The $PbtO_2$ monitor is inserted into the brain parenchyma typically at the time of ICP monitor placement; it has a low complication rate. Regional brain tissue oxygen goals are a $PbtO_2$ of 25 to 35 mm Hg. This device provides information regarding regional ischemia;

its position in the brain may be helpful in improving ischemia to specific areas of brain at risk, that is, penumbra. There is an association between a low $PbtO_2$ and a poor neurologic outcome.

Jugular bulb catheters for $SjvO_2$ monitoring, on the other hand, provide information regarding global cerebral oxygenation. A cervical spine x-ray is helpful in confirming placement to avoid extracerebral contamination by inadvertent placement into the dilated portion of a vein just below base of skull. SjvO2 is responsive to changes in CPP and ICP. The SjvO2 goal is 55% to 75%. In patients with TBI, there appears to be an association between a low SjvO2 (<50%) and a high SjvO2 (>75%) and a worse neurologic outcome.

Cerebral oxygenation monitoring values of the noninvasive near-infra red spectroscopy does not correlate well with other monitors. The variability of results is related to artifacts from light, the extracranial circulation, skin, and skull conditions.

Oddo M, Bösel J. Participants in the International Multidisciplinary Consensus Conference on Multimodality Monitoring. Monitoring of brain and systemic oxygenation in neurocritical care patients. *Neurocrit Care*. 2014;2:103-120.

Schell RM, Cole DJ. Cerebral monitoring: jugular venous oximetry. *Anesth Anal*. 2000;90:559-566.

D.6. What methods can be used in the neurointensive care unit to prevent hyperthermia?

Fever (>38.3°C) occurs in approximately 70% of patients with brain injury and may last weeks after injury. After ruling out nosocomial infections, approximately one-third of patients will require treatment for central fever due to their injured brain. Damage to or irritation of the hypothalamus, the center for thermoregulation, and increased sympathetic tone cause this elevation in temperature. The elevated temperature exacerbates the brain injury by increasing neurotransmitter release, oxygen free radicals, high glutamate concentrations, ischemic damage in the penumbra, and BBB breakdown. Fever after TBI is associated with a poor long-term outcome.

Antipyretic agents (e.g., acetaminophen, aspirin, and nonsteroidal anti-inflammatory drugs) inhibit cyclooxygenase-mediated prostaglandin synthesis in the brain and lower the hypothalamic temperature set point. The limited benefit of this treatment relates to damage to the thermoregulatory center in head trauma patients.

Nonpharmacologic interventions include external and intravascular cooling. External cooling includes four modes of promoting heat loss: evaporation via sponge baths, conductive heat loss with water-circulating cooling blankets, convective heat loss using fans and air-circulating cooling blankets, and radiation or exposure of the patients' skin. Combining these modalities appears to be more effective than any single method for decreasing temperature in patients without brain injury. A new system of surface cooling includes tightly wrapped pads that circulate cold water to promote conductive heat loss. This mode of conductive heat loss reduces fever better and faster than the conventional water-circulating cooling blanket. Intravascular cooling works by infusing cooled saline intravascularly. This method is more effective at cooling than other nonpharmacologic methods. The solution extracts heat from the blood thereby lowering body temperature. Infusion of NS at 4°C will decrease core temperature by 2.5°C within an hour after the infusion is started with no untoward effects on the patient.

The hyperthermic patient must be continuously monitored for any signs of infection and hypothermia. At temperatures less than 35°C, the risk of dysrhythmias, coagulopathy, electrolyte abnormalities, and hypovolemia will increase. Shivering and vasoconstriction (at <36°C) may complicate the cooling process with a significant increase in metabolic demand and unwanted tachycardia and hypertension. The injured hypothalamus may reset so that these effects may manifest at normothermia.

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Badjatia N. Hyperthermia and fever control in brain injury. *Crit Care Med*. 2009;37(7 suppl):S250-S257.

Badjatia N, Bodock M, Guanci M, et al. Rapid infusion of cold saline (4°C) as adjunctive treatment of fever in patients with brain injury. *Neurology*. 2006;66:1739-1741.

Greer DM, Funk SE, Reaven NL, et al. Impact of fever on outcome in patients with stroke and neurologic injury. *Stroke*. 2008;39:3029-3035.

Mayer SA, Kowalski RG, Presciutti M, et al. Clinical trial of a novel surface cooling system for fever control in neurocritical care patients. *Crit Care Med*. 2004;32:2508-2515.

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Chapter 21
Cerebral Aneurysm

Patricia Fogarty Mack

A 43-year-old woman presented to the emergency room 2 days ago, complaining of severe headache, nausea, and vomiting, followed by a witnessed 3-minute loss of consciousness. On regaining consciousness, the patient was noted by her family to be confused. A computed tomography (CT) scan showed subarachnoid bleeding. You are called to the angiography suite because four-vessel angiography has revealed an 18-mm basilar tip aneurysm and a 10-mm right middle cerebral artery aneurysm. The interventional neuroradiologist wishes to coil the basilar tip aneurysm but believes the middle cerebral artery aneurysm will require a craniotomy and clipping. At present, she was oriented only to person. She had no previous medical history; however, she had smoked one pack of cigarettes per day for the last 20 years. Her blood pressure was 130/80 mm Hg, pulse 90 beats per minute, and respiration 18 breaths per minute. She had no focal neurologic deficits. Laboratory examination revealed normal electrolytes and complete blood count but elevated CPK-MB and troponin. Electrocardiogram demonstrated normal sinus rhythm with flipped T waves throughout the precordium.

A. Medical Disease and Differential Diagnosis

1. What are the incidence, prevalence, and causes of subarachnoid hemorrhage (SAH) and what are the risk factors associated with rupture of intracranial aneurysms?
2. What are common sizes and locations of intracranial aneurysms?
3. What is the pathophysiology of aneurysmal rupture and SAH?
4. What are symptoms and signs of SAH?
5. How does one assess the severity of SAH?
6. What are the cardiovascular effects of SAH?
7. How is the diagnosis of SAH made?
8. What is the risk for rebleeding for a patient with SAH?

B. Preoperative Evaluation and Preparation

1. What are some concerns in going to the interventional neuroradiology suite in the midst of an angiogram to follow immediately with coiling of an aneurysm?
2. What type of anesthesia is required for coiling of an aneurysm?
3. Should one proceed with induction of general anesthesia under these circumstances?
4. What types of emergencies can occur during coiling of an aneurysm and how should they be managed?
5. A craniotomy is planned for the following day to clip the middle cerebral artery aneurysm. Should surgery be postponed because of the patient's elevated troponin and creatine phosphokinase (CPK) myocardial-bound (MB) fractions?
6. Would you premedicate this patient before craniotomy?

C. Intraoperative Management

1. What are the goals of the induction and maintenance of anesthesia for this patient?
2. Is placement of an arterial line necessary for induction of anesthesia in this patient in the interventional neuroradiology suite?
3. How would you assess fluid status in this patient?

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4. Would monitoring central venous pressure (CVP) be useful in this patient for craniotomy for clipping?
5. What other forms of monitoring would you consider?
6. What are your particular concerns during induction of anesthesia in this patient?
7. How would you accomplish a smooth and safe induction and intubation in this patient?
8. Would you perform a rapid sequence induction and intubation on this patient?
9. What are the effects of hypoxemia and hypercapnia, such as would be seen with loss of the airway on induction, on cerebral blood flow (CBF)?
10. What is optimal fluid management for aneurysm clipping? Would you use a dextrose-containing solution?
11. After the bone plate was removed and as the dura was being opened, the surgeon complained that the brain was "tight." What could you do to achieve better brain relaxation and facilitate surgical exposure?
12. How might transmural pressure be decreased to allow for aneurysm clip placement?
13. What is the purpose of controlled hypotension and how is it achieved?
14. What are some of the drawbacks of controlled hypotension?
15. What methods of cerebral protection might you use during this operation?
16. Would you induce mild hypothermia as a means of cerebral protection?
17. What are the indications for deep hypothermic circulatory arrest?
18. What steps should be taken in the case of intraoperative rupture of an intracranial aneurysm?
19. How would you plan the emergence from an anesthetic for aneurysm clipping?

D. Postoperative Management

1. Would you extubate the patient postoperatively?
2. What would be the differential diagnosis if the patient did not return to her preoperative neurologic condition?
3. On postoperative day 2, the patient became disoriented and developed hemiplegia. A CT scan was obtained, which shows no new intracranial bleeding. What other diagnostic studies should be performed?
4. What is cerebral vasospasm and what causes it?
5. What are pathophysiologic changes seen in cerebral vasospasm?
6. How is the diagnosis of cerebral vasospasm made?
7. What steps can be taken to prevent cerebral vasospasm?
8. What treatments can be undertaken once a diagnosis of cerebral vasospasm is made?
9. What are other neurologic complications following SAH and aneurysm clipping?
10. What other organ systems may manifest problems postoperatively in aneurysm clipping patients?

A. Medical Disease and Differential Diagnosis

A.1. What are the incidence, prevalence, and causes of subarachnoid hemorrhage (SAH) and what are the risk factors associated with rupture of intracranial aneurysms?

The prevalence of SAH is 2% to 5% with an incidence of 10 to 15 per 100,000 people. Each year, 25,000 cases of SAH occur in the United States, comprising 5% to 10% of all cases of

stroke. In China and South America, the incidence is only 2 to 4 cases per 100,000 people, whereas higher rates of 19 to 23 per 100,000 are reported in Finland and Japan. Sixty percent of the cases occur in young individuals between the ages of 40 and 60 years. Therefore, a poor neurologic outcome is a devastating condition to be endured over a potentially long period.

Approximately one-third of patients die as a result of the acute bleed. Of the two-thirds who survive the acute bleed, one-

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half (one-third of total) later die or are severely disabled and half (one-third of total) have an acceptable outcome.

Cerebral aneurysms account for 75% to 80% of SAH; arteriovenous malformations are the cause in 4% to 5%, whereas no specific cause can be found in 15% to 20% of SAH. Other causes of SAH include trauma, mycotic aneurysm, sickle cell disease, cocaine use, and coagulation disorders.

The four strongest independent predictors of aneurysmal SAH are smoking (OR 6.0; 95% CI 4.1 to 8.6), family history of aneurysmal SAH (4.0; 95% CI 2.3 to 7.0), hypertension (2.4; 95% CI 1.5 to 3.8), and hypercholesterolemia (0.2; 95% CI 0.1 to 0.4) according to a recent case control study. Other risk factors include pregnancy and vascular abnormalities (e.g., type III collagen deficiency and elastase abnormalities). One-third of patients with polycystic kidney disease have been found to have intracranial aneurysms at autopsy. Genetic predisposition plays a role: Seven percent of berry aneurysms are familial, and 5% to 10% of patients with a ruptured aneurysm have a first-order relative with a ruptured aneurysm. The rupture rate for aneurysm has been estimated at 0.14% per year for a 5-mm lesion to 1.1% per year for a 10-mm lesion.

Smoking and alcohol abuse also appear to predispose to aneurysm formation and rupture. Smoking at any time and female gender are related to the presence of multiple intracranial aneurysms as well as accelerated aneurysm growth. Cocaine abuse and resultant episodic hypertension may predispose to aneurysmal rupture at an early age.

Death and disability are primarily due to the initial bleed, vasospasm, and rebleeding. Other causes include surgical complications, parenchymal hemorrhage, hydrocephalus, and complications of medical therapy.

Chang HS. Simulation of the natural history of cerebral aneurysms based on data from the International Study of Unruptured Intracranial Aneurysms. *J Neurosurg*. 2006;104:188-194.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:218-246.

de Rooij NK, Linn FH, van der Plas JA, et al. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. *J Neurol Neurosurg Psychiatry*. 2007;78(12):1365-1372.

Vlak MH, Rinkel GJ, Greebe P, et al. Lifetime risks for aneurysmal subarachnoid haemorrhage: multivariable risk stratification. *J Neurol Neurosurg Psychiatry*. 2013;84(6):619-623.

Yoshimoto Y. A mathematical model of the natural history of intracranial aneurysm: quantification of the benefit of prophylactic treatment. *J Neurosurg*. 2006;104:195-200.

A.2. What are common sizes and locations of intracranial aneurysms?

Small (less than 12 mm) aneurysms make up 78% of the total, whereas large (12 to 24 mm) are 20%, and giant (greater than 24 mm) comprise 2%. Most aneurysms are located in the anterior circulation, with the junction of the anterior communicating and anterior cerebral arteries being the most common (39%). Thirty percent of aneurysms occur in the internal carotid artery, 22% in the middle cerebral artery, and 8% in the posterior circulation (posterior cerebral, basilar, and vertebral arteries).

Kasell NF, Torner JC, Haley C, et al. The international cooperative study on the timing of aneurysm surgery. Part 1: overall management results. *J Neurosurg*. 1990;73:18-32.

A.3. What is the pathophysiology of aneurysmal rupture and SAH?

On the basis of experimental models, aneurysmal rupture leads to the leakage of arterial blood and a rapid increase in intracranial pressure (ICP), approaching diastolic blood pressure in the proximal intracerebral arteries. This increase in ICP causes a decrease in cerebral perfusion pressure (CPP) and a fall in CBF, leading to a loss of consciousness. The decrease in CBF diminishes bleeding and stops the SAH. A gradual reduction in ICP and an

increase in CBF indicates improved cerebral function and possibly a return to consciousness. A persistent increase in ICP (perhaps resulting from thrombi in the cranial cisterns), however, indicates a persistent no-flow pattern with acute vasospasm, cell swelling, and death.

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A.4. What are symptoms and signs of SAH?

Headache occurs in 85% to 95% of patients. Often, a brief loss of consciousness occurs, followed by diminished mentation; consciousness may be impaired to any degree or may be unaffected at the time of presentation. Symptoms secondary to subarachnoid blood may be similar to those of infectious meningitis (nausea, vomiting, and photophobia). The patient may also experience motor and sensory deficits, visual field disturbances, and cranial nerve palsies. Finally, blood in the subarachnoid space may cause an elevated temperature.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:218-246.

A.5. How does one assess the severity of SAH?

Two grading scales are commonly used to assess neurologic status following SAH, the Hunt and Hess grade (Table 21.1) and the World Federation of Neurologic Surgeons' grade (Table 21.2), based on the Glasgow Coma Scale. The scales are useful in identifying a baseline neurologic status from which any acute changes should be assessed. In addition, the scales may correlate with physiologic status. Patients who are Hunt and Hess grades I and II have near-normal cerebral autoregulation and ICP.

Drake CG. Report of World Federation of Neurological Surgeons committee on a universal subarachnoid hemorrhage grading scale. *J Neurosurg*. 1988;68:985-986.

Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *J Neurosurg*. 1968;28:14-20.

A.6. What are the cardiovascular effects of SAH?

Injury to the posterior hypothalamus from SAH causes the release of norepinephrine from the adrenal medulla and cardiac sympathetic efferents. Norepinephrine can cause an increase in afterload and direct myocardial toxicity, leading to subendocardial ischemia. Pathologic analysis of the myocardium of patients who have died of acute SAH has revealed microscopic subendocardial hemorrhage and myocytolysis.

Electrocardiographic abnormalities are present in 50% to 80% of patients with SAH. Most commonly, these involve ST-segment changes and T-wave inversions but also include prolonged QT interval, U waves, and P-wave changes. ST-T wave changes are usually scattered and not related to a particular distribution.

TABLE 21.1 Modified Hunt and Hess Clinical Grades

GRADE[a]	CRITERIA
0	Unruptured aneurysm
I	Asymptomatic or minimal headache and slight nuchal rigidity
II	Moderate to severe headache, nuchal rigidity, but no neurologic deficit other than cranial nerve palsy
III	Drowsiness, confusion, or mild focal deficit
IV	Stupor, mild to severe hemiparesis, possible early decerebrate rigidity, vegetative disturbance

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V	Deep coma, decerebrate rigidity, moribund appearance

[a] Serious systemic disease such as hypertension, diabetes, severe arteriosclerosis, chronic pulmonary disease, and severe vasospasm seen on arteriography result in placement of the patient in the next less favorable category.

From Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *J Neurosurg*. 1968;28:14-20, with permission.

TABLE 21.2 World Federation of Neurological Surgeons (WFNS) Grading Scale

WFNS GRADE	GLASGOW COMA SCALE	MOTOR DEFICIT
I	15	Absent
II	14-13	Absent
III	14-13	Present
IV	12-7	Present or absent
V	6-3	Present or absent

From Drake CG. Report of World Federation of Neurological Surgeons committee on a universal subarachnoid hemorrhage grading scale. *J Neurosurg*. 1988;68:985-986, with permission.

Dysrhythmias occur in 80% of patients, usually in the first 48 hours. Premature ventricular contractions are the most common abnormality, but any type of dysrhythmia is possible. They include severely prolonged QT interval, torsades de pointes, and ventricular fibrillation. In one series, 66% of the arrhythmias were considered mild, 29% moderate, and 5% severe. In addition to increased catecholamine secretion, hypercortisolism and hypokalemia have been suggested as causes for the dysrhythmias seen with SAH.

Ventricular dysfunction, possibly leading to pulmonary edema, is present in approximately 30% of patients with SAH.

Cardiac troponin I predicts myocardial dysfunction in SAH with a sensitivity of 100% and a specificity of 91%. This compares with a sensitivity and specificity of 60% and 94% for CPK-MB in predicting myocardial dysfunction. In order to plan optional anesthetic management, it is important to determine if any cardiac dysfunction is due to a myocardial infarction or reversible neurogenic left ventricular dysfunction. A retrospective study from Duke determined that reversible neurogenic cardiac dysfunction was associated with a troponin level of 0.22 to 0.25 ng per mL and an ejection fraction of less than 40% by echocardiogram.

Bulsara KR, McGirt MJ, Liao L, et al. Use of peak troponin value to differentiate myocardial infarction from reversible neurogenic left ventricular dysfunction associated with aneurysmal subarachnoid hemorrhage. *J Neurosurg*. 2003;98:524-528.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:218-246.

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A.7. How is the diagnosis of SAH made?

Noncontrast CT scan can determine the magnitude and location of the bleed. It may also be useful in assessing ventricular size and aneurysm location. High-resolution CT (CT angiogram) with contrast can more precisely determine the location of the aneurysm.

Lumbar puncture can be used to diagnose SAH if CT is negative, especially when the patient presents more than 1 week after an initial bleed. Xanthochromia, a yellow discoloration of the cerebrospinal fluid (CSF) after centrifugation, is present from 4 hours to 3 weeks after SAH. A lumbar puncture can cause herniation or rebleeding. Therefore, a CT scan should be performed first if the patient presents within 72 hours of suspected SAH.

Four-vessel angiography (right and left carotid and vertebral arteries) has been considered the gold standard in the diagnosis of a intracranial aneurysm; however, CT angiography has been used with increasing frequency. The goal is to visualize all of the intracranial vessels, to localize the source of bleeding, and to rule out multiple aneurysms (5% to 33% of patients). Three-dimensional reconstructive angiograms and magnetic resonance angiography also may be used.

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage: part 1. Operative management. *Anesth Analg*. 1995;81:1060-1072.

Zhang LJ, Wu SY, Niu JB, et al. Dual energy CT angiography in the evaluation of intracranial aneurysms: image quality, radiation dose, and comparison with 3D rotational digital subtraction angiography. *AJR Am J Roentgenol*. 2010;194:23-30.

A.8. What is the risk for rebleeding for a patient with SAH?

The risk of rebleeding from a ruptured aneurysm is highest, 4%, in the first 24 hours after the initial bleed and 1.5% per day thereafter. The cumulative risk is 19% in 14 days and 50% at 6 months. After 6 months, the rebleeding risk is 3% per year.

Kassell NF, Torner JC. Aneurysmal rebleeding: a preliminary report from the Cooperative Aneurysm Study. *Neurosurgery*. 1983;13:479-481.

B. Preoperative Evaluation and Preparation

B.1. What are some concerns in going to the interventional neuroradiology suite in the midst of an angiogram to follow immediately with coiling of an aneurysm?

Whenever an anesthesiologist assumes care of a patient when the patient is already sedated, it may be more difficult to obtain an accurate medical history. In addition, the physical examination will be limited by the patient's position for the diagnostic study. Finally, the patient's capacity to consent may also be impaired by previous sedation.

B.2. What type of anesthesia is required for coiling of an aneurysm?

In most institutions, general anesthesia is required for coiling of an intracranial aneurysm. First, intraoperative neurologic testing is generally not required. Second, akinesis is very important not only when the coils are actually deployed but also while the interventionist is navigating the intracranial vessels to reach the aneurysm.

B.3. Should one proceed with induction of general anesthesia under these circumstances?

Obliteration of the aneurysm with coils has become the standard of care for basilar tip aneurysm, and it would be best for the patient to have this done in the same setting as the angiography, provided there were no contraindications to induction of general anesthesia (e.g., hemodynamic instability).

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. St. Louis, MO: Mosby; 2010:218-246.

Lee CZ, Young WL. Anesthetic considerations for interventional neuroradiology. In: *ASA Refresher Courses in*

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Anesthesiology. 2005;33:145-154.

B.4. What types of emergencies can occur during coiling of an aneurysm and how should they be managed?

Basically, intraoperative emergencies can be divided into two categories—hemorrhage and thrombosis. Appropriate management requires constant communication between the radiologist, surgeon, and anesthesiologist. If an intracranial hemorrhage occurs, the interventionalist may try to "glue" the hole in the aneurysm or embolize the parent vessel. If this is not possible, heparin should be rapidly reversed with protamine, and a ventriculostomy will generally be placed by the surgical team. Management of arterial carbon dioxide partial pressure ($PaCO_2$) can then be guided by the ICP. In the case of catheter-induced thrombosis, induced hypertension is usually desirable while tissue plasminogen activator or glycoprotein IIb/IIIa therapy is considered.

If a coil is malpositioned, anticoagulation would be continued while the interventional radiologist attempts to snare the coil. As with a thrombosis, it may be desirable to augment the blood pressure.

B.5. A craniotomy is planned for the following day to clip the middle cerebral artery aneurysm. Should surgery be postponed because of the patient's elevated troponin and creatine phosphokinase (CPK) myocardial-bound (MB) fractions?

Fifty percent of patients will have an increase in CPK-MB fraction; however, CPK-MB per total CPK fraction is usually not consistent with a transmural myocardial infarction. As discussed previously, troponin I levels are more sensitive. In addition, although some patients (0.7%) do sustain a myocardial infarction in the setting of SAH, little correlation is found between electrocardiographic abnormalities and ischemia in this population.

An echocardiogram may be useful in determining the severity of reversible neurogenic left ventricular dysfunction. If left ventricular function is found to be depressed, a pulmonary artery catheter or intraoperative transesophageal echocardiography may be helpful for intraoperative management.

The desire to delay surgery because of cardiac abnormalities must be weighed against the risk of rebleeding and vasospasm. In most cases, the risk of recurrent hemorrhage outweighs the risk of perioperative myocardial infarction. Furthermore, even if coronary artery disease is present, these patients are not candidates for angioplasty or myocardial revascularization, which requires heparinization. If pulmonary edema or malignant dysrhythmias are present, it may be prudent to postpone surgery until such problems are controlled medically. However, if these problems are not present, then clipping of the aneurysm may be indicated. Bulsara et al. found that 2.9% of patients had severe cardiac dysfunction. In this study, neurogenic left ventricular dysfunction resolved over 4 to 5 days.

Bulsara KR, McGirt MJ, Liao L, et al. Use of peak troponin value to differentiate myocardial infarction from reversible neurogenic left ventricular dysfunction associated with aneurysmal subarachnoid hemorrhage. *J Neurosurg*. 2003;98:524-528.

B.6. Would you premedicate this patient before craniotomy?

No. When the patient is in a Hunt and Hess grade III to V state, anxiety is unlikely. Furthermore, heavy sedation may decrease ventilation, raising $PaCO_2$ and increasing CBF and ICP, which, at the very least, may hinder preoperative and postoperative neurologic evaluation. If patients are Hunt and Hess grade I to II and it appears that preoperative anxiety might lead to hemodynamic instability, a small dose of benzodiazepine may be appropriate.

Medications such as calcium channel blockers (nicardipine), anticonvulsants, and corticosteroids should be continued preoperatively on the day of surgery.

If the patient is at risk for aspiration, medications to decrease gastric acidity and volume are appropriate. Most patients will already be receiving a histamine-2 blocker or proton pump inhibitor if they are on dexamethasone.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:218-246.

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C. Intraoperative Management

C.1. What are the goals of the induction and maintenance of anesthesia for this patient?

The primary goal is to prevent aneurysm rupture on induction or intraoperatively while maintaining adequate CPP. The goal of matching anesthetic depth to surgical stimulation is more important than which specific drugs are used. In general, the anesthesiologist should provide for rapid and reversible titration of blood pressure, maintain CPP, and protect against cerebral ischemia. An additional goal is to provide a relaxed brain for ease of surgical exposure with minimal brain retraction. Finally, the anesthetic should be planned to achieve a rapid, smooth emergence, allowing prompt neurologic assessment. This can be accomplished with a combination of balanced anesthesia, muscle relaxation, and sympathetic blockers as well as with total intravenous anesthesia.

Bendo AA. Intracranial vascular surgery. *Anesthesiol Clin North Am*. 2002;20:377-388.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:218-246.

C.2. Is placement of an arterial line necessary for induction of anesthesia in this patient in the interventional neuroradiology suite?

In this case, because a femoral sheath is in place at the time that anesthesia is being induced, one may transduce femoral arterial pressure during induction. However, because the patient has two aneurysms and because the sheath will be removed at the end of the procedure, it

would be prudent to place an additional arterial line at some point before the removal of the sheath. When a large coaxial catheter is placed through the femoral sheath, systolic pressure is underestimated. The mean pressure, though, should be accurate. Studies have suggested that the placement of an arterial line prior to induction is not essential when an unruptured aneurysm is to be coiled.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:247.

Lai YC, Manninen PH. Anesthesia for cerebral aneurysms: a comparison between interventional neuroradiology and surgery. *Can J Anaesth*. 2001;48:391-395.

C.3. How would you assess fluid status in this patient?

Several issues in interventional radiology complicate fluid management. First, contrast material acts as an osmotic diuretic. Often, these patients have had a CT scan with contrast before the angiograms and may become intravascularly depleted. Second, the femoral sheath and other catheters are constantly flushed with a heparinized saline solution. It is not uncommon for a patient to receive 1,000 mL or more of flush fluid during the case. This must be taken into account when calculating fluid balance.

C.4. Would monitoring central venous pressure (CVP) be useful in this patient for craniotomy for clipping?

Many have suggested that CVP monitoring is essential in assessing volume replacement needs because urine output will be affected by osmotic or loop diuretics administered to facilitate surgical exposure. In addition, should vasoactive medication become necessary, it may be most effectively administered through a central venous catheter.

One disadvantage of CVP monitoring in the neurosurgical patient is catheter placement. Some clinicians are concerned that placement of an internal jugular venous CVP will compromise venous outflow of the head, thereby predisposing to bleeding or brain swelling, although this remains controversial. A “long-arm” or antecubital CVP line may be more difficult to insert and have a higher incidence of thrombophlebitis. Multiple studies have shown the complication rate of central catheter placement to be as high as 14%. When including failure to place the catheter, the complication rate rises to 54%.

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Nevertheless, use of an ultrasound-guided approach to placement of central venous catheters reduces the complication rates to less than 2% to 5% and should be the standard of care whenever possible.

Finally, a poor correlation between CVP and left ventricular end-diastolic pressure has been documented in SAH, so a pulmonary artery catheter may be more useful in assessing volume status as well as providing a monitor of cardiac output in those patients who have had preoperative cardiac problems. Patients who are expected to be candidates for hypertensive hypervolemic hemodilution therapy for vasospasm or for barbiturate coma may also benefit from placement of a pulmonary artery catheter.

Central pressure monitoring is usually instituted after the patient is asleep to minimize patient stress. One should be careful to use the minimal degree of head-down tilt necessary to access the central circulation because the Trendelenburg position may have deleterious effects on ICP and CPP.

Based on the risk and benefits of central venous and pulmonary artery access, placement of CVP and pulmonary artery catheters is reserved for those patients who have documented cardiac dysfunction, cerebral vasospasm or who have poor peripheral intravenous access. Volume status may be assessed by noninvasive monitors or by careful assessment of the arterial waveform utilizing calculated pulse pressure variation available on many monitoring systems.

Akmal AH, Hasan M, Mariam A. The incidence of complications of central venous catheters at an intensive care unit. *Ann Thorac Med*. 2007;2:61-63.

Eisen LA, Narasimhan M, Berger JS, et al. Mechanical complications of central venous catheters. *J Intensive Care Med*. 2006;21:40-46.

Marik PE, Cavallazzi R, Vasu T, et al. Dynamic change in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med*. 2009;37:2642-2647.

C.5. What other forms of monitoring would you consider?

Electroencephalography (EEG) and somatosensory evoked potentials (SSEPs) have been advocated by some authors, although they are not standard monitoring in most hospitals. Although EEG has been used to monitor cerebral ischemia, scalp electrodes may not reflect activity of brain areas most at risk. Cortical electrodes, such as those used in epilepsy surgery, may avoid the problem of attenuation of the scalp electroencephalographic signal by CSF drainage and air between scalp electrodes and brain surface during surgery. EEG is useful in a titrating barbiturate or propofol infusion if burst suppression is desired during temporary clipping.

SSEPs may detect reversible ischemia during temporary vessel occlusion, but they may not detect ischemia in subcortical structures and motor cortex. Furthermore, SSEPs have relatively high false-positive (38% to 60%) and false-negative (5% to 34%) rates. Brainstem auditory evoked responses may be useful for monitoring during posterior circulation aneurysm clipping. Motor evoked potentials may be superior in detecting subcortical ischemia. The use of SSEP and motor evoked potential monitoring usually warrants the use of total intravenous anesthesia and elimination of muscle relaxants from the anesthetic.

Microvascular Doppler ultrasound evaluation may detect inadvertent vessel occlusion, but it cannot assess the adequacy of collateral perfusion.

Monitoring of ICP is common, with the probability of increased ICP being greatest at 24 to 48 hours after SAH. An intraventricular catheter not only allows for ICP monitoring but also allows for CSF drainage to improve operating conditions. If an intraventricular catheter is not present, lumbar spinal drain may be placed. One must be careful not to allow substantial CSF drainage before dural opening because this may decrease ICP allowing for an increase in transmural pressure and possible rupture.

Intraoperative angiography is one means by which to ensure complete obliteration of the aneurysm without clip occlusion of the parent artery or perforating branches. Use of this modality may increase with the installation of more “hybrid” operating rooms, which are fully equipped with advanced angiography equipment in the operating room suite.

Horiuchi K, Suzuki K, Sasaki T, et al. Intraoperative monitoring of blood flow insufficiency during surgery of middle

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cerebral artery aneurysms. *J Neurosurg*. 2005;103:275-283.

Neuloh G, Schramm J. Monitoring of motor evoked potentials compared with somatosensory evoked potentials and microvascular Doppler ultrasonography in cerebral aneurysm surgery. *J Neurosurg*. 2004;100;389-399.

Szelényi A, Langer D, Kothbauer K, et al. Monitoring of muscle motor evoked potentials during cerebral aneurysm surgery: intraoperative changes and postoperative outcome. *J Neurosurg*. 2006;105:675-681.

C.6. What are your particular concerns during induction of anesthesia in this patient?

If an aneurysm ruptures during anesthetic induction, mortality is high (approximately 75%). Therefore, precise control of transmural pressure is important in preventing aneurysm rupture.

Transmural pressure = CPP = MAP - ICP or CVP (whichever is greater), where MAP = mean arterial pressure

On the other hand, one does not want CPP to be so low that ischemia develops, especially in areas of vasospasm.

Chowdhury T, Cappellani RB, Sandu N, et al. Perioperative variables contributing to the rupture of intracranial aneurysm: an update. *ScientificWorldJournal*. 2013;2013:396404.

Tsementzis SA, Hitchcock ER. Outcome from “rescue clipping” of ruptured intracranial aneurysms during induction of anesthesia and endotracheal intubation. *J Neurol Neurosurg Psychiatry*. 1985;48:160-163.

C.7. How would you accomplish a smooth and safe induction and intubation in this patient?

Assuming that evaluation of the airway indicated that intubation would not be difficult, one would begin with preoxygenation. Propofol 1.5 to 2.5 mg per kg, thiopental 3 to 5 mg per kg, and etomidate 0.5 to 1 mg per kg have similar effects on CBF and cerebral metabolic rate. Given that this patient had no other medical problems, propofol is a reasonable choice. One may want to avoid ketamine for induction because of its associated increase in CBF and ICP.

After loss of consciousness and apnea, care must be taken to maintain a normal $PaCO_2$ and avoid extreme hyperventilation. Vigorous hyperventilation will lower $PaCO_2$, decreasing CBF. This may lower ICP to such a degree that if MAP is maintained or increased, transmural pressure may be increased, leading to rupture of the aneurysm.

A nondepolarizing muscle relaxant, which has no effect on ICP or CBF, should be added to facilitate intubation. The neuromuscular junction should be monitored to ensure that paralysis is adequate to avoid coughing with intubation.

Fentanyl 3 to 5 μg per kg, sufentanil 0.5 to 1 μg per kg, or remifentanil 0.25 to 1 μg per kg can be added 3 to 5 minutes before laryngoscopy to blunt the hemodynamic response. Isoflurane, desflurane, or sevoflurane is added to deepen the anesthetic. Finally, approximately 90 seconds before laryngoscopy, lidocaine 1.5 to 2 mg per kg or esmolol 0.5 mg per kg can be added to further blunt the hemodynamic response to intubation.

Lidocaine decreases both CBF and cerebral metabolic rate for oxygen ($CMRO_2$), and at high concentrations, it can cause seizures. Esmolol and labetalol have no effect on CBF and ICP, even in brain areas where autoregulation may not be intact. Extreme reductions in MAP (greater than 35%) may compromise CPP in patients with increased ICP.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:218-246.

C.8. Would you perform a rapid sequence induction and intubation on this patient?

No indication is seen for a rapid sequence induction and intubation in this patient. Overall risk of aspiration during general anesthesia has been estimated at 0.05%; nevertheless, the risk of aneurysm rupture during induction is 1% to 2%.

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Therefore, unless a clear indication exists for rapid sequence induction, it is best avoided.

If a rapid sequence induction is indicated, one may consider using vecuronium 0.15 to 0.20 mg per kg or rocuronium 0.9 mg per kg rather than succinylcholine. Succinylcholine may cause an increase in ICP, although some recent studies have noted no increase in ICP with administration of succinylcholine, but rather with intubation. The increase in ICP can be attenuated or eliminated by deep anesthesia or prior defasciculation. Succinylcholine, more importantly, may lead to hyperkalemia and possibly ventricular fibrillation in those patients presenting with motor deficits following SAH or in those patients who have been bedridden for some time.

In the case of a full stomach or an anticipated difficult airway, a careful awake fiberoptic intubation, with the use of appropriate sedation and topical application of local anesthesia, may be an appropriate alternative. Under such circumstances, it is useful to have an assistant so that while one person is securing the airway, the other is solely focused on controlling the hemodynamics with titration of appropriate medication.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:218-246.

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage: part 1. Operative management. *Anesth Analg*. 1995;81:1060-1072.

Zura A. Succinylcholine in the patient with increased intracranial pressure. In: Mashour GA, Farag E, eds. *Case Studies in Neuroanesthesia and Neurocritical Care*. Cambridge, United Kingdom: Cambridge University Press; 2011:309-310.

C.9. What are the effects of hypoxemia and hypercapnia, such as would be seen with loss of the airway on induction, on cerebral blood flow (CBF)?

Each millimeter of mercury increase in $PaCO_2$ increases CBF 3% to 4%, when $PaCO_2$ is in the range of 20 to 80 mm Hg. In addition, the hypoxia that will ensue if the airway is not secured in a timely manner will also cause an increase in CBF once arterial oxygen partial pressure (PaO_2) is less than 60 mm Hg (Fig. 21.1).

C.10. What is optimal fluid management for aneurysm clipping? Would you use a dextrose-containing solution?

Maintenance fluid requirements and blood loss should be replaced. One wants to avoid profound hypovolemia not only for its detrimental cardiovascular effects but also because it is

associated with cerebral ischemia and perioperative neurologic deficits resulting from vasospasm. Some authors advocate mild hypervolemia to maximize cerebral CBF and minimize vasospasm; however, one must keep in mind the possibility of cerebral edema as well as acute congestive heart failure.

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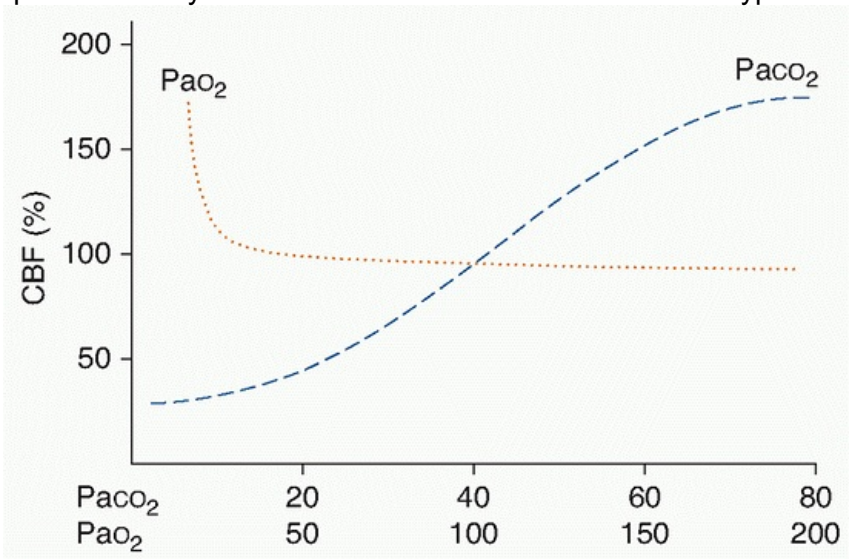


FIGURE 21.1 Change in cerebral blood flow as a function of arterial carbon dioxide partial pressure ($Paco_2$) and arterial oxygen partial pressure (Pao_2) tension. CBF, cerebral blood flow. (From Albin MS, ed. *Textbook of Neuroanesthesia: With Neurosurgical and Neuroscience Perspectives.* New York: McGraw-Hill; 1997:30, with permission.)

In general, dextrose-containing solutions should be avoided because an increased incidence of neurologic deficits associated with glucose administration has been found in experimental models of focal cerebral ischemia. Blood glucose should be maintained less than 180 mg per dL.

Use of crystalloid versus colloid for fluid management and which type of crystalloid solution has long been a matter of controversy. Although some authors advocate colloid solutions to diminish the risk of brain swelling, evidence exists that the solution may predispose to brain edema and contribute to hyponatremia, which may increase the incidence of delayed ischemic neurologic deficits. As far as crystalloid solutions are concerned, hypotonic solutions are avoided in the neurosurgical patient. Acceptable solutions include normal saline, Normosol®, and Plasmalyte®.

A moderate degree of hemodilution to a hematocrit of 30% to 35% usually lowers blood viscosity, thereby increasing CBF. The goal is to increase oxygen delivery by increasing CBF, without allowing the hematocrit to decrease to the degree that reduction in oxygen content negates the increase in CBF. Hematocrit, serum sodium, and serum osmolality measurements may be followed to guide fluid therapy. Serum sodium should be maintained within normal limits, both to maintain serum oncotic pressure and to avoid the hyponatremia associated with cerebral salt wasting.

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage: part 1. Operative management. *Anesth Analg*. 1995;81:1060-1072.

Ibrahim GM, Macdonald RL. The effects of fluid balance and colloid administration on outcomes in patients with aneurysmal subarachnoid hemorrhage: a propensity score-matched analysis. *Neurocrit Care*. 2013;19:140-149.

Lanier WL, Stangland KJ, Scheithauer BW, et al. The effects of dextrose infusion and head position on neurologic outcome after complete cerebral ischemia in primates: examination of a model. *Anesthesiology*. 1987;66:39-48.

Perel P, Roberts I, Ker K. Colloids versus crystalloids for fluid resuscitation in critically ill patients. *Cochrane Database Syst Rev*. 2013;(2):CD000567.

C.11. After the bone plate was removed and as the dura was being opened, the surgeon complained that the brain was "tight." What could you do to achieve better brain relaxation and facilitate surgical exposure?

Any method that rapidly decreases ICP before dural opening may suddenly increase transmural pressure and lead to

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aneurysm rupture. After dural opening, one of the fastest ways

to decrease cerebral blood volume and improve exposure is through hyperventilation. Mild hypocarbia ($PaCO_2$ = 30 to 35 mm Hg) can usually be established before dural opening, with moderate hypocarbia ($PaCO_2$ = 25 to 30 mm Hg) after dural opening. Because of the risk for cerebral ischemia secondary to diminished CBF, normocarbia should be maintained whenever possible in patients with vasospasm.

Mannitol is the most frequently used diuretic at our institution. It is given as an infusion for a total dose of 0.7 g per kg (0.25 to 1 g per kg). Its immediate effect is a transient rise in intravascular volume, which may pose problems in patients with impaired ventricular function. In addition, too rapid infusion can lead to decreases in systemic vascular resistance. Its onset of diuretic action is in 10 to 15 minutes, with peak effect occurring at 60 to 90 minutes. If mannitol does not produce the desired brain relaxation and the serum osmolality is greater than 320 mOsm, additional mannitol is unlikely to produce additional effect. In those patients who may not tolerate the initial effects of mannitol, intravenous furosemide 0.1 to 0.3 mg per kg can be substituted. Both medications can cause derangements in fluid status and serum electrolytes that require close monitoring.

Drainage of CSF from either a lumbar drain or an intraventricular catheter is usually effective in optimizing surgical exposure. One must be careful to avoid significant CSF drainage before dural opening to prevent either brainstem herniation or a sudden decrease in transmural pressure. Similarly, hemodynamic instability can ensue if CSF is drained too rapidly at any point in the operation.

If tight brain remains a problem, one must ascertain that there is no hypoxemia or hypercarbia. In addition, one should consider eliminating nitrous oxide (N_2O) if it is in use and reducing the amount of volatile anesthetic because all inhalational agents are cerebral vasodilators and may potentially increase ICP. Of course, if inhaled agents are reduced, appropriate intravenous agents should be substituted to ensure adequate anesthesia. Total intravenous anesthesia technique may be useful in this situation.

One may give a bolus of propofol or thiopental to decrease $CMRO_2$ and CBF; nevertheless, one must maintain MAP to maintain CPP. At the time of patient positioning, one must ensure that no impediment exists to venous outflow of the brain (i.e., extreme flexion or rotation of the head should be avoided and no monitor cables [electrocardiogram] should be draped across the neck). Even 10 degrees of head-up positioning has been found to be effective at reducing ICP.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:218-246.

Sullivan HG, Keenan RL, Isrow L. The critical importance of $PaCO_2$ during intracranial aneurysm surgery. *J Neurosurg*. 1980;52:426-430.

C.12. How might transmural pressure be decreased to allow for aneurysm clip placement?

The most widely accepted method for producing a slack aneurysm to allow for clip placement is the use of temporary clip occlusion of one or more parent vessels. For example, to place a permanent clip on an anterior communicating artery aneurysm, a temporary clip can be placed on either the right or left anterior cerebral artery or both. Advantages of temporary clip use include a greater reduction in transmural pressure, a greater ease in clipping, a decreased incidence of intraoperative rupture, and the avoidance of controlled hypotension.

The maximal duration of temporary clip application before a neurologic deficit occurs is unknown, but it is probably related to the location of the aneurysm and distribution of perforating vessels distal to the temporary clip. White matter and major deep nuclei are likely to be more susceptible than gray matter to temporary ischemia. Risk factors for neurologic deficit following temporary clip placement include poor preoperative neurologic condition, age older than 61 years, and distribution of perforating arteries in distal basilar and horizontal segments of middle cerebral artery. Recent studies suggest that there are regional differences in brain oxygenation during temporary clip occlusion, with the middle cerebral artery distribution being more susceptible to ischemia than the anterior cerebral artery distribution. In addition, patients who underwent multiple brief periods of temporary occlusion

had less ischemia than those who underwent a single temporary artery occlusion of greater than 10 minutes.

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Adenosine-induced temporary flow arrest has also been reported as a mechanism to produce a slack aneurysm to facilitate clipping.

Bendok BR, Gupta DK, Rahme RJ, et al. Adenosine for temporary flow arrest during intracranial aneurysm surgery: a single center retrospective review. *Neurosurgery*. 2011;69:815-820.

Ha SK, Lim DJ, Seok BG, et al. Risk of stroke with temporary arterial occlusion in patients undergoing craniotomy for cerebral aneurysm. *J Korean Neurosurg Soc*. 2009;46:31-37.

Silva PA, Cerejo A, Vilarinho A, et al. Regional variations in brain oxygenation during temporary clipping in aneurysm surgery. *Neurol Res*. 2012;34:971-976.

C.13. What is the purpose of controlled hypotension and how is it achieved?

In the past, controlled hypotension was used to decrease transmural pressure, making the aneurysm neck slack enough to allow placement of a clip without vessel rupture. Various agents were used to achieve controlled hypotension, including volatile agent, nitroprusside, esmolol, labetalol, nitroglycerin, and trimethaphan. Specific agents were selected based on the patient's preexisting medical conditions, especially coronary ischemia or poor ventricular function. In an otherwise healthy patient, sodium nitroprusside infusion may be used for its rapid onset, easy titratability, and quick offset. An esmolol infusion can be added to augment hypotension and counteract the reflex tachycardia; by decreasing the amount of nitroprusside needed to induce hypotension, the likelihood of cyanide toxicity diminishes. Side effects of nitroprusside include cyanide toxicity, rebound hypertension, and intrapulmonary shunting. Direct measurement of CVP is useful when planning to use controlled hypotension in these patients.

During controlled hypotension, MAP is usually maintained at a minimum of 50 mm Hg in previously normotensive individuals. Neurologic function monitors (EEG, SSEP, brainstem auditory evoked response, and cerebral oximetry) may be useful in guiding target level of MAP.

Albin MS, ed. *Textbook of Neuroanesthesia: With Neurosurgical and Neuroscience Perspectives*. New York: McGraw-Hill; 1997:877-878.

Ornstein E, Young WL, Ostapkovich N, et al. Deliberate hypotension in patients with intracranial arteriovenous malformations: esmolol compared with isoflurane and sodium nitroprusside. *Anesth Analg*. 1991;72:639-644.

C.14. What are some of the drawbacks of controlled hypotension?

The main drawback of controlled hypotension is that it leads to a global decrease in CPP. CPP is then further diminished in the presence of vasospasm or in areas of brain retraction. In a retrospective study, multiple regression analysis indicated that patients who underwent even limited periods of controlled hypotension had a worse outcome, both in terms of Glasgow Outcome Scale (multiple regression) and higher incidence and severity of vasospasm. Although further studies indicated that this effect was not seen when corrected for age, controlled hypotension usually is avoided in neurosurgery.

Connolly ES, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of anuerysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2012;43:11-27.

C.15. What methods of cerebral protection might you use during this operation?

Cerebral protection has long been a matter of much investigation and controversy. Barbiturate loading has been shown in animals to be protective against focal ischemia, although no controlled human studies have been performed. Barbiturates decrease cerebral metabolic rate for glucose and oxygen and lower CBF and ICP. The dose is usually titrated to electroencephalographic silence or burst suppression. At doses used to suppress electroencephalographic activity, the

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patient may experience cardiovascular depression. The dose of barbiturate traditionally used for cerebral protection may also prolong emergence and hinder postoperative neurologic evaluation. Although barbiturates were originally thought to protect against ischemia through metabolic depression, other factors such as redistribution

of blood flow to ischemic areas, blockade of the sodium channels and glutamate receptors, attenuation of *N*-methyl D-aspartate (NMDA), and *α*-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA)-mediated glutamate toxicity all play a role.

Propofol has also been used as an alternative to thiopental sodium. Cerebral protection from propofol is thought to result from scavenging of free radicals, inhibition of glutamate release, and prevention of lipid peroxidation. In studies involving both volatile anesthetics and propofol, apoptotic cell death is delayed, but not prevented, if the ischemic result is mild.

Etomidate decreases cerebral metabolic rate at electroencephalographic burst suppression and prevents an increase in excitatory neurotransmitters during cerebral ischemia in animal models; nevertheless, it has been associated with a greater volume of injured brain than thiopental and control groups in focal ischemia in hypertensive rats.

Deliberate mild hypothermia (32.5°C to 35.5°C), although promising in animal models, did not demonstrate efficacy with patients with good-grade aneurysm in the Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST) 2, although there was a suggestion of a trend toward benefit in subgroup analysis.

While many pharmacologic targets for cerebral protection are under investigation and show promising results in laboratory analysis, none have proven effective in the clinical setting.

Engelhard K, Werner C, Eberspächer E, et al. Influence of propofol on neuronal damage and apoptotic factors after incomplete cerebral ischemia and reperfusion in rats: a long-term observation. *Anesthesiology*. 2004;101:912-917.

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage: part 1. Operative management. *Anesth Analg*. 1995;81:1060-1072. Kawaguchi M, Furuya H, Patel PM. Neuroprotective effects of anesthetic agents. *J Anesth*. 2005;19:150-156.

Todd MM, Hindman BJ, Clarke WR, et al. Intraoperative hypothermia for aneurysm surgery trial. *N Engl J Med*. 2005;352:135-145.

C.16. Would you induce mild hypothermia as a means of cerebral protection?

Hypothermia causes a greater reduction in cerebral metabolic rate for glucose and oxygen than the level attained at electroencephalographic silence because its reduction of metabolism is caused by a reduction in both neuronal electrical activity and enzyme activity related to maintenance of cellular function. Hypothermia also reduces the release of excitatory neurotransmitters. Significant reduction in infarct size after global and focal ischemia has been demonstrated in several animal studies. Unfortunately, these advantages have not been documented in clinical trial. The IHAST study showed no differences in Glasgow Outcome Scale at 3 months in patients at good grade.

Disadvantages of unintentional hypothermia documented in the literature include an increased incidence of myocardial ischemia in peripheral vascular surgery, increased incidence of postoperative wound infection in abdominal surgery, coagulopathy, prolonged drug clearance, and hyperglycemia. In the IHAST study, the hypothermic group had a small increase in infection rate. As a result of IHAST, we no longer deliberately induce hypothermia in patients at good grade for aneurysm clippings.

Frank SM, Beattie C, Christopherson R, et al. Unintentional hypothermia is associated with postoperative myocardial ischemia. *Anesthesiology*. 1993;78:468-476.

Todd MM, Hindman BJ, Clarke WR, et al. Intraoperative hypothermia for aneurysm surgery trial. *N Engl J Med*. 2005;352:135-145.

C.17. What are the indications for deep hypothermic circulatory arrest?

Hypothermic circulatory arrest at body temperature less than 22°C (71.6°F) is reserved for giant aneurysms, difficult

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basilar artery aneurysms, and anatomically complex aneurysms that are not clippable without complete cessation of blood flow and are not amenable to the use of temporary clips. Deep hypothermic circulatory arrest requires cooperation between several services, including anesthesiology, neurosurgery, cardiac surgery, and perfusionists. In addition to the concerns mentioned regarding anesthesia for the person with an intracranial aneurysm and the need for prompt awakening for ease of neurologic assessment, deep

hypothermic circulatory arrest adds concerns regarding institution of and separation from cardiopulmonary bypass, systemic heparinization and protamine reversal, and, of course, rewarming from profound hypothermia. This is rarely performed now that coil embolization is possible for many of these aneurysms. For those aneurysms that are not amenable to coiling, flow diversion endovascular therapy is now an option. Flow diversion is an endovascular technique whereby instead of placing a device inside the aneurysm sac, such as with coiling, a stent is placed in the parent blood vessel to divert blood flow away from the aneurysm itself. Long-term data regarding outcome and rebleeding risk are pending.

Gross BA, Frerichs KU. Stent usage in the treatment of intracranial aneurysms: past, present and future. *J Neurol Neurosurg Psychiatry*. 2013;84:244-253.

Young WL, Lawton MI, Gupta DK, et al. Anesthetic management of deep hypothermic circulatory arrest for cerebral aneurysm clipping. *Anesthesiology*. 2002;96:497-503.

C.18. What steps should be taken in the case of intraoperative rupture of an intracranial aneurysm?

The incidence of intraoperative rupture is 2% to 19%. The stage of the operation at which rupture occurs affects outcome, with rupture at induction being the worst. After induction, the most common times for rupture are when the dura mater or arachnoid mater are being opened, during intracranial hematoma removal, and, of course, during dissection exposure of the aneurysm. At any point in the operation, a sudden sustained increase in blood pressure with or without bradycardia is suggestive of rupture. If rupture is suspected on induction, one must institute measures to control ICP while maintaining CPP.

If rupture occurs during surgical dissection, mortality is lower. The primary concern is to control bleeding while maintaining systemic perfusion. Bleeding is controlled by placement of temporary clips or by clamping or compression of the ipsilateral carotid artery in the neck if the aneurysm is too proximal. If bleeding is not controlled in a timely manner and a significant amount of blood accumulates in the subarachnoid space, severe brain swelling that is refractory to all treatment may develop.

Houkin K, Kuroda S, Takahashi A, et al. Intra-operative premature rupture of the cerebral aneurysms: analysis of the causes and management. *Acta Neurochir (Wien)*. 1999;141:1255-1263.

Lin BF, Kuo CY, Wu ZF. Review of aneurysmal subarachnoid hemorrhage—focus on treatment, anesthesia, cerebral vasospasm prophylaxis, and therapy. *Acta Anaesthesiol Taiwan*. 2014;52:77-84.

C.19. How would you plan the emergence from an anesthetic for aneurysm clipping?

The goal is to have a patient comfortable and not coughing or straining or subject to hypercarbia or wide variations in blood pressure.

After discontinuing all anesthetic agents and reversing neuromuscular blockade, the use of a lidocaine 1.5 mg per kg bolus may minimize bucking and reaction to the endotracheal tube. Strict control of blood pressure must be observed especially in the presence of ischemic heart disease or in patients suspected of having multiple aneurysms. One should keep the blood pressure within 20% of the patient's normal measurement.

D. Postoperative Management

D.1. Would you extubate the patient postoperatively?

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Most patients who are in Hunt and Hess grades I and II can be extubated postoperatively with no need for airway support. Patients in grades IV and V usually require mechanical ventilation postoperatively, whereas grade III patients may or may not require intubation and mechanical ventilation. Patients with vertebral or basilar artery aneurysms may require airway protection secondary to cranial nerve damage and loss of protective reflexes.

If this patient was able to follow commands, was clinically recovered from the effects of muscle relaxants, and had established an adequate ventilatory pattern with return of protective airway reflexes, extubation would be appropriate.

Bendo AA. Intracranial vascular surgery. *Anesthesiol Clin North Am*. 2002;20:377-388.

D.2. What would be the differential diagnosis if the patient did not return to her preoperative neurologic condition?

If the patient had a focal neurologic deficit on awakening in the operating room, the cause most likely would be a surgical one, although new-onset vasospasm is also a possibility. If the patient failed to awaken, the first step would be to ensure that all inhalational and infused anesthetics had been discontinued. Second, one should make sure that neuromuscular blockade was fully reversed. One should make sure that the patient had been appropriately rewarmed because hypothermia would prolong the duration of action of intravenous medications. While considering reversal of benzodiazepines and narcotics, one should rule out other causes such as hypoxia, hypercarbia, hyponatremia, and hypoglycemia. One should consider the possibility of intraoperative seizure, with delayed emergence resulting from a postictal state. If after reversal of all anesthetic agents, the patient had not awakened, a CT scan should be obtained to rule out subdural hematoma, intracranial hemorrhage, hydrocephalus, and pneumocephalus. An angiogram may also be obtained to rule out vascular occlusion. An electroencephalogram might be appropriate to rule out subconvulsive status epileptics.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:218-246.

D.3. On postoperative day 2, the patient became disoriented and developed hemiplegia. A CT scan was obtained, which shows no new intracranial bleeding. What other diagnostic studies should be performed?

If transcranial Doppler is available, an increased value for cerebral arterial flow velocity would be suggestive for vasospasm, leading to delayed cerebral ischemia/infarction (DCI). Tissue oximetry may also be useful as a monitor for vasospasm. Angiography is the gold standard for the diagnosis of cerebral vasospasm and should be performed to confirm the diagnosis and characterize the number and location of the vessels involved.

Cerebral vasospasm may be localized to the area of aneurysm rupture or in an area of the brain remote from SAH. The worst prognosis is in those patients in whom vasospasm is diffuse. Of course, as these studies are being done, laboratory values should be checked to make sure no new or worsening metabolic derangement is contributing to the neurologic deterioration.

D.4. What is cerebral vasospasm and what causes it?

Vasospasm, which occurs in 35% of patients with SAH, is a segmental or diffuse narrowing of the lumen of one or more intracranial arteries. It is the most common cause of DCI and may be seen angiographically in 60% of patients, even if clinical manifestations are not apparent.

The severity of vasospasm is apparently related to the amount and location of subarachnoid blood. Injection of blood into the subarachnoid space causes vasospasm in experimental animals and antifibrinolytics apparently worsen the spasm. On a molecular level, one theory is that oxyhemoglobin causes the production of superoxide radicals that lead to a decrease in nitric oxide production in endothelial cells. This decrease in nitric oxide increases protein kinase C and intracellular calcium, resulting in myofilament activation and vasospasm. Other theories involve prostaglandins and lipid peroxidases. There may also be a genetic predisposition to development of vasospasm. Preliminary studies suggest that patients with the polymorphism of haptoglobin ($\alpha_1\alpha_1$) may be protected against vasospasm compared to patients with haptoglobin $\alpha_2\alpha_2$, which is less effective at neutralizing free radical formation by free hemoglobin. It is clear that endothelial

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dysfunction is present, particularly in the microcirculation.

Borosody M, Burke A, Caplin W, et al. Haptoglobin and the development of cerebral artery vasospasm after subarachnoid hemorrhage. *Neurology*. 2006;66:634-640.

D.5. What are pathophysiologic changes seen in cerebral vasospasm?

Structurally, leukocytes, red blood cells, and macrophages are seen in arterial walls. Inflammatory mediators, such as eicosanoids, interleukin 1, and immune complexes, are increased.

Eventually, the vessel wall thickens, and smooth muscle proliferation and collagen deposition accompany degenerative changes in the tunica intima and media.

Functionally, carbon dioxide reactivity is impaired, and autoregulation is often impaired, perhaps correlating to the degree of DCI. CBF in some areas appears to be pressure dependent, hence the reasoning behind hypertensive therapy.

Weyer GW, Nolan CP, Macdonald RL. Evidence-based cerebral vasospasm management. *Neurosurg Focus*. 2006;21:E8.

D.6. How is the diagnosis of cerebral vasospasm made?

The clinical diagnosis of cerebral vasospasm is made when the patient experiences an altered level of consciousness (drowsiness, disorientation) or a new focal neurologic deficit. These may be accompanied by increasing headache, meningismus, and fever. Vasospasm is rare in the first 3 days following SAH. It reaches peak incidence at 3 to 10 days and usually resolves by 10 to 14 days after SAH. In this patient, the new onset of hemiplegia suggests that the middle cerebral artery is involved. If vessels in the posterior fossa are involved, respiratory and hemodynamic abnormalities may develop.

The differential diagnosis includes rebleeding, hydrocephalus, seizure, hyponatremia, and drug effects. Transcranial Doppler, CBF, velocity greater than 120 cm per second in association with a new focal neurologic deficit are usually sufficient to make the diagnosis of cerebral vasospasm; however, a change in transcranial Doppler values over time may be more useful than an absolute value. CBF velocity greater than 200 cm per second is associated with a high risk of cerebral infarct, whereas a velocity less than 100 cm per second indicates that cerebral vasospasm is unlikely. Recent evidence shows that transcranial Doppler had only 63% sensitivity in identifying DCI, with a positive predictive value of only 22% in grade II and III patients. Cerebral perfusion imaging may be necessary in patients of poor grade who are unable to participate in neurologic examination.

Angiographic cerebral vasospasm can be found in 60% of patients following SAH, but only 50% of these patients will develop clinical focal neurologic deficits.

Connolly ES, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2012;43:11-27.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:218-246.

D.7. What steps can be taken to prevent cerebral vasospasm?

Calcium channel blockers are standard prophylactic therapy to prevent vasospasm. The mechanism is unknown, but presumably, calcium channel blockers aid in maintaining cellular integrity by preventing calcium entry into ischemic cells. Nimodipine, taken orally, improves neurologic outcome. Patients given nimodipine have no change in overall incidence of vasospasm, but they have a lower incidence of severe narrowing. In addition, although no improvement is found in mortality, there is improvement in outcome for survivors. Intravenous nimodipine is not available in the United States.

Nicardipine, an intravenous agent, showed a lower incidence of vasospasm, but no improvement in outcome versus a placebo group; both groups received hypertensive hypervolemic hemodilution therapy. The main complication of calcium

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channel blocker therapy is hypotension (0% to 8%), which may make this therapy difficult to achieve.

Other steps to limit cerebral vasospasm include the removal of subarachnoid blood as quickly as possible, instillation of thrombolytic agents (e.g., tissue plasminogen activator), and use of pharmacologic agents to reduce inflammatory response (high-dose glucocorticoids, ibuprofen). In Europe and Japan, protease inhibitors have been used in the treatment of vasospasm.

Connolly ES, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2012;43:11-27.

D.8. What treatments can be undertaken once a diagnosis of cerebral vasospasm is made?

Treatment for cerebral vasospasm is multifactorial and includes continuation of prophylactic measures. In the past, hypertensive hypervolemic hemodilution (HHH) therapy is a plan to augment CBF past the stenotic areas. It begins with hypervolemic hypertension, with intravascular volume expansion with crystalloid or colloid to increase cardiac output. Some recommended target values are CVP of 10 to 12 mm Hg, pulmonary artery occlusion pressure of 15 to 18 mm Hg, cardiac index of 3.0 to 3.5 L/min/m^2, and hematocrit of 30% to 35%. Various blood pressure targets have been reported, but a reasonable plan is systolic blood pressure 160 to 200 mm Hg if the aneurysm is clipped and 120 to 150 mm Hg if unclipped. Vasoactive infusions are added if hypervolemia alone is inadequate. End points of therapy are resolution of neurologic deficits or occurrence of complications of therapy, such as pulmonary edema (26%), myocardial ischemia, and rebleeding or rupture of a secondary aneurysm. A pulmonary artery catheter is often indicated.

Fluid used for HHH should be isotonic and have enough sodium to avoid hyponatremia. Vasopressin, fludrocortisone, or hydrocortisone may be administered to counteract excessive sodium and fluid loss.

Recent literature has proven the benefit of maintenance of euvolemia with induced hypertension in contrast to strict HHH.

Other treatments for vasospasm, including intra-arterial vasodilators or angioplasty, are utilized if the patient does not demonstrate prompt improvement with hypertensive therapy.

In spite of all attempted therapy, the outcome in patients with significant vasospasm is often poor. Most medications investigated to ameliorate the devastating consequences of vasospasm have had limited efficacy. Nimodipine, a calcium channel antagonist, has been found to have some efficacy in treating vasospasm and improving outcome. A recent target of pharmacologic therapy has been endothelin, a potent long-lasting vasoconstrictor. An endothelin receptor antagonist is now in clinical trials.

Connolly ES, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2012;43:11-27.

Dorhout Mees SMD, Rinkel GJ, Feigin VL, et al. Calcium antagonists for aneurismal subarachnoid hemorrhage. *Cochrane Database Syst Rev*. 2005;(3):CD000277.

Hoh BL, Ogilvy CS. Endovascular treatment of cerebral vasospasm: transluminal balloon angioplasty, intra-arterial papaverine, and intra-arterial nicardipine. *Neurosurg Clin North Am*. 2005;16:501-516.

Macdonald RL, Kassell NF, Mayer S, et al. Clazosentan to overcome neurological ischemia and infarction occurring after subarachnoid hemorrhage (CONSCIOUS-1): randomized, double-blind, placebo-controlled phase 2 dose-finding trial. *Stroke*. 2008;39:3015-3021.

Muench E, Horn P, Bauhuf C, et al. Effects of hypervolemia and hypertension on regional cerebral blood flow, intracranial pressure, and brain tissue oxygenation after subarachnoid hemorrhage. *Crit Care Med*. 2007;35:1844-1851.

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Raabe A, Beck J, Keller M, et al. Relative importance of hypertension compared with hypervolemia for increasing cerebral oxygenation in patients with cerebral vasospasm after subarachnoid hemorrhage. *J Neurosurg*. 2005;103:974-981.

D.9. What are other neurologic complications following SAH and aneurysm clipping?

Hydrocephalus, manifesting with a gradual decrease in level of consciousness, occurs in 25% of patients surviving SAH. Diagnosis is confirmed by CT scan. Treatment is by ventricular drainage.

Seizures, which occur in 13% of patients with SAH, may herald rebleeding or vasospasm. Seizures cause an increase in MAP, CBF, ICP, and lactate production, predisposing to rebleeding in those patients with unclipped aneurysms and cerebral ischemia in those patients with vasospasm. Most patients receive prophylactic anticonvulsants.

Hyponatremia occurs in 10% to 34% of patients with SAH in a time course that parallels that of vasospasm. It may be due to syndrome of inappropriate antidiuretic hormone secretion, “cerebral salt wasting,” or prolonged or excessive mannitol use. Cerebral salt wasting syndrome is thought to be mediated by release of atrial natriuretic factor by the

hypothalamus secondary to distention of the cerebral ventricles from hydrocephalus. After SAH, patients also have elevated plasma volume. In these patients, fluid restriction is not the treatment of choice because hypovolemia may predispose to vasospasm. Serum brain natriuretic peptide, which causes diuresis and natriuresis, is elevated after SAH, and patients may require treatment with an isotonic or hypertonic salt-containing fluid. In addition, treatment with hydrocortisone may be considered.

Finally, patients may experience brain swelling or edema, which is treated with hypertonic saline, mannitol, and/or dexamethasone.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010:218-246.

D.10. What other organ systems may manifest problems postoperatively in aneurysm clipping patients?

The lungs can be affected by pneumonia or neurogenic pulmonary edema, in which disruption of the pulmonary capillary membrane occurs secondary to increased sympathetic nervous system activity. Because of inactivity, patients may be predisposed to developing deep venous thrombosis (DVT) and pulmonary embolism. Patients (approximately 5%) may develop heparin-induced thrombocytopenia, possibly due to heparin exposure during angiography. These patients tend to have increased rates of both vasospasm and DVT. There appears to be a relationship between the use of hypertonic saline in the SAH patient and the incidence of acute kidney injury. Patients may have a fever secondary to subarachnoid blood, which may make the workup of postoperative infection more difficult. Finally, as in most patients with head injury, those with SAH may have increased metabolic rate.

Connolly ES, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2012;43:11-27.

Kumar AB, Shi Y, Shotwell MS, et al. Hypernatremia is a significant risk factor for acute kidney injury after subarachnoid hemorrhage: a retrospective analysis. *Neurocrit Care*. 2015;22:184-191.

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Chapter 22
Pheochromocytoma

Anup Pamnani

Vinod Malhotra

A 39-year-old man has a history of recurrent headaches, diaphoresis, and severe hypertension for several weeks. During a physical examination, he was found to have an exceptionally high blood pressure (BP) of 230/150 mm Hg with a heart rate of 112 beats per minute. Prior to this, the patient claims to have been in good health. Further studies were obtained to evaluate the etiology of his arterial hypertension and headaches.

A. Medical Disease and Differential Diagnosis

1. What are some common differential diagnoses for arterial hypertension?
2. What is a pheochromocytoma?
3. Describe the anatomy of the adrenal gland.
4. What substances does the adrenal medulla excrete?
5. What are the mechanisms of action of epinephrine and norepinephrine?
6. What is the pathway for synthesis and breakdown of catecholamines?
7. What does the adrenal cortex secrete?
8. What are the metabolic actions of the glucocorticoids and the mineralocorticoids?
9. What are some clinical features associated with a pheochromocytoma?
10. What is the prevalence of pheochromocytomas and paragangliomas?

B. Preoperative Evaluation and Preparation

1. How can you diagnose and localize the tumor preoperatively?
2. How do you pharmacologically prepare the patient with a pheochromocytoma for surgery?
3. What other aspects of preoperative management are important?

C. Intraoperative Management

1. What drugs should be avoided during the operation?
2. How would you monitor this patient?
3. Describe the anesthetic management of the patient with pheochromocytoma.
4. What drugs are used to control the effects of catecholamine stimulation during surgery?

5. What are some management concerns after the tumor is removed?
6. What are some of the concerns with laparoscopic adrenalectomy?

D. Postoperative Management

1. What is the significance of postoperative hypotension? How is it treated?
2. What other problems can arise in the postoperative period?

A. Medical Disease and Differential Diagnosis

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A.1. What are some common differential diagnoses for arterial hypertension?

The following is a partial list of differential diagnosis of hypertension:

- *Essential hypertension* of unknown etiology
- *Primary renal disease*: nephritis, renal artery stenosis, and renal infarction
- *Endocrine*: adrenocortical *hyperfunction*, hyperthyroidism, pheochromocytoma, acromegaly
- *Sympathetic stimulation*: light anesthesia, hypoxia, hypercarbia, pain
- *Neurogenic*: seizure activity, elevated intracranial pressure, and denervation of the carotid sinus
- *Miscellaneous*: malignant hyperthermia, neuroleptic malignant syndrome, carcinoid syndrome, and toxemia of pregnancy

Longo DL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 12th ed. New York: McGraw Hill; 2012:2042-2059.

A.2. What is a pheochromocytoma?

Pheochromocytomas are catecholamine-secreting tumors of chromaffin tissue. The precise etiology of these tumors is unknown. They are usually located in the adrenal medulla or sympathetic paraganglia but may be found anywhere chromaffin tissue exists. These locations extend from the base of the skull to the anus. Traditionally, it was thought that 90% of pheochromocytomas were found in the adrenal medulla and 10% occurred elsewhere. Prevalence of extra-adrenal tumors is now thought to be as high as 20%. These are commonly called *paragangliomas*.

Pheochromocytomas account for only 0.1% of all cases of arterial hypertension. They are prevalent in 0.005% to 0.01% of the population. When unsuspected or improperly managed during surgery, the hemodynamic effects of the released catecholamines can be profound.

Chen H, Sippel RS, O'Dorisio MS, et al. The North American Neuroendocrine Tumor Society consensus guideline for the diagnosis and management of neuroendocrine tumors: pheochromocytoma, paraganglioma, and medullary thyroid cancer. *Pancreas*. 2010;39(6):775-783.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier; 2012:376-406.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2002;16(3):359-369.

A.3. Describe the anatomy of the adrenal gland.

The adrenal glands are paired, mustard-colored structures positioned superior and slightly medial to the kidneys in the retroperitoneal space. Each gland is supplied by three arteries: the superior adrenal arteries derived from the inferior phrenic artery, the middle adrenal arteries derived from the aorta, and the inferior adrenal arteries derived from the renal artery. In contrast to the arterial supply, each adrenal gland usually is drained by a single, major adrenal vein. The right adrenal vein is usually short and drains into the inferior vena cava (IVC), whereas the left adrenal vein is longer and empties into the left renal vein. Accessory veins occur in 5% to 10% of patients and are an important consideration during pheochromocytoma resection.

In most respects, the cortex and medulla of the adrenal gland can be considered as two completely distinct organs that happen to colocalize during development. They are of separate

embryologic origin; the medullary portion is derived from the chromaffin ectodermal cells of the neural crest and develops in parallel with the sympathetic system during development, and the cortex originates around the fifth week of gestation from mesodermal tissue near the gonads on the adrenogenital ridge.

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The chromaffin cells become enclosed within the cortex to form the medulla. The organs of Zuckerkandl are paraganglia around the aorta at the level of the kidney anterior to the inferior aorta. Accessory areas for the occurrence of pheochromocytoma are in the mediastinum, in the bladder, occasionally in the neck, in the sacrococcygeal region, or in the anal or vaginal areas.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery* . 10th ed. New York: McGraw Hill; 2015:1343-1407.

Townsend CM, Beauchamp RD, Evers MB, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: WB Saunders; 2012:963-994.

A.4. What substances does the adrenal medulla excrete?

The adrenal medulla primarily secretes three substances, all of which are catecholamines: epinephrine, norepinephrine, and dopamine. These three compounds are found in all the chromaffin cells of the sympathetic nervous system, which includes the adrenal medulla, aberrant tissue along the sympathetic chain, and paraganglia. Both norepinephrine and dopamine are found at the endings of the postganglionic fibers of the sympathetic nervous system and in the central nervous system.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery* . 10th ed. New York: McGraw Hill; 2015:1343-1407.

Townsend CM, Beauchamp RD, Evers MB, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: WB Saunders; 2012:963-994.

A.5. What are the mechanisms of action of epinephrine and norepinephrine?

These catecholamines exert their effects by acting on β-adrenergic and α-adrenergic receptors. β-Receptor stimulation results in G protein-mediated activation of adenylate (adenylyl) cyclase, which increases cyclic adenosine monophosphate (cAMP) levels.

Stimulation of the α_1 subtype of the α-receptor results in G protein-mediated hydrolysis of phospholipid membranes, which cause an increase in cytoplasmic Ca^{2+} levels and subsequent smooth muscle contraction. The stimulation of α_2 receptors, conversely, inhibits the action of adenylate cyclase and decreases cAMP (Fig. 22.1).

The pharmacologic response is dependent on the location of the catecholamine receptors throughout the body. The distribution and density of the receptors will determine the predominant response to each catecholamine.

Brunton L, Chabner B, Knollman B, eds. *Goodman and Gillman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw Hill; 2010:277-334.

Hemmings HC Jr, Egan TD, eds. *Pharmacology and Physiology for Anesthesia* . Philadelphia, PA: Elsevier; 2013:218-234.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier; 2012:376-406.

A.6. What is the pathway for synthesis and breakdown of catecholamines?

The synthesis of endogenous catecholamines begins with the active transport of the amino acid tyrosine from the circulation into postganglionic sympathetic nerve endings. The hydroxylation of tyrosine is regarded as the rate-limiting step of the pathway (Fig. 22.2). The termination of the action of catecholamines occurs primarily through reuptake at nerve

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terminals. Diffusion and metabolism, by the enzymes catechol-*O*-methyltransferase (COMT) and monoamine oxidase (MAO), also play a role in termination of action.

Hemmings HC Jr, Egan TD, eds. *Pharmacology and Physiology for Anesthesia* . Philadelphia, PA: Elsevier; 2013:218-234.

Schulz C, Eisenhofer G, Lehnert H. Principles of catecholamine biosynthesis, metabolism and release. *Front Horm Res*. 2004;31:1-25.

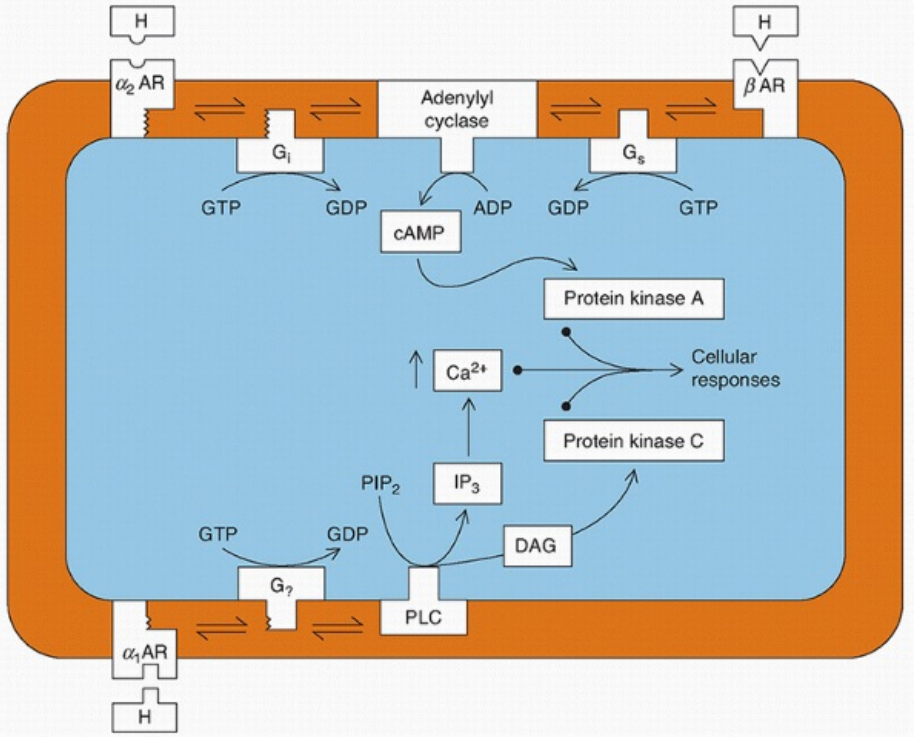


FIGURE 22.1 α_2-Receptor inhibition of adenylate cyclase. ADP, adenosine diphosphate; AR, adrenergic receptor; cAMP, cyclic adenosine monophosphate; Ca^{2+}, calcium; DAG, diacylglycerol; Gi, regulatory protein that, along with GTP, inhibits adenylate cyclase; G_s, regulatory protein that interacts with liganded β-adrenergic receptor to stimulate adenylate cyclase; GDP, guanosine diphosphate; GTP, guanosine triphosphate; H, neurotransmitter or hormone; IP_3, inositol triphosphate; PIP_2, phosphatidyl inositol biphosphate; PLC, phospholipase C. (Reprinted with permission from Goodman AG, Rall TW, Nies AS, et al, eds. *The Pharmacologic Basis of Therapeutics*. 8th ed. New York: MacMillan; 1993:109.)

A.7. What does the adrenal cortex secrete?

The adrenal cortex secretes more than 30 different corticosteroids. These can be divided into three major classes: mineralocorticoids, glucocorticoids, and sex steroids (the androgens and estrogen).

The precursor of all corticosteroids is cholesterol. Aldosterone is the most important mineralocorticoid secreted by the adrenal cortex, whereas cortisol is the most important glucocorticoid secreted. The adrenal cortex is also responsible for secreting sex steroids.

Each of these substances is secreted by different zones. The mineralocorticoids are secreted by the zona glomerulosa, glucocorticoids are secreted by the zona fasciculata, and sex steroids are secreted by the zona reticularis.

Brunton L, Chabner B, Knollman B, eds. *Goodman and Gillman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw Hill; 2010:277-334.

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Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier; 2012:376-406.

A.8. What are the metabolic actions of the glucocorticoids and the mineralocorticoids?

The glucocorticoids have their predominant mechanism of action on intermediary metabolism. These effects include increased gluconeogenesis, fatty acid mobilization, protein

catabolism, and anti-inflammatory effects. Cortisol may improve cardiac function by improving responsiveness of β-adrenergic receptors. Approximately 95% of the glucocorticoid activity is from the secretion of cortisol.

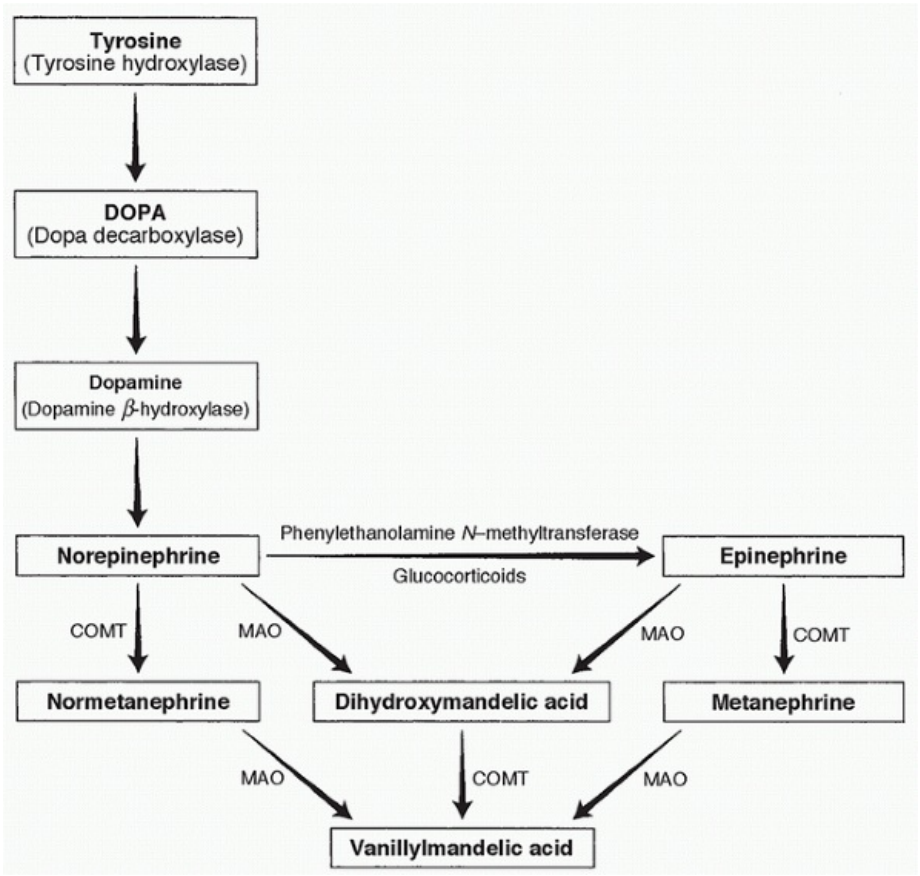


FIGURE 22.2 Synthesis and metabolism of endogenous catecholamine. COMT, catechol-*O*-methyltransferase; MAO, monoamine oxidase. (Reprinted with permission from Pullerits J, Ein S, Balfe JW. Anesthesia for phaeochromocytoma. *Can J Anesth*. 1988;35[5]: 526-534.)

The mineralocorticoids predominantly act on the body minerals, such as sodium and potassium. By conserving sodium ions, they sustain extracellular fluid volume. They also help maintain normal potassium plasma concentrations.

Barnes PJ. Molecular mechanisms and cellular effects of glucocorticosteroids. *Immunol Allergy Clin North Am*. 2005;25(3):451-468.

Brunton L, Chabner B, Knollman B, eds. *Goodman and Gillman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw Hill; 2010:277-334.

Czock D, Keller F, Rasche FM, et al. Pharmacokinetics and pharmacodynamics of systemically administered glucocorticoids. *Clin Pharmacokinet*. 2005;44(1):61-98.

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A.9. What are some clinical features associated with a pheochromocytoma?

The classic triad is severe headache, diaphoresis, and palpitations. One or more of the following often signal the presence of a pheochromocytoma: sudden severe headaches, perspiration, weight loss, paroxysmal hypertension, pallor, palpitations, diabetes-like syndrome with elevated fasting blood sugar, nausea, vomiting, fever, encephalopathy, anxiety, myocardial infarction, stroke, or acute renal failure. The aforementioned symptoms are usually paroxysmal in nature. These "attacks" may last from a few moments to hours. Although hypertension can be paroxysmal, 65% of adults demonstrate sustained hypertension.

TABLE 22.1 Syndromes Associated with Pheochromocytoma

MEN Type IIa (Sipple syndrome)	Parathyroid adenoma/hyperplasia
	Medullary carcinoma of thyroid
	Pheochromocytoma
MEN Type IIb	Medullary carcinoma of the thyroid
	Mucosal adenomas
	Marfanoid appearance
	Pheochromocytoma
von Hippel-Landau syndrome	Hemangioblastoma of the retina, cerebellum, or other parts of the CNS, pheochromocytoma
Neurofibromatosis	Neurofibromas, café-au-lait spots, axillary or inguinal freckling, optic nerve glioma, pheochromocytoma

CNS, central nervous system; MEN, multiple endocrine neoplasia.

A pressor response to particular drugs suggests the presence of this tumor. These drugs include histamine, glucagon, droperidol, tyramine, metoclopramide, cytotoxic drugs, saralasin, tricyclic antidepressants, and phenothiazines.

Manger WM. An overview of pheochromocytoma: history, current concepts, vagaries, and diagnostic challenges. *Ann N Y Acad Sci*. 2006;1073:1-20.

Townsend CM, Beauchamp RD, Evers MB, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: WB Saunders; 2012:963-994.

A.10. What is the prevalence of pheochromocytomas and paragangliomas?

Pheochromocytomas occur in both sexes with peak incidence in the third to fifth decades of life. Advances in diagnosis

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and genetics now challenge the traditional “rule of 10” for pheochromocytomas (10% bilateral, 10% extra-adrenal, 10% familial, 10% malignant). Prevalence of bilateral adrenal tumors is higher than 10% in some familial pheochromocytoma syndromes such as multiple endocrine neoplasia type 2 and von Hippel-Lindau syndrome (see Table 22.1 for complete list). Prevalence of extra-adrenal tumors (paragangliomas) is thought to reach as high as 20%. Nearly 25% of these tumors are thought to be hereditary.

Metastases is low for adrenal pheochromocytomas (up to 5%). The prevalence of malignant disease is about 33% for extra-adrenal pheochromocytomas and even higher in patients with specific mutations such as those causing some forms of familial paragangliomas.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2002;16(3):359-369.

Lenders JW, Eisenhofer G, Mannelli M, et al. Phaeochromocytoma. *Lancet*. 2005;366(9486):665-675.

Widimský J Jr. Recent advances in the diagnosis and treatment of pheochromocytoma. *Kidney Blood Press Res*. 2006;29(5):321-326.

B. Preoperative Evaluation and Preparation

B.1. How can you diagnose and localize the tumor preoperatively?

The laboratory tests for pheochromocytoma are shown in Table 22.2. Biochemical diagnosis is based on the excess catecholamines and their metabolites released by the tumor.

In theory, the hydroxy-methoxy-mandelic acid (often misnamed as vanillylmandelic acid [VMA]) level should be the most reliable laboratory test because it is the final common product of both catecholamine metabolic pathways. In practice, however, the intermediate metanephrines have proved to be better discriminators of pheochromocytomas. Hydroxymethoxy-mandelic acid is often used as an initial “case-finding” test because it has “acceptable” specificity and sensitivity and is relatively inexpensive.

TABLE 22.2 Biochemical Tests for Diagnosis of Pheochromocytoma

URINE TESTS
Norepinephrine
Epinephrine
Dopamine
Total metanephrines
Fractionated metanephrines
Vanillylmandelic acid
PLASMA TESTS
Norepinephrine

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Epinephrine
Dopamine
Plasma-free metanephrines
Clonidine suppression of norepinephrine secretion

Historically, 24-hour urine tests were generally considered superior to plasma tests in the diagnosis of pheochromocytomas because the tumor secretes catecholamines only intermittently and the catecholamines have a short half-life. These combined factors could result in relatively normal plasma catecholamine levels in the presence of an active tumor.

Measurement of total metanephrines gives the highest true-positive results, approximately 98% to 99%. Compelling evidence now indicates that initial screening for pheochromocytomas and paragangliomas can include measurements of plasma-free metanephrines or urinefractionated metanephrines. The plasma test offers advantages over the urine test in that it can additionally help predict size and adrenal versus extra-adrenal locations of tumors as well as presence of metastases and underlying germline mutations of tumor susceptibility genes. However, the plasma test is difficult to implement correctly, rendering the urine test preferable for mainstream use and the plasma test more appropriate for specialized endocrine centers.

Computed tomography (CT) with or without iodine 131 (^{131}I)-labeled metaiodobenzylguanidine (MIBG) is extremely accurate in diagnosing and localizing the tumor. Use of arteriography, once popular, should be performed cautiously because dye can stimulate catecholamine release. CT scanning and magnetic resonance imaging (MRI) scanning are excellent imaging techniques that visualize normal adrenal glands when the diagnosis is equivocal. For extra-adrenal locations and in pregnant patients, MRI scanning may be a more desirable choice.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw Hill; 2015:1343-1407.

Chen H, Sippel RS, O'Dorisio MS, et al. The North American Neuroendocrine Tumor Society consensus guideline for the diagnosis and management of neuroendocrine tumors: pheochromocytoma, paraganglioma and medullary thyroid cancer. *Pancreas*. 2010;39(6):775-783.

Eisenhofer G, Peitzsch M. Laboratory evaluation of pheochromocytoma and paraganglioma. *Clin Chem*. 2014;60(12):1486-1499.

Widimský J Jr. Recent advances in the diagnosis and treatment of pheochromocytoma. *Kidney Blood Press Res*. 2006;29(5):321-326.

B.2. How do you pharmacologically prepare the patient with a pheochromocytoma for surgery?

The major goals of pharmacologic therapy in the preoperative period are to control hypertension and to facilitate intravascular volume expansion.

Administration of *α*-adrenergic blockers has been the cornerstone of preoperative management. Phenoxybenzamine, prazosin, terazosin, and doxazosin may all be employed to

facilitate preoperative *α*-blockade. Phenoxybenzamine is most commonly used due to its relatively long duration of action and ease of administration. It irreversibly and nonselectively alkylates *α*-adrenergic receptors, including α_1-receptors on vascular smooth muscle, rendering them nonfunctional. Preoperative medical therapy is started 1 to 3 weeks prior to surgery. Therapy is titrated to resolution of symptoms and decrease of BP to low normal values for age. During this period, the patient is encouraged to liberally imbibe fluids and salt in order to facilitate volume replacement and minimize

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postural hypotension.

Reflex tachycardia is a frequent side effect of preoperative *α*-blockade. Tachycardia can be managed by subsequent addition of *β*-blocker therapy. It is worth noting, however, that *β*-blockade is best avoided in the initial phases of treatment. In the absence of adequate *α*-blockade, inhibition of *β*-receptor-mediated vasodilation, can result in unopposed *α*-receptor-mediated vasoconstriction due to catecholamines secreted by the tumor. This can precipitate a hypertensive crisis, heart failure, and possibly end-organ damage.

Recently, the calcium channel blocker nicardipine has been used as an alternative to phenoxybenzamine for preoperative management. Preoperative use of phenoxybenzamine can often be limited by its frequent and sometimes severe side effect profile (postural hypotension, reflex tachycardia, nasal stuffiness, syncope, etc.), as well as its uncommon use and high cost. Oral nicardipine therapy appears to be an equivalent alternative to phenoxybenzamine therapy and may better tolerated, cheaper, and more accessible.

Brunaud L, Boutami M, Nguyen-Thi PL, et al. Both preoperative alpha and calcium channel blockade impact intraoperative hemodynamic stability similarly in the management of pheochromocytoma. *Surgery*. 2014;156(6):1410-1417.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier; 2012:376-406.

Lenders JW, Duh QY, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99(6):1915-1942.

Siddiqi HK, Yang HY, Laird AM, et al. Utility of oral nicardipine and magnesium sulfate infusion during preparation and resection of pheochromocytomas. *Surgery*. 2012;152(6):1027-1036.

B.3. What other aspects of preoperative management are important?

The circulating blood volume is frequently decreased in these patients due to vasoconstriction from high levels of circulating catecholamines. Patients are encouraged to consume fluid and salt in order to facilitate volume expansion once *α*-blocker therapy is initiated. However, volume expansion should be undertaken with caution in those with decreased myocardial function to avoid precipitating congestive heart failure.

Sedation in the immediate preoperative period can be particularly helpful to attenuate catecholamine release secondary to anxiety. It may also help reduce vasodilator requirement subsequently in the intraoperative phase. Adequate sedation and analgesia should also be provided during invasive procedures such as arterial line access. Preoperative treatment of the airway with nebulized lidocaine can help significantly attenuate the tracheal response to intubation.

Lenders JW, Duh QY, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99(6):1915-1942.

Pacak K. Preoperative management of the pheochromocytoma patient. *J Clin Endocrinol Metab*. 2007;92(11):4069-4079.

C. Intraoperative Management

C.1. What drugs should be avoided during the operation?

Some of the commonly administered drugs that should be avoided in patients with pheochromocytoma are listed in Table 22.3. Many of these agents release histamine (e.g., morphine, curare, atracurium), which is a potent catalyst of catecholamine release from the tumor. Agents that cause indirect increase of catecholamine levels (e.g., pancuronium, ketamine, ephedrine) should also be avoided. It should be noted, however, that these are not absolute

contraindications and many of these agents can be used if clinically necessary, provided they are used judiciously with close monitoring.

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TABLE 22.3 Suggested Drugs to Avoid in Patients with Pheochromocytoma

Droperidol
Morphine
Atracurium
Pancuronium
Ketamine
Ephedrine
Halothane
Cocaine
Metoclopramide
Curare

Connery LE, Coursin DB. Assessment and therapy of selected endocrine disorders. *Anesthesiol Clin North America*. 2004;22(1):93-123.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2002;16(3):359-369.

C.2. How would you monitor this patient?

Monitoring in these patients generally includes an electrocardiogram with a V_5 lead, core temperature, pulse oximetry, intra-arterial BP monitoring, central venous pressure monitoring, and a urinary catheter. For patients with known or suspected myocardial dysfunction, a pulmonary artery catheter or transesophageal echocardiography should be considered. Devices that measure cardiac output and stroke volume variation noninvasively can be particularly helpful in titrating fluid therapy.

Most tumors nowadays are excised using laparoscopic technique with minimal blood loss. With the increasing availability of noninvasive monitors of cardiac function, patients who are adequately optimized in the preoperative period and display minimal hemodynamic perturbation may not require central venous pressure monitoring.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier; 2012:376-406.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2002;16(3):359-369.

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C.3. Describe the anesthetic management of the patient with pheochromocytoma.

General anesthesia is frequently employed for tumor resection because most resections are performed by laparoscopic technique. Neuromuscular relaxation and controlled ventilation allow for adequate gas exchange during CO_2 insufflation for pneumoperitoneum.

The anesthetic induction technique should minimize hemodynamic changes and allow for adequate depth of anesthesia during tracheal intubation. Lidocaine 4% solution administered prior to intubation, via mucosal atomizer device, or 1.5 mg per kg intravenously 2 minutes before laryngoscopy can significantly attenuate the response to tracheal intubation. Other measures to attenuate hemodynamic responses to intubation are described in Chapter 11, sections C.5 and C.6. Most of the inhaled agents can be employed during the maintenance phase. However, caution should be used when desflurane is utilized because it may provoke sympathetic stimulation and subsequent catecholamine release. Halothane, now infrequently used in most clinical settings, should be avoided because it has the potential to incite arrhythmias in the presence of high levels of circulating catecholamines.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier; 2012:376-406.

TABLE 22.4 Intravenous Drugs to Control Intraoperative Hypertension

DRUG	DOSE
Nicardipine	Infusion of 5-15 mg/hr. Increase by 2.5 mg/hr q15min to effect.
Phentolamine	1-mg IV boluses q5-10min. Start infusion 0.1-2 mg/min and titrate to effect.
Nitroglycerin	20-40 μg boluses q5-10 mins to effect. Infusion 5-20 μg/min initial (maximum dose 400 μg/min)
Nitroprusside	Infuse initially with 0.5-1.5 μg/kg/min to maximum of 8 μg/kg/min over 1-3 hr
Propranolol	1-mg boluses to total 10 mg
Esmolol	Load with 5-10-mg boluses and infuse at 0.25-0.5 μg/kg/min.
Labetalol	5-10-mg boluses q20-30min to maximum dose 150 mg

C.4. What drugs are used to control the effects of catecholamine stimulation during surgery?

Drugs used to control intraoperative hypertension are listed in Table 22.4.

Nicardipine infusion can be easily titrated and is particularly effective at achieving systemic vasodilation. It is a good choice in patients that have already been started on oral nicardipine in the preoperative period. Sodium nitroprusside was used extensively previously. Concerns over toxic metabolites and handling precautions to prevent its degradation by light have largely resulted in nicardipine replacing it as a first-line agent. Phentolamine, a shortacting α-blocking agent, can also be given as a bolus medication or a continuous infusion to control BP.

$MgSO_4$ has been occasionally used in selected cases as an adjunct vasodilator. Data is still being gathered on its efficacy. Administration of $MgSO_4$ should be accompanied by close monitoring of plasma magnesium levels and other

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clinical signs of hypermagnesemia.

β-Blockers can be a useful adjunct to control BP in the intraoperative phase, particularly if tachycardia accompanies use of systemic vasodilators. They should, however, not be used as the first-line agent for treatment of intraoperative hypertension due to the concern about unopposed *α*-agonism.

Hodin R, Lubitz C, Phitayakorn R, et al. Diagnosis and management of pheochromocytoma. *Curr Probl Surg*. 2014;51(4):151-187.

James MF, Cronjé L. Pheochromocytoma crisis: the use of magnesium sulfate. *Anesth Analg*. 2004;99(3): 680-686.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2002;16(3):359-369.

C.5. What are some management concerns after the tumor is removed?

It is important to be aware of the fact that BP may decrease very quickly after venous drainage of the tumor is interrupted. Any vasodilators being administered should be discontinued. BP support may be maintained by administering vasopressors, such as norepinephrine and vasopressin, and administering fluids. Norepinephrine requirements can be substantial in the post-tumor resection period due to receptor insensitivity from chronic catecholamine release. Close communication between the anesthesia and surgical teams is essential during this period. Continued vasodilator support may indicate inadequate resection or previously undiagnosed extra-adrenal tumor.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier; 2012:376-406.

Hodin R, Lubitz C, Phitayakorn R, et al. Diagnosis and management of pheochromocytoma. *Curr Probl Surg*. 2014;51(4):151-187.

C.6. What are some of the concerns with laparoscopic adrenalectomy?

Insufflation of CO_2, to facilitate pneumoperitoneum, is typically associated with an elevation in catecholamine levels in patients undergoing laparoscopic adrenalectomy, resulting in an associated increase in cardiac output and BP. Close monitoring of vital signs is essential once pneumoperitoneum is initiated. Use of lower intra-abdominal pressures during laparoscopy has been associated with decreased release of catecholamines and less hemodynamic fluctuation. If hemodynamic instability is sustained or refractory, insufflation should be terminated.

Lombardi CP, Raffaelli M, De Crea C, et al. Role of laparoscopy in the management of adrenal malignancies. *J Surg Oncol*. 2006;94(2):128-131.

Sood J, Jayaraman L, Kumra VP, et al. Laparoscopic approach to pheochromocytoma: is a lower intraabdominal pressure helpful? *Anesth Analg*. 2006;102(2):637-641.

Sprung J, O'Hara JF Jr, Gill IS, et al. Anesthetic aspects of laparoscopic and open adrenalectomy for pheochromocytoma. *Urology*. 2000;55(3):339-343.

D. Postoperative Management

D.1. What is the significance of postoperative hypotension? How is it treated?

Postoperative hypotension can be due to reduced circulating catecholamine levels post-tumor resection, hypovolemia, or residual effects of phenoxybenzamine (which has a long half-life). In addition, downregulation of catecholamine receptors,

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due to chronically elevated levels of catecholamines, renders administered catecholamines less effective. Post-adrenalectomy hypotension should be treated with volume administration and, if needed, norepinephrine. Vasopressin can be used to treat catecholamine-resistant hypotension. It is important that the clinician rule out other etiologies of hypotension, such as postoperative bleeding as well.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier; 2012:376-406.

D.2. What other problems can arise in the postoperative period?

Occasionally, patients may be somnolent in the postoperative period. This is possibly due to the sudden removal of activating catecholamines. Narcotic requirement may also be decreased.

Hypoglycemia is another significant concern. Severe hypoglycemia may cause loss of consciousness and respiratory arrest. Hypoglycemia is the result of decreased catecholamine levels (particularly when the tumor is epinephrine-secreting). Neoglycogenesis and glycogenolysis, the result of chronic β-agonism, are no longer present, and chronically elevated insulin plasma level may decrease more gradually. Close monitoring of plasma glucose levels is essential in the first 24-hours post-tumor resection.

Persistent hypertension after removal of a pheochromocytoma occasionally signifies that a residual pheochromocytoma tumor is present. Be aware that plasma catecholamine levels (norepinephrine) may not decrease to normal levels for many days after removal of the tumor.

Davies MJ, McGlade DP, Banting SW. A comparison of open and laparoscopic approaches to adrenalectomy in patients with phaeochromocytoma. *Anaesth Intensive Care*. 2004;32(2):224-229.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier; 2012:376-406.

Wilhelm SM, Prinz RA, Barbu AM, et al. Analysis of large versus small pheochromocytomas: operative approaches and patient outcomes. *Surgery*. 2006;140(4):553-559; discussion 559-560.

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Chapter 23
Diabetes Mellitus

Mark E. Nunnally

Vinod Malhotra

A 59-year-old woman presents for vaginal hysterectomy for cervical cancer. She is obese (body mass index 32 kg per m^2) and has had diabetes mellitus (DM) type 2, hypertension, and dyslipidemia for 20 years. She takes enalapril, metoprolol, atorvastatin, metformin, sitagliptin, and recently, insulin glargine, 20 units subcuta-neous, daily for refractory hyperglycemia. She measures her serum glucose inter-mittently at home. Values are generally 150 to 220 mg per dL. She experiences an early and prolonged sense of fullness after meals and an unpleasant sour taste at night two or three times per week. Laboratory values are notable for a serum creatinine of 2.2 mg per dL and a serum glucose of 206 mg per dL. She has not taken any medications today and has had nothing to eat since midnight.

A. Medical Disease and Differential Diagnosis

1. What is the epidemiology of DM in the general population?
2. What are the factors in the etiology of the disease?
3. How is DM classified?
4. What are the complications of DM?
5. How are the different forms of this illness treated?
6. How is control of the disease adequately monitored?
7. What are some of the factors that alter insulin requirements?
8. What are the principles of management of diabetic ketoacidosis (DKA)?
9. What is a hyperglycemic hyperosmolar state?

B. Preoperative Evaluation and Preparation

1. How should this patient be evaluated?
2. How would the stiff joint syndrome affect her airway management?
3. What are the signs and implications of autonomic neuropathy in the diabetic patient?
4. How should this patient be prepared for anesthesia and surgery?
5. For elective surgery, how are insulin and glucose requirements managed on the day of surgery?
6. How should this patient be premedicated?

C. Intraoperative Management

1. What are the effects of anesthesia and surgery on insulin and glucose metabolism?
2. What anesthetic techniques should be considered?
3. How should this patient be monitored?
4. How is hyperglycemia treated intraoperatively?
5. How is hypoglycemic shock recognized and treated intraoperatively?

D. Postoperative Management

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1. How is diabetes controlled in this patient postoperatively?
2. Does diabetes increase perioperative risk?
3. What are the common postoperative complications to be expected in a diabetic patient?
4. Is it necessary to achieve tight perioperative control of glucose?

A. Medical Disease and Differential Diagnosis

A.1. What is the epidemiology of DM in the general population?

DM, literally "sweet urine," is a group of metabolic disorders defined by elevated serum glucose. Data from the National Health and Nutrition Examination Survey from 2007 to 2010 suggest a prevalence of DM in the adult population of 11.4%, with more than a quarter of those undiagnosed. For patients 65 years or older, the prevalence is 25.7%. National Health Interview Survey (NHIS) data suggest a doubling of prevalence between 1990 and 2008, but no significant change between 2008 and 2012.

A majority of patients with diabetes (approximately 90%) have type 2 diabetes (DM2); a minority (approximately 10%) have type 1 diabetes (DM1). Finally, 1% to 14% of pregnant women develop gestational diabetes. DM1 and DM2 are very different diseases. In DM1, ex-ogenous insulin is essential for cellular metabolism. Untreated, DM1 is a wasting disease associated with ketoacidosis and severe cumulative organ failure. DM2 is a metabolic disorder associated with resistance to insulin effects. Because of the presence of circulating insulin, ketoacidosis is rare in DM2. However, a hyperglycemic hyperosmolar state is a risk in the inadequately treated patient.

Diabetes prevalence and glycemic control among adults aged 20 and over, by sex, age, and race and Hispanic origin: United States, selected years 1988-1994 through 2007-2010. http://www.cdc.gov/nchs/data/hus/2013/046.pdf. Accessed September 15, 2015.

Geiss LS, Wang J, Cheng YJ, et al. Prevalence and incidence trends for diagnosed diabetes among adults aged 20 to 79 years, United States, 1980-2012. *JAMA*. 2014;312(12):1218-1226.

Hillier TA, Vesco KK, Pedula KL, et al. Screening for gestational diabetes mellitus: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2008;148:766-775.

A.2. What are the factors in the etiology of the disease?

Because hyperglycemia defines DM, it is too easy to focus on elevations in serum glucose, ignoring other effects. Lipid and protein metabolism are deranged in both varieties of DM. Tissue growth, signaling, and function are likewise impaired. Simple control of blood sugar may not adequately treat the complex hormonal and metabolic derangements of DM. Inflammation and immune dysfunction are also components of the disease.

In DM1, the immune system destroys insulin-secreting pancreatic beta cells. The diagnosis of DM1 is frequently made in childhood. DM2 manifests in a variety of conditions that decrease the hypoglycemic effects of insulin. Among these are obesity and endocrine and inflammatory conditions. In both cases, genetic association is incomplete and there is association with other diseases, including autoimmune disorders, hypertension, and dyslipidemias. Gestational diabetes reflects insulin resistance exacerbated by the effects of pregnancy. It likely signals patients who are at risk of developing DM2.

Cowie CC, Rust KF, Byrd-Holt DD, et al. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health and Nutrition Examination Survey 1999-2002. *Diabetes Care.* 2006;29(6):1263-1268.

McDonald M, Hertz RP, Unger AN, et al. Prevalence, awareness, and management of hypertension, dyslipidemia, and diabetes among United States adults aged 65 and older. *J Gerontol A Biol Sci Med Sci.* 2009;64(2):256-263.

A.3. How is DM classified?

Table 23.1 lists the criteria for the diagnosis of DM1, DM2, and gestational diabetes. Elevated (≥6.5%) hemoglobin (Hgb)

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to confirm metabolic derangement, but random hyperglycemia accompanied by classic symptoms (such as polyuria and polydipsia), or the inability to manage a glucose load, are sufficient to make the diagnosis. Ketoacidosis and the need for insulin reflect DM1, whereas obesity, gradual onset (usually at an older age), and hyperosmolality without ketosis suggest DM2. Gestational diabetes resembles DM2 only in the setting of pregnancy.

TABLE 23.1 American Diabetes Association Diagnostic Criteria for Diabetes Mellitus

1. Symptoms of diabetes plus random plasma glucose level >200 mg/dL (11.1 mmol/L)

2. Hemoglobin A_1C ≥6.5%

3. Fasting plasma glucose level ≥126 mg/dL (7.0 mmol/L)

4. Two-hour plasma glucose level ≥200 mg/dL (11.1 mmol/L) during oral glucose tolerance test

From American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2010;33(suppl 1): S62-S69.

Therapy for DM varies by type. Insulin is essential in DM1. In DM2 and gestational diabetes, diet, exercise, and drugs that modify insulin secretion or sensitivity can help correct hyperglycemia, although exogenous insulin may be necessary.

American Diabetes Association. Standards of medical care in diabetes—2013. *Diabetes Care.* 2013;36 (suppl 1): S11-S66.

A.4. What are the complications of DM?

Acute complications of DM include DKA and a hyperglycemic hyperosmolar state. Both are associated with severe systemic illness and a high mortality and will be discussed separately. Hypoglycemia is a serious risk of several diabetes therapies.

Chronically, DM impacts virtually every organ system. Of most concern to the anesthetist are macrovascular disease, including accelerated atherosclerosis, and microvascular nephropathy, neuropathy, and cardiomyopathy. Tissues fail from a combination of advanced glycation end products, inflammation, connective tissue proliferation, and impaired perfusion. Renal failure, neuropathy, and accelerated coronary, cerebral, and peripheral vascular disease are common. Autonomic neuropathy and the stiff joint syndrome are both factors for preoperative evaluation (see later discussion). Hypertension frequently accompanies DM, exacerbating organ failure. Impaired immune function predisposes to infection. Hypercoagulability exacerbates macrovascular disease. Dyslipidemias accelerate atherosclerotic lesions and may directly contribute to metabolic toxicities.

Cumulatively, the systemic lesions caused or exacerbated by DM reduce life expectancy. When diagnosed before the age of 35 years, DM causes an estimated mean of 25.9 years of lost life. Because complications worsen with time, this effect decreases. About 50% of mortality in diabetic patients comes from cardiovascular disease.

Although it would be helpful to stratify diabetic patients according to their risk of complications, the complexity of the disease and its management makes risk stratification difficult. The safest assumption is that a diabetic is at high risk for coronary and other macrovascular disease, congestive heart failure, and renal insufficiency.

Ford ES, Zhao G, Li C. Pre-diabetes and the risk for cardiovascular disease: a systematic review of evidence. *J Am Coll Cardiol.* 2010;55:1310-1317. Stolar M. Glycemic control and complications in type 2 diabetes mellitus. *Am J Med.* 2010;123:S3-S11.

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A.5. How are the different forms of this illness treated?

Diabetes care is different in chronic and acute settings. It is essential to differentiate between the agents used chronically and during acute perioperative stress.

Care of DM1 requires exogenous insulin. Figure 23.1 illustrates the pharmacodynamics of several insulin preparations. A combination of a short- and a long-acting insulin preparation can help achieve the goals of resting and postprandial glycemic control. In contrast, DM2

responds to insulin, oral insulin secretagogues, insulin sensitizers, glucose uptake inhibitors, gastrointestinal hormones, weight loss, dietary management, and exercise. Table 23.2 lists the major classes of drugs for the treatment of DM2, their mechanisms of action, pharmacokinetics, and particular concerns for the anesthetist.

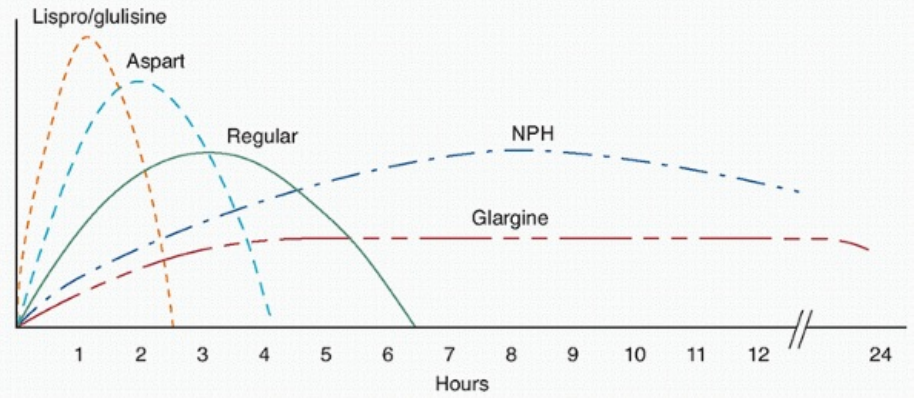


FIGURE 23.1 Onset and duration of action graphic for common subcutaneous insulin preparations. Regular insulin given intravenously fits the best profile for a titratable drug in the operating room, as onset peak and offset all occur within an hour. NPH, neutral protein hagedorn.

Certain medications have adverse effects that deserve consideration. Biguanides, such as metformin, increase peripheral glucose uptake but also predispose patients to greater production of lactic acid and acidosis. The significance of this finding is not clear, but many recommend discontinuing these drugs perioperatively because they might increase the risk of lactic acidosis with hypoperfusion during surgery. Because of its long half-life, metformin may take up to 72 hours to clear from the bloodstream, so discontinuation on the day of surgery does not minimize the risk of acidosis. Thiazolidinediones have been associated with hepatic injury and congestive heart failure. Exenatide is associated with reports of kidney dysfunction. Sulfonylureas, pramlintide, and sitagliptin may be associated with hypoglycemia. Glucose transporter type 2 inhibitors, such as dapagliflozin, may be associated with urogenital infections. Long-term risks remain poorly characterized for this and other new agents, such as glucagon-like peptide agonists and inhaled insulin preparations.

For these reasons, as well as unreliable pharmacokinetics, the best option for acute treatment of all types of diabetic hyperglycemia is insulin. Although subcutaneous dosing is often used in the hospital setting, intravenous insulin best meets the profile of an ideal titratable agent. It has a short time to onset (10 to 15 minutes), peak effect (less than 30 minutes), and duration of action (45 minutes). Frequent glucose monitoring is essential to titrate the therapy.

Although serum glucose or other markers of chronic hyperglycemia, such as Hgb A_1C are currently standard end points for chronic therapy, other factors such as serum lipid and blood pressure management may be just as important. Anesthesiologists should inquire about agents treating these conditions during preoperative evaluation.

Bagry HS, Raghavendran S, Carli F. Metabolic syndrome and insulin resistance: perioperative considerations. *Anesthesiology.* 2008;108:506-523.

Chen D, Lee SL, Peterfreund RA. New therapeutic agents for diabetes mellitus: implications for anesthetic management. *Anesth Analg.* 2009;108:1803-1810.

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Jung CH, Chung EJ, Park JY. A novel therapeutic agent for type 2 diabetes mellitus: SGLT2 inhibitor. *Diabetes Metab J.* 2014;38:261-273.

A.6. How is control of the disease adequately monitored?

Self-monitoring of blood glucose is possible in all forms of diabetes, usually by using fingerstick blood samples and portable monitors. This method is the established standard of care in DM1 for carefully titrated control to prevent hypoglycemia and ketoacidosis. Many advocate

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self-monitoring for patients with DM2, especially if they take insulin, but compliance varies, and self-monitoring may not be beneficial in all patients. Hgb A_1C, the product of hemoglobin exposure to hyperglycemic conditions, is a marker of long-term glycemic control. It may help identify subgroups of patients for whom the risk for complications is higher and can be a marker of disease control. The relationship between levels of glycemic control and Hgb A_1C is not linear, so a single laboratory value does not completely reveal the glycemic profile over time. Patients with DM have blood pressure and serum lipid profiles monitored as part of their long-term care because these factors increase the risk of lifetime complications.

TABLE 23.2 Common Therapies for Type 2 Diabetes[a]

DRUG NAME/CLASS	MECHANISM	ROUTE	ONSET	DURATION	IMPORTANT CONSIDERATIONS
First-Generation Sulfonylureas	↑ Beta cell insulin secretion	PO			Hypoglycemia risk
Tolbutamide			1 hr	12 hr	
Acetohexamide			3 hr	24 hr	
Tolazamide			4 hr	16 hr	
Chlorpropamide			2 hr	24 hr	
Second-Generation Sulfonylureas	↑ Beta cell insulin secretion	PO			Hypoglycemia risk
Glyburide (Micronase)			30 min	24 hr	
Glipizide IR (Glucotrol)			30 min	24 hr	
Glipizide ER (Glucotrol XL)			2-4 hr	24 hr	

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Glimepiride (Amaryl)			2-3 hr	24 hr	
Biguanides	↑ Peripheral glucose uptake in response to insulin	PO			Lactic acidosis risk may extend up to 72 hr after administration
Metformin (Glucophage)			1-3 hr	17 hr	
α-Glucosidase Inhibitors	↓ Digestive carbohydrate breakdown	PO			No known adverse effects
Acarbose (Precose)			2 hr	NA	
Miglitol (Glyset)			2-3 hr	NA	
Thiazolidinediones (PPAR-γ mediators)	↑ Peripheral glucose uptake	PO			Risk for hepatic injury, fluid retention; ongoing concerns about myocardial ischemia
Pioglitazone (Actos)			hours	$T_{1/2}$ 3-7 hr	
Rosiglitazone (Avandia)			hours	$T_{1/2}$ 3-4 hr	
Glinides	↑ Beta cell insulin secretion	PO			Hypoglycemia risk
Repaglinide (Prandin)			15-60 min	4-6 hr	
Nateglinide (Starlix)			20 min	$T_{1/2}$ 1.5 hr	
Incretin-Mimetics	↑ Insulin, ↓ glucagon, hepatic glucose production, gastric emptying, and appetite	SC			Observational data associate with renal failure
Exenatide (Byetta)			10 min	6-8 hr	

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Liraglutide (Victoza)			minutes	$T_{1/2}$ 13 hr	
DPP-IV Inhibitors	Inhibits incretin breakdown	PO			May have effects on immune function
Sitagliptin (Januvia)			hours	days	
Saxagliptin (Onglyza)			hours	24 hr	
Amylin Analogues	↑ Satiety, ↓ glucagon, and appetite	SC			No confirmed hypoglycemia risk
Pramlintide (Symlin)			minutes	hours	

[a]Onset and duration data are approximate only and subject to variability.

PO, per os (by mouth); PPAR, peroxisome proliferator-activated receptor; SC, subcutaneous; DPP-IV, dipeptidyl peptidase - 4.

In the operating room, serum glucose can be measured by pinprick or vascular blood sample. Samples from a venous or arterial line offer greater reliability during low perfusion. If insulin is being used, monitoring is recommended every hour.

Kolb H, Kempf K, Martin S, et al. On what evidence-base do we recommend self-monitoring of blood glucose? *Diabetes Res Clin Pract.* 2010;87:150-156.

Moitra V, Sladen RN. Monitoring endocrine function. *Anesthesiol Clin.* 2009;27:355-364.

A.7. What are some of the factors that alter insulin requirements?

Insulin responsiveness is dynamic during stress or illness. Tissue injury from surgery, trauma, or inflammatory states, such as infection, decrease responsiveness to insulin as part of the stress response. Under ideal circumstances, these effects are maximal 2 to 3 days after injury and resolve over the course of a week, but there is substantial variability. Besides stress, any other condition that increases counter-regulatory hormones such as glucagon, cortisol, and catecholamines decreases insulin sensitivity and increases insulin requirements. Cushing disease and pheochromocytoma are examples of conditions that cause insulin resistance. Several medications, including corticosteroids, thyroid replacement preparations, oral contraceptives, and thiazide diuretics also increase insulin resistance. In solid organ transplant recipients, steroids and the calcineurin inhibitors tacrolimus and cyclosporine have been associated with insulin resistance or onset diabetes. Exercise and ethanol can decrease insulin requirements.

Shah T, Kasravi A, Huang E, et al. Risk factors for development of new-onset diabetes mellitus after kidney transplantation. *Transplantation.* 2006;82:1673-1676. Tanaka T, Nabatame H, Tanifuji Y. Insulin secretion and glucose utilization are impaired under general anesthesia with sevoflurane as well as isoflurane in a concentration-independent manner. *J Anesth.* 2005;19:277-281.

Thorell A, Nygren J, Ljungqvist O. Insulin resistance: a marker of surgical stress. *Curr Opin Clin Nutr Metab Care.* 1999;2(1):69-78.

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A.8. What are the principles of management of diabetic ketoacidosis (DKA)?

A hyperglycemic patient should be assessed for DKA before surgery. Because DKA is associated with higher perioperative mortality, patients should be monitored for intravascular volume and electrolyte abnormalities.

Withholding insulin contributes to DKA. Infection or tissue injury exacerbates diabetes and sets off a chain of events that can result in DKA. Because of increased risk to the patient, DKA is corrected before surgery. When it is triggered by a surgical condition, time to correct it may be limited by the urgency of the surgery.

Patients with DKA have an anion gap metabolic acidosis in addition to hyperglycemia. Elevated serum ketone levels can help confirm the diagnosis, but urine ketones are frequently easier to assay. Commonly, a patient will be hypovolemic from polyuria and incomplete hydration, and resuscitation with isotonic fluids is appropriate. Lactate and acetate are converted to glucose by the liver, and this fact should be considered in selecting solutions for the initial resuscitation weighed against the risks of hyperchloremic acidosis. Ketosis is corrected with insulin, which is best as an intravenous infusion. Because glucose levels frequently normalize before ketosis clears, insulin therapy is continued even after hyperglycemia corrects. Dextrose is administered simultaneously to avoid hypoglycemia. During acidemia, hyperkalemia is common, resulting from shifts in body stores. However, a patient will frequently have a net potassium deficit. Hypokalemia during correction, which can reflect a deficit of up to

10 mEq potassium per kg body mass, should be treated aggressively. Likewise, hypocalcemia and hypomagnesemia should be anticipated and treated.

Kitabchi AE, Murphy MB, Spencer J, et al. Is a priming dose of insulin necessary in a low-dose insulin protocol for the treatment of diabetic ketoacidosis? *Diabetes Care.* 2008;31:2081-2085.

Kitabchi AE, Nyenwe EA. Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Endocrinol Metab Clin North Am.* 2006;35:725-751.

A.9. What is a hyperglycemic hyperosmolar state?

Any hyperglycemic patient should be evaluated for a hyperglycemic hyperosmolar state, another potentially fatal condition. The syndrome is more frequent in DM2. It includes hyperglycemia, hyperosmolarity, volume depletion, and changes in mental status. Adverse effects result from hyperosmolarity and hypovolemic shock. Glucose levels exceeding 1,000 mg per dL have been described. Mortality can be high. Glycosuria and inadequate fluid intake contribute to the condition. Treatment consists of fluid resuscitation and intravenous insulin to correct the hyperglycemia. Sodium, potassium, calcium, and magnesium levels should be evaluated and normalized.

Kitabchi AE, Nyenwe EA. Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Endocrinol Metab Clin North Am.* 2006;35:725-751.

B. Preoperative Evaluation and Preparation

B.1. How should this patient be evaluated?

The goals of preoperative evaluation are to stratify perioperative risk, ensure optimal management of concurrent illness, and screen for specific anesthetic-related problems. A diabetic patient is evaluated for cardiovascular disease, renal function, stiff joint syndrome, autonomic neuropathy, aspiration risk, and acute diabetic emergencies.

Both DM1 and DM2 increase the risk of coronary artery disease. The 2014 American College of Cardiology (ACC)/American Heart Association (AHA) Guideline on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery recommend the use of the Revised Cardiac Risk Index (RCRI). This index uses a history of diabetes, ischemic heart disease, heart failure, cerebrovascular disease, and renal insufficiency to predict perioperative cardiovascular risk. According to the 2014 guidelines, patients are triaged based on risk for major adverse cardiac events (MACE). The RCRI, the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) Surgical Risk Calculator, and the Myocardial Infarction and Cardiac Arrest (MICA) calculators are three tools to measure

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this risk. In the case of the RCRI, diabetes requiring insulin is one of six criteria used in the score. In the Surgical Risk Calculator, risk is calculated from a larger group of factors, including surgery type and a diagnosis of diabetes. The MICA calculator risk is calculated based on surgery type, American Society of Anesthesiologists patient classification, serum creatinine, and patient age. If MACE risk from these indices is greater than or equal to 1%, poor or unknown exercise tolerance and whether the results will change perioperative care determine the need for stress testing. A diagnosis of diabetes is thus a major factor for deciding whether to supplement a patient assessment preoperatively because of cardiovascular risk. Preoperative β-blocker therapy is recommended (level of evidence: B) in diabetic patients with two or more RCRI risk factors, although starting these agents on the day of surgery in patients who have never had the therapy is discouraged.

Optimizing the patient's medical status is a consideration for all patients but particularly for diabetics who have many comorbidities. Optimal management of coexisting hypertension and congestive heart failure can minimize perioperative risk. The decision to proceed or delay a procedure for medical management depends on the urgency of the surgery and the potential for improving the patient's medical condition.

Diabetes is a leading cause of renal insufficiency and failure. Because this patient already has an increased serum creatinine, she should be screened for renal insufficiency and any fluid and metabolic derangements should be corrected. A metabolic panel, including serum

creatinine, blood urea nitrogen, potassium, sodium, chloride, bicarbonate, and base deficit can be useful, especially because angiotensin mediators, β-blockers, and insulin itself can affect serum potassium levels. Joint stiffness is assessed with a comprehensive airway examination and the “prayer sign,” in which a patient's hands are placed against each other at the palmar surface to see whether the fingers touch. Other considerations in the diabetic include the risks of aspiration and autonomic instability. Although Hgb A_1C levels correlate with perioperative risk, the test does not add any information to the decision paradigm.

In addition to its chronic consequences, diabetes may produce a hyperglycemic hyperosmolar state and DKA. Both syndromes reflect severe metabolic abnormalities, most commonly infection. Because these syndromes may manifest as a result of a surgical emergency, patients with these conditions will present for perioperative management. Ideally, metabolic derangements should be corrected before anesthetic induction, but sometimes, patients must go to surgery urgently or emergently. Anesthesia providers should be prepared for hemodynamic instability, rapid fluid infusion, electrolyte repletion, and frequent monitoring of serum glucose and electrolytes. In both conditions, intravenous insulin infusion is indicated, titrated to normoglycemia in the hyperglycemic hyperosmolar state and the clearance of ketones in DKA. Supplemental dextrose is usually necessary to maintain insulin infusion in DKA.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management for patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2014;64:e77-e137.
Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation.* 1999;100(10):1043-1049.

B.2. How would the stiff joint syndrome affect her airway management?

The stiff joint syndrome is thought to result from glycation of connective tissue with chronic exposure to hyperglycemia. The range of motion may be reduced in the cervical spine, temporomandibular, and arytenoid joints, making endotracheal intubation difficult. As a screening tool, the prayer sign suggests the presence of joint stiffness. If the patient cannot completely oppose the palmar surface of her hands, she may also have reduced mobility in her glottic structures. Neck range of motion and oral aperture should be assessed; the prayer sign might suggest the need for a small endotracheal tube for a narrow glottis or difficult airway adjuncts.

Hogan K, Rusy D, Springman SR. Difficult laryngoscopy and diabetes mellitus. *Anesth Analg.* 1988;67: 1162-1165.
Salzarulo HH, Taylor LA. Diabetic “stiff joint syndrome” as a cause of difficult endotracheal intubation. *Anesthesiology.* 1986;64:366-368.

B.3. What are the signs and implications of autonomic neuropathy in the diabetic patient?

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Diabetic neuropathy involves both the peripheral and autonomic nervous system. In the autonomic system, gastric motility, heart rate, and vasomotor tone may be impaired. Cardiac ischemia can be asymptomatic. This patient is at risk for pulmonary aspiration of gastric contents and hemodynamic instability. A history will elicit early satiety, prolonged postprandial fullness, and significant reflux symptoms. Potential difficulties with mask ventilation and intubation are assessed. Heart rate variability, best seen on an electrocardiogram (ECG) tracing in response to deep breathing, Valsalva maneuver, or position changes, identifies patients at risk for hemodynamic instability. Preparation is made to control hemodynamic instability, especially because this patient is taking an angiotensin-converting enzyme inhibitor. Angiotensin-receptor blocking agents also increase the risk of postinduction hypotension. Because of a high likelihood of hemodynamic instability, the anesthesiologist should prepare to use slow titration of anesthetic agents, frequent blood pressure monitoring, and vasoactive agents, if necessary.

Huang CJ, Kuok CH, Kuo TB, et al. Pre-operative measurement of heart rate variability predicts hypotension during general anesthesia. *Acta Anaesthesiol Scand.* 2006;50:542-548.

B.4. How should this patient be prepared for anesthesia and surgery?

This patient's cardiovascular risk is elevated. Her RCRI puts her risk for MACE between 6% and 11%, but the NSQIP Surgical Risk Calculator puts it at 0.2%. If her exercise tolerance is below 4 metabolic equivalents (METs), about the equivalent of climbing a flight of stairs with a bag of groceries or performing heavy work around the house, noninvasive stress testing may be considered. Insulin therapy is given for hyperglycemia. Because of her elevated serum glucose, she is asked about polyuria, a sign that she might be dehydrated from hyperglycemic diuresis. DKA is unlikely because she has DM2, but a metabolic panel is indicated to rule out electrolyte abnormalities. An ECG may be indicated based on her risk factors for cardiovascular disease.

Her symptoms, consistent with gastroparesis and gastroesophageal reflux, will influence premedication and airway management. Results from a comprehensive airway examination, including assessment of neck and jaw mobility and a check for the prayer sign, affect anesthetic management decisions. A rapid sequence intubation could minimize aspiration risk but only if intubation is easy. If a difficult airway is suspected, awake intubation techniques should be considered.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management for patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2014;64:e77-e137.

B.5. For elective surgery, how are insulin and glucose requirements managed on the day of surgery?

The risk of hypoglycemia is balanced against the benefit of tight glycemic control. Anesthetized patients can have occult hypoglycemia, so serum glucose is checked frequently. Intravenous insulin is titrated for glycemic control. When administered intravenously, either as an infusion or as intermittent boluses, insulin has a fast onset and a short duration of action. Subcutaneous insulin, with longer lasting effects, is less predictable, especially during the hemodynamic changes of anesthesia and surgery. Subcutaneous insulin pumps should be turned down or off for all but the most minor procedures. Similarly, oral agents should be withheld on the day of surgery, except for minor procedures. Ideally, metformin should be withheld for 72 hours to minimize the risk of lactic acidosis.

Initial enthusiasm for tight glycemic control in critically ill patients has given way to a much more cautious approach. Perioperatively, hyperglycemia is associated with worsened neurologic and cardiac ischemia and poor wound healing. Even though tight control of serum glucose has been associated with better outcomes in some settings, there is risk associated with insulin therapy. Hypoglycemia is a serious risk, and insulin has multiple other effects that remain poorly described.

Evidence is limited to support glycemic control to a “normal” range of 80 to 110 mg per dL in the operating room. Higher targets minimize hypoglycemia. Levels higher than 180 mg per dL may cause protein glycation and osmotic diuresis. Targets within the range of 100 to 180 mg per dL are considered satisfactory.

Preoperative infusion of dextrose minimizes peripheral insulin resistance and reduces the risks of hypoglycemia. When dextrose causes hyperglycemia, the amount of insulin needed is increased. Given that insulin resistance and hyperglycemia are parts of the stress response to surgery, hyperglycemia may be a sign that exogenous carbohydrate

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infusion is not necessary.

Coursin DB, Connery LE, Ketzler JT. Perioperative diabetic and hyperglycemic management issues. *Crit Care Med.* 2004;32(4 suppl):S116-S125.

Lipshutz AK, Gropper MA. Perioperative glycemic control: an evidence based-review. *Anesthesiology.* 2009;110:408-421.

B.6. How should this patient be premedicated?

Concerns with premedication include sensitivity to sedatives and aspiration risk. Preexisting cardiovascular, cerebrovascular, and renal disease temper the aggressiveness of administration of benzodiazepines and opioids. Because of the symptoms of gastroesophageal reflux

and gastroparesis, histamine blockers, liquid antacids, or metoclopramide may be given. Metoclopramide, famotidine, and a liquid antacid like sodium citrate may minimize aspiration risk in this patient.

C. Intraoperative Management

C.1. What are the effects of anesthesia and surgery on insulin and glucose metabolism?

As part of the stress response to surgery, metabolism increases and resistance develops to the hypoglycemic effects of insulin. The response includes the mobilization of protein stores (mostly muscle), more hepatic gluconeogenesis, and greater breakdown and synthesis of triglycerides. Hormones, including catecholamines, cortisol, glucagon, and even insulin, contribute to the metabolic changes. Although glucose metabolism increases, so too does glucose production, adding to the risk of hyperglycemia. Administration of exogenous dextrose can exacerbate hyperglycemia in diabetic patients.

Anesthetic techniques influence metabolism but generally to a lesser extent than the stress from surgical injury. Techniques that mitigate stress hormones, such as neuraxial anesthesia, also may mitigate hyperglycemia. Some drugs affect regulatory hormones directly. Etomidate blocks cortisol synthesis. Benzodiazepines can decrease cortisol secretion. Halogenated agents have in vitro effects on insulin secretion. However, none of these effects impact postoperative glycemic control as much as will the surgery itself.

McAnulty GR, Robertshaw HJ, Hall GM. Anaesthetic management of patients with diabetes mellitus. *Br J Anaesth.* 2000;85(1):80-90.

C.2. What anesthetic techniques should be considered?

Factors other than glycemic control may influence the choice of anesthetic technique in the patient with diabetes. Regional techniques are chosen based on provider skill, patient preferences, and postoperative pain control. Techniques that speed the time to oral intake by reducing nausea or minimizing ileus make glycemic management easier postoperatively. For this reason, antiemetics and the spare use of opioids might be beneficial. Although not a contraindication to nerve blockade, peripheral neuropathy should be documented in a preoperative neurologic examination. Nerve injury from local anesthetics or abnormalities on neurologic examination may complicate postoperative management. Infection risk from regional techniques may be increased in patient with diabetes.

Sedated or anesthetized patients cannot complain of hypoglycemic symptoms the same way unsedated patients do. Serum glucose is monitored regularly in all but the shortest cases.

In this patient, general endotracheal anesthesia with precautions to prevent aspiration, intravenous insulin titrated to a serum glucose of less than 180 mg per dL, and frequent blood glucose monitoring is a satisfactory choice.

Ljungqvist O, Nygren J, Soop M, et al. Metabolic perioperative management: novel concepts. *Curr Opin Crit Care.* 2005;11:295-299. McAnulty GR, Robertshaw HJ, Hall GM. Anaesthetic management of patients with diabetes mellitus. *Br J Anaesth.* 2000;85(1):80-90.

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C.3. How should this patient be monitored?

If preoperative evaluation reveals a risk of hemodynamic instability, cardiac ischemia, or congestive heart failure, added cardiovascular monitoring should be considered, depending on the procedure. Peripheral vascular disease can complicate placement of an arterial catheter but is not a contraindication because in patients who have cardiovascular comorbidities, the benefits of monitoring outweigh the risks.

Frequent glucose monitoring is recommended in cases lasting longer than an hour or when hypoglycemic agents are being used. Serum glucose by finger stick or, ideally, venous or arterial sample should be measured at least every hour when giving intravenous insulin.

In this patient, pulse oximetry, continuous ECG monitoring, end-tidal carbon dioxide and gas analysis, and noninvasive blood pressure monitoring are satisfactory, if no further concerns arise from cardiovascular evaluation or surgical complexity.

McAnulty GR, Robertshaw HJ, Hall GM. Anaesthetic management of patients with diabetes mellitus. *Br J Anaesth.* 2000;85(1):80-90.

C.4. How is hyperglycemia treated intraoperatively?

The high end of a normal range for fasting serum glucose is 110 mg per dL; however, hyperglycemia in inpatients need not be treated until it reaches a higher level.

The one good agent for treating intraoperative hyperglycemia is intravenous insulin. Onset takes minutes, peak effect is achieved in 15 to 30 minutes, and duration of effect is less than an hour, facilitating titration. Insulin may be administered by continuous infusion or as intermittent boluses; the bolus consumes less lead time and eliminates the risk of pump misprogramming or malfunction. Subcutaneous insulin is less ideal for use during general anesthetics or complex procedures because variable peripheral blood flow will alter the uptake and duration of action. Most other therapies for DM2 are not fit for intraoperative use. Oral agents cannot be easily administered, are not reliably absorbed, and have too long a duration of action to be practical perioperatively. They may be taken on the day of surgery before minor procedures. In this case, sitagliptin should be discontinued to avoid hypoglycemia. Metformin, a biguanide, increases the risk of lactic acidosis during periods of hypoperfusion. Metformin is discontinued for 3 or more days before extensive procedures when a large-volume blood loss is possible.

Smiley DD, Umpierrez GE. Perioperative glucose control in the diabetic or nondiabetic patient. *South Med J.* 2006;99(6):580-589.

C.5. How is hypoglycemic shock recognized and treated intraoperatively?

Hypoglycemia can lead to tissue energy failure and has been associated with hemodynamic collapse and brain injury. Any patient receiving insulin, pramlintide, sitagliptin, or sulfonylureas is at risk for hypoglycemia. Because risk is usually known beforehand, hourly or more frequent monitoring of serum glucose should detect hypoglycemia. If glucose levels are low or decrease rapidly, the fastest treatment is a bolus of intravenous dextrose, 50% solution, administered slowly. In an emergency, one full ampule is the starting dose. In less urgent settings when the serum glucose level is low but not critical, smaller doses can be titrated to serum glucose values.

Dierdorf SF. Anesthesia for patients with diabetes mellitus. *Curr Opin Anaesthesiol.* 2002;15:351-357.

D. Postoperative Management

D.1. How is diabetes controlled in this patient postoperatively?

Unless there is a change in disease status as a consequence of surgery or preoperative care was inadequate, this patient should be transitioned back to her preoperative regimen. Before transitioning, she must recover from the stress response to the surgery. If this were a simple outpatient procedure, such as a cataract extraction, she could return home on her outpatient medication regimen. In this case, however, the effects of tissue injury may not peak for days; diabetes control is

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thus a dynamic challenge. Regular monitoring of glucose is required (at a minimum checks should be made every 6 hours).

She is monitored for hyperglycemia, and her nutrition regimen is adjusted to serum glucose measurements. Hourly glucose measurements and insulin infusion can control hyperglycemia. Most patients can be effectively managed with subcutaneous insulin and less frequent measurements. Insulin dose should take into account preoperative requirements, insulin resistance from the stress response, and caloric intake. Many patients receive intravenous dextrose postoperatively; if they are hyperglycemic on this regimen, dextrose is discontinued.

Oral diabetes medications can be reintroduced once the acute stress response begins to wane and the patient is cleared for a normal diet. Resumption of an oral diet can increase the risk of hyperglycemia, so ongoing monitoring is essential.

Smiley DD, Umpierrez GE. Perioperative glucose control in the diabetic or nondiabetic patient. *South Med J.* 2006;99(6):580-589.

D.2. Does diabetes increase perioperative risk?

Because patients with diabetes are at a greater risk of atherosclerosis, infection, autonomic and cardiovascular instability, and metabolic abnormalities than those without diabetes, perioperative risk is higher in this patient population. After surgery, the diabetic patient is monitored for hyperglycemia and hypoglycemia, ischemic complications, circulatory compromise, and wound and nosocomial infection. As a group, patients with diabetes have an increased risk for complications and poor outcomes from complications.

Lipshutz AK, Gropper MA. Perioperative glycemic control: an evidence-based review. *Anesthesiology.* 2009;110: 408-421.

D.3. What are the common postoperative complications to be expected in a diabetic patient?

Hyperglycemia and hypoglycemia, wound infections, and organ ischemia are the most common and worrisome postoperative complications in patients with diabetes. Following myocardial infarction or cerebrovascular accident, hyperglycemia is associated with a worse prognosis.

Smiley DD, Umpierrez GE. Perioperative glucose control in the diabetic or nondiabetic patient. *South Med J.* 2006;99(6):580-589.

D.4. Is it necessary to achieve tight perioperative control of glucose?

In the critical care setting, there is evidence for improved outcomes with tight glycemic control, variably defined as serum glucose between 80 and 120 mg per dL or higher; other evidence has shown no benefit or even harm. Some advocate for tight glycemic control in cardiac and noncardiac surgery. The risks of hypoglycemia and data from more recent studies have tempered the enthusiasm for tight glycemic control.

Potential benefits from tight glycemic control include improvement in metabolic, anti-inflammatory, organ, and circulatory function. Unfortunately, there is little evidence to suggest these benefits are substantial perioperatively. Unresolved issues are the best time for tight control, the goals of therapy, the effect of nutrition, and the magnitude and factors in the potential for significant hypoglycemia. The patient is transitioned to her preoperative level of control during recovery, and severe hyperglycemia is prevented by monitoring glucose closely. Glucose levels above 180 mg per dL increase the risk of protein glycation and osmotic diuresis; targeting serum glucose below this value makes physiologic sense.

Gandhi GY, Nuttall GA, Abel MD, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery: a randomized trial. *Ann Intern Med.* 2007;146:233-243.

NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med.* 2009;360:1283-1297.

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van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med.* 2001;345(19):1359-1367.

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Chapter 24
Transurethral Resection of the Prostate

Anuj Malhotra
Vinod Malhotra
Fun-Sun F. Yao

A 79-year-old man with benign prostatic hypertrophy was scheduled for transurethral resection of the prostate (TURP). His past medical history includes myocardial infarction (MI) 7 months ago requiring drug-eluting coronary stent placement and an implantable cardioverter-defibrillator (ICD) inserted for episodes of ventricular tachycardia. His current left ventricular ejection fraction is 25%. The patient is taking diuretics, a β-blocker, ticlopidine (an antiplatelet agent), aspirin, and an angiotensin-converting enzyme (ACE) inhibitor. Medical assessment advice was to continue platelet therapy for 1 year postcardiac stent.

A. Medical Disease and Differential Diagnosis

1. Are there differences in morbidity and mortality rates between TURP and suprapubic or retropubic prostatectomy?
2. What comorbidities are common in patients undergoing TURP?
3. Does a history of prior MI increase the patient's risk of perioperative reinfarction?
4. In patients with a history of recent MI, would you recommend that the surgery be postponed for a certain period? If so, why? If not, why not?

B. Preoperative Evaluation and Preparation

1. How would you evaluate the patient's cardiac condition? What additional tests would you have liked to order? Would you recommend that the patient undergo coronary angiography before surgery? Explain.
2. Are patients with a Q-wave infarction at greater risk of reinfarction than those with a non-Q-wave infarction? If so, why? If not, why not?
3. Would you discontinue any antihypertensives or any medications for angina? Why or why not?
4. For a patient with an ICD, what information should you know? What precautions should be taken?
5. What types of coronary stents are available? What is their perioperative relevance?
6. What is the conventional recommendation for antiplatelet therapy in a patient with previous percutaneous coronary intervention (PCI) undergoing noncardiac surgery?
7. What risk is associated with perioperative antiplatelet therapy?
8. How should patients with coronary stents undergoing noncardiac surgery be approached?

C. Intraoperative Management

1. What monitors would you use for this patient?
2. What anesthetic technique is preferable for patients undergoing TURP, and why?
3. Does regional anesthesia result in a lower incidence of perioperative mortality than general anesthesia? Whether yes or no, explain why or why not.
4. What intravenous fluid would you use during TURP?
5. Forty minutes after a sensory level of T10 was established with intrathecal anesthesia, and monopolar TURP resection was initiated with the use of glycine as the bladder irrigating solution, the patient becomes agitated and complains of nausea. Further sedation along with an antiemetic is administered. However, shortly thereafter, the patient becomes

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very restless, blood pressure rises, and heart rate decreases. The patient becomes cyanotic and obtunded, blood pressure precipitously falls, and pupils are dilated and unresponsive to light. What is the most likely cause of these signs and symptoms, and would these occur during bipolar or laser TURP resection?

6. What are the important characteristics of irrigation solutions used during TURP?
7. Why is plain distilled water rarely used for irrigation during TURP? What types of irrigation solutions are available?
8. What is the effect on body temperature of continuous bladder irrigation during TURP?
9. What is the definition of TURP syndrome? What are the signs and symptoms of the syndrome?
10. How can hyponatremia occur if the bladder irrigating fluid is not absorbed via the prostatic vessels?
11. How does the patient absorb irrigation solution during TURP? How much irrigation solution is typically absorbed?
12. How can one estimate the volume of irrigation solution absorbed during TURP?
13. What is the relation between the duration of surgery and the incidence of TURP syndrome?
14. What factors increase the incidence of TURP syndrome?
15. What is the effect on cardiopulmonary, renal, and central nervous system (CNS) functions of excessive absorption of irrigation solution during TURP?
16. What causes CNS dysfunction in patients who have undergone TURP?
17. What is the physiologic role of sodium ions in the body? What is the effect of excessive absorption of irrigation solution on serum sodium level?
18. What is the relation between serum sodium level and the incidence of neurologic symptoms in patients who have undergone TURP?
19. How does acute hyponatremia affect the cardiovascular system?
20. What prophylactic measures may reduce the incidence of TURP syndrome?
21. What therapeutic measures are recommended for patients with TURP syndrome?
22. Is normal saline administration always necessary to correct hyponatremia? Explain. What are the risks of rapidly correcting hyponatremia?
23. What are the toxic effects of glycine? Is there an antidote to glycine toxicity? What are the metabolic by-products of glycine?
24. What are the symptoms and clinical course of TURP-induced hyperammonemia?
25. Why do some patients who have undergone TURP develop hyperammonemia and others do not? Is there a preventive treatment for hyperammonemia in these patients?
26. What are the clinical characteristics, causes, and prognosis of TURP-related blindness?
27. What gynecologic procedure has been associated with a syndrome similar to TURP syndrome?

28. What are the causes of excessive bleeding during TURP?
29. What triggers disseminated intravascular coagulopathy in patients undergoing TURP? How would you treat it?
30. What are the causes, signs, symptoms, and treatment of bladder perforation during TURP?
31. What are the causes, signs, symptoms, and preventive measures for bladder explosion during TURP?
32. What are the causes of hypotension during TURP?

D. Postoperative Management

1. What is the source of postoperative bacteremia in patients who have undergone TURP? What factors increase the incidence of bacteremia?
2. What are the signs of post-TURP septicemia? What preventive measures are generally recommended?
3. What bacteria-related cause may possibly lead to sudden postoperative shock in patients who have undergone TURP?

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4. Is postoperative hypothermia a risk factor for myocardial ischemia?
5. How would you diagnose perioperative MI?

E. Comparing Monopolar, Bipolar, and Laser TURP

1. What differentiates monopolar from bipolar TURP?
2. Are decreased morbidity and mortality associated more closely with monopolar TURP or with bipolar TURP?
3. What differentiates the technologies for laser TURP?

F. Are There Preferred Anesthetic and Preferred Surgical TURP Techniques for This Patient?

A. Medical Disease and Differential Diagnosis

A.1. Are there differences in morbidity and mortality rates between TURP and suprapubic or retropubic prostatectomy?

Many anesthesiologists and urologists consider TURP to be a simpler and safer procedure than open prostatectomy; however, no differences have been reported in mortality rates between patients who have undergone monopolar TURP and those who have undergone retropubic or suprapubic prostatectomy. With recent advances in TURP, including bipolar and laser, the overall mortality has declined to 0.10%.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18:883-897. Reich O, Gratzke C, Bachmann A, et al. Morbidity, mortality, and early outcome of transurethral resection of the prostrate: a prospective multicenter evaluation of 10,654 patients. *J Urol.* 2008;180:246-249.

Roos NP, Wennberg JE, Malenka DJ, et al. Mortality and reoperation after open and transurethral resection of the prostate for benign prostatic hyperplasia. *N Engl J Med.* 1989;320:1120-1124.

A.2. What comorbidities are common in patients undergoing TURP?

TURP patients often are elderly and suffer from cardiac, pulmonary, vascular, and endocrine disorders. The incidence of cardiac disease is 67%; cardiovascular disease, 50%; abnormal electrocardiogram (ECG), 77%; chronic obstructive pulmonary disease, 29%; and diabetes mellitus, 8%. Occasionally, these patients are dehydrated and depleted of essential electrolytes because of long-term diuretic therapy and restricted fluid intake.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438-446.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18:883-897.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

A.3. Does a history of prior MI increase the patient's risk of perioperative reinfarction?

Yes, a history of prior MI or ischemic heart disease is considered an intermediate predictor of perioperative cardiac morbidity. Unstable coronary syndrome, severe angina, or recent MI indicates major clinical risks. Also see Chapter 14, section A.1.

A.4. In patients with a history of recent MI, would you recommend that the surgery be postponed for a certain period? If so, why? If not, why

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not?

An acute MI (7 days or less), or a recent MI (more than 7 days but less than or equal to 1 month), is considered an event requiring evaluation to determine if there is residual myocardium at risk. The stratification is based on the presentation of the disease; patients with active ischemia are at highest risk. Therefore, it is advocated to wait at least 6 weeks after an MI before elective surgery is performed, although no evidence supports this precaution. Also see Chapter 14, section A.7.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2014;130:e278-e333.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient's cardiac condition? What additional tests would you have liked to order? Would you recommend that the patient undergo coronary angiography before surgery? Explain.

The American College of Cardiology/American Heart Association guidelines suggest a stepwise approach that takes into account the clinical markers of cardiac risk, functional capacity, and surgery risk. The patient's medical history should focus on information about previous cardiac evaluations and interventions (coronary stent and automatic implantable cardioverter-defibrillator [AICD] placement). During physical examination of all organ systems, attention should be paid to the circulatory functions, especially in the presence of active cardiac conditions such as unstable coronary syndromes, decompensated congestive heart failure (CHF), significant arrhythmias, or severe valvular disease. The functional capacity of the patient is best evaluated by the activity history. Minimally, a routine ECG and chest radiograph should be obtained. If the patient presents signs and symptoms of CHF, angina, syncope, or arrhythmia, further cardiac testing should be considered if the results would impact the patient's management. Traditional indications for coronary angiography apply regardless of future surgical interventions. Also see Chapter 14, section B.1.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2014;130:e278-e333.

B.2. Are patients with a Q-wave infarction at greater risk of reinfarction than those with a non-Q-wave infarction? If so, why? If not, why not?

Studies suggest that patients who survive a non-Q-wave infarction are at greater risk of reinfarction than those who survive a Q-wave infarction.

Landesberg G. The pathophysiology of perioperative myocardial infarction: facts and perspectives. *J Cardiothorac Vasc Anesth.* 2003;17:90-100.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine.* 10th ed. Philadelphia, PA: WB Saunders; 2015:1227-1252.

Priebe HJ. Perioperative myocardial infarction—aetiology and prevention. *Br J Anaesth.* 2005;95:3-19.

B.3. Would you discontinue any antihypertensives or any medications for angina? Why or why not?

Antianginal agents and β-blockers should be continued until the day of the surgery to prevent rebound hypertension and tachycardia that may result from sudden withdrawal of these drugs. Patients taking ACE inhibitors or angiotensin II receptor antagonists might present intraoperative hypotension due to a decrease of intravascular volume. It has been suggested that ACE inhibitors or angiotensin II receptor antagonists be withheld on the day before surgery and restarted after adequate intravascular volume has been established in order to avoid renal dysfunction.

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Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2014;130:e278-e333.

B.4. For a patient with an ICD, what information should you know? What precautions should be taken?

Patients undergoing surgery with an ICD need to have the device interrogated prior to surgery. Recent and accurate information should be collected about the device's features, the date of insertion, and the indication for placement. On the day of surgery, the device should be assessed for settings, pacer dependency, baseline rhythm and rate, tachyarrhythmia history, effect of magnet, and battery status.

In the event of potential electromagnetic interference, the antitachycardia algorithm of the ICD should be turned off and external cardioversion paddles should be placed until the device is reset to its initial functions after the procedure. Also see Chapter 8, sections B and C.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pace makers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology.* 2011;114:247-261.

B.5. What types of coronary stents are available? What is their perioperative relevance?

PCI is a common procedure in the United States. Coronary stent placement was introduced in order to reduce the risk of thrombosis, dissection, and restenosis after angioplasty. Two types of coronary stents have been used: bare metal stents (BMS) and drug-eluting stents (DES). Two types of DES—sirolimus and paclitaxel-eluting stents—have been used extensively to reduce the neointimal hyperplasic reaction seen with the use of BMS, which is the main cause of restenosis. Evidence suggests that DES delay the endothelialization of coronary stent struts. Patients with DES are at risk for late thrombosis if the antiplatelet therapy is prematurely interrupted.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2014;130:2215-2245.

B.6. What is the conventional recommendation for antiplatelet therapy in a patient with previous percutaneous coronary intervention (PCI) undergoing noncardiac surgery?

Therapy with thienopyridines (ticlopidine or clopidogrel) and aspirin is recommended for 2 to 4 weeks after dilatation without stenting; elective surgery should be postponed for 2 to 4 weeks. After BMS, antiplatelet therapy for 4 to 6 weeks is recommended; elective surgery should be postponed for 4 to 6 weeks. After the implantation of DES, at least 12 months of antiplatelet therapy is required; elective surgery should be delayed for 12 months. Of note, newer DES may not require the same duration of dual therapy, and in these cases, consultation with the patient's cardiologist can help guide the timing of discontinuation. In patients with an indication for PCI and a projected need for surgery within the next 12 months, a balloon angioplasty or BMS may be considered. Daily aspirin should be continued during the

perioperative period. Continuation of aspirin is not a contraindication to neuraxial anesthesia. For more details, see Chapter 10, section A.5 and Figure 10.1 and Chapter 14, section A.8.

Abualsaud AO, Eisenberg MJ. Perioperative management of patients with drug-eluting stents. *JACC Cardiovasc Interv.* 2010;3:131-142.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American

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College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2014;130:2215-2245.

Narouze S, Benzon HT, Provenzano DA, et al. Interventional spine and pain procedures in patients on antiplatelet and anticoagulant medications: guidelines from the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society, and the World Institute of Pain. *Reg Anesth Pain Med.* 2015;40:182-212.

B.7. What risk is associated with perioperative antiplatelet therapy?

The results of studies on the risk of surgical bleeding with aspirin are inconsistent. In Burger's review and meta-analysis (aspirin withdrawal vs. low-dose aspirin), the low-dose group's relative risk of bleeding increased by a factor of 1.5, but there was no increase in bleeding complications or in perioperative mortality, with the possible exceptions of intracranial surgery and prostatectomy. Studies with ticlopidine or clopidogrel are also contradictory. Although some data support increased risk of major perioperative bleeding with dual-antiplatelet therapy (0.4% to 1%), there is no consensus regarding withholding thienopyridines. The risk of perioperative bleeding must be balanced against protection from a coronary event.

Burger W, Chemnitius JM, Kneissl GD, et al. Low-dose aspirin for secondary cardiovascular prevention—cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation—review and meta-analysis. *J Intern Med.* 2005;257(5):399-414.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2014;130:2215-2245.

B.8. How should patients with coronary stents undergoing noncardiac surgery be approached?

The preoperative evaluation of patients with coronary stents should include information regarding the date of stent placement, the coronary anatomy before the intervention, the type of coronary stent, the localization of the intervention, complications (if any) during the procedure, the residual anatomy after the intervention (e.g., possibility of incomplete revascularization), and the antiplatelet strategy. Multidisciplinary discussions regarding how the risk of bleeding compares with the risk of coronary stent thrombosis are strongly encouraged. The most recently published *Practice Alert* indicates, “Elective surgery with a significant risk of bleeding should be postponed until the recommended course of thienopyridine therapy has been completed.” If surgery must be performed and if thienopyridine therapy must be interrupted (surgery with high risk of perioperative bleeding), aspirin should be continued and thienopyridine should be readministered as soon as possible after the procedure. Bridge therapies have been proposed for patients who undergo surgical procedures, but this practice has not been shown to reduce the risk of thrombosis. Currently, continuing double antiplatelet therapy is recommended in patients with DES for surgery with minor or intermediate risk of perioperative bleeding. A careful “case-by-case” consideration is advisable. Discussion between the anesthesiologist, the surgeon, and the treating cardiologist is recommended. For more details, see Chapter 10, section A.5 and Figure 10.1.

Abualsaud AO, Eisenberg MJ. Perioperative management of patients with drug-eluting stents. *JACC Cardiovasc Interv.* 2010;3:131-142.

Caplan RA, Connis RT, Nickinovich DG, et al. Practice alert for the perioperative management of patients with coronary artery stents: A report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology.* 2009;100(1):22-23.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American

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College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2014;130:2215-2245.

C. Intraoperative Management

C.1. What monitors would you use for this patient?

The following monitors would be used for this patient:

- American Society of Anesthesiologists standard monitors, including multiple-lead ST-segment analysis
- Temperature
- Consider direct arterial blood pressure.
- Consider transthoracic echocardiography, if necessary.

C.2. What anesthetic technique is preferable for patients undergoing TURP, and why?

Regional anesthesia has advantages for patients undergoing monopolar electrode TURP for the following reasons:

- It allows monitoring of the patient's mentation, thereby facilitating early detection of signs of TURP syndrome.
- It can allow for earlier detection of prostate capsular tears or bladder perforation via patient reports of peritoneal or diaphragmatic (shoulder) pain, provided spinal level is below T10.
- It promotes vasodilation and peripheral pooling of blood, thereby reducing the severity of circulatory overloading.
- It reduces blood loss by lowering arterial and venous blood pressure during surgery.
- It provides postoperative analgesia, thereby reducing the incidence of postoperative hypertension and tachycardia, which often accompanies recovery from general anesthesia.
- Currently, less emphasis is placed on regional anesthesia (vs. general anesthesia) for TURP because of the increased use of bipolar electrode and laser resection surgical techniques.
- Regional anesthesia may not be a safe option in an anticoagulated patient.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18:883-897.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

O'Donnell AM, Foo ITH. Anaesthesia for transurethral resection of the prostrate. *Contin Educ Anaesth Crit Care Pain.* 2009;9(3):92-96.

C.3. Does regional anesthesia result in a lower incidence of perioperative mortality than general anesthesia? Whether yes or no, explain why or why not.

Although spinal anesthesia offers distinct advantages over general anesthesia for TURP surgery, mortality and many markers of patient outcome have been similar for both groups. The 30-day mortality rate associated with TURP has steadily declined from 2.5% in 1962 to 0.10% in 2003. Mortality rates are reported to be similar in patients receiving regional anesthesia or general anesthesia. Increased morbidity was found in patients with resections exceeding 90 minutes, gland size greater than 45 g, acute urinary retention, and age older than 80 years. The incidence of postoperative complications, specifically MI, pulmonary embolism, cerebrovascular accidents, transient ischemic attacks, renal failure, hepatic insufficiency, and the need for prolonged ventilation, is similar in patients receiving regional anesthesia and those receiving general anesthesia. More recently, with the use of laser TURP resection surgical techniques, less emphasis has been placed on regional anesthesia as the preferred anesthetic technique given minimal absorption of irrigating fluid.

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Hanson RA, Zornow MH, Conlin MJ, et al. Laser resection of the prostate: implications for anesthesia. *Anesth Analg.* 2007;105:475-479.

Hawary A, Mukhtar K, Sinclair A, et al. Transurethral resection of the prostate syndrome: almost gone but not forgotten. *J Endourol.* 2009;23:2013-2020.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

Wasson JH, Bubolz TA, Lu-Yao GL, et al. Transurethral resection of the prostate among medicare beneficiaries: 1984 to 1997. For the Patient Outcomes Research Team for Prostatic Diseases. *J Urol.* 2000;164:1212-1215.

C.4. What intravenous fluid would you use during TURP?

Because dilutional hyponatremia commonly occurs in patients undergoing monopolar electrode TURP, the intravenous fluid of choice perioperatively is normal saline that contains sodium, 154 mEq per L. It is important to remember, however, that circulatory overloading from absorbed irrigant is common in patients who have undergone monopolar or bipolar electrode TURP (but not laser TURP); therefore, the amount of intravenous fluid administered during surgery should be carefully monitored.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.5. Forty minutes after a sensory level of T10 was established with intrathecal anesthesia, and monopolar TURP resection was initiated with the use of glycine as the bladder irrigating solution, the patient becomes agitated and complains of nausea. Further sedation along with an antiemetic is administered. However, shortly thereafter, the patient becomes very restless, blood pressure rises, and heart rate decreases. The patient becomes cyanotic and obtunded, blood pressure precipitously falls, and pupils are dilated and unresponsive to light. What is the most likely cause of these signs and symptoms, and would these occur during bipolar or laser TURP resection?

Restlessness and incoherence during TURP are particularly ominous signs of TURP syndrome. These are often caused by subtle pulmonary edema, hypoxemia, and cerebral edema. These signs must not be misinterpreted as signs of inadequate anesthesia. The administration of sedatives or general anesthesia in the presence of TURP syndrome is often fraught with severe complications, even death. In bipolar and laser TURP, normal saline can be used as the bladder irrigating solution and hyponatremia is not expected. In bipolar TURP, absorption of the intravascular bladder irrigating solution can occur via the prostatic venous sinuses but is not expected in laser TURP as the treatment zone is rapidly coagulated.

Chen Q, Zhang L, Fan QL, et al. Bipolar transurethral resection in saline vs traditional monopolar resection of the prostate: results of a randomized trial with a 2-year follow-up. *BJU Int.* 2010;106(9):1339-1343.

Geavlete B, Multescu R, Dragutescu M, et al. Transurethral resection (TUR) in saline plasma vaporization of the prostate vs standard TUR of the prostate: 'the better choice' in benign prostatic hyperplasia? *BJU Int.* 2010;106(11):1695-1699.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438-446.

O'Hara J. Anesthesia for select urologic procedures. In: *ASA Refresher Courses in Anesthesiology.*

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2011;39(1):115-119.

C.6. What are the important characteristics of irrigation solutions used during TURP?

Ideal TURP irrigation solutions are either isotonic or nearly isotonic, electrically inert, nontoxic, and transparent. Electrolyte-containing solutions are avoided in monopolar electrode TURP because they can conduct electrical current to surrounding tissues and cause burns. Because significant absorption of bladder irrigating solution can occur during TURP, only solutions with nontoxic solutes are used. The solution must be transparent to allow the surgeon to visualize the surgical site. If intravascular hypotonic bladder irrigating solution is absorbed, absorption can lead to hyponatremia, hypoosmolality, and, in severe cases, hemolysis. These complications are avoided when normal saline is used with bipolar electrode and laser resection TURP.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438-446.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.7. Why is plain distilled water rarely used for irrigation during TURP? What types of irrigation solutions are available?

Although distilled water is totally transparent and electrically inert and was regularly used decades ago for irrigation during monopolar TURP, it is extremely hypotonic. Therefore, when it is absorbed, it may cause hemolysis, shock, and renal failure.

Over the years, a number of isotonic and nearly isotonic irrigation solutions have been introduced and they have almost totally replaced plain distilled water. The most commonly used solution currently is glycine (1.2% and 1.5%). Mannitol (3%), glucose (2.5% to 4%), Cytal (a mixture of sorbitol 2.7% and mannitol 0.54%), and urea (1%) solutions are also occasionally used. For maintenance of their transparency, these solutions are purposely prepared moderately hypotonic. Sterile water and glycine have been used as the bladder irrigation solution in laser resection TURP because they are minimally absorbed, but TURP syndrome has been reported when bladder perforation or urethral trauma occurred.

Dilger JA, Walsh MT, Warner ME, et al. Urethral injury during potassium-titanyl-phosphate laser prostatectomy complicated by transurethral resection syndrome. *Anesth Analg.* 2008;107:1438-1440.

Farag E, Baccala AA Jr, Doutt RF, et al. Laser bladder perforation from photoselective vaporization of prostate resulting in rhabdomyolysis induced acute renal failure. *Minerva Anesthesiol.* 2008;74:277-280.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.8. What is the effect on body temperature of continuous bladder irrigation during TURP?

Several liters of irrigation solution pass through the bladder during TURP. This can reduce body temperature at the rate of 1°C per hour (Fig. 24.1). Approximately half of patients undergoing TURP become hypothermic and shiver at the conclusion of surgery.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

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C.9. What is the definition of TURP syndrome? What are the signs and symptoms of the syndrome?

Rapid absorption of a large-volume, hypotonic bladder irrigation solution during TURP can lead to TURP syndrome. TURP syndrome is characterized by intravascular volume shifts and plasma-solute (osmolarity) effects. The signs and symptoms of TURP syndrome are as follows:

Cardiopulmonary

Hypertension

Bradycardia

Dysrhythmia

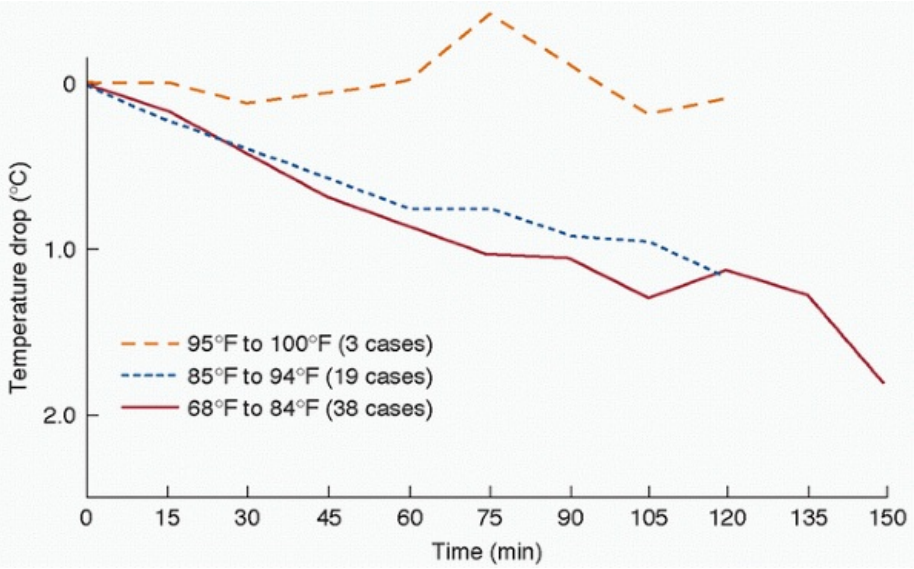


FIGURE 24.1 The decrease in body temperature during transurethral resection of the prostate (TURP) is related to the temperature of the irrigating solution and to the duration of surgery. (Modified from Allen TD. Body temperature changes during prostatic resection as related to the temperature of the irrigating solution. *J Urol*. 1973;110:433-535, with permission.)

Respiratory distress

Cyanosis

Hypotension

Shock

Death

Hematologic and renal

Hyperglycinemia

Hyperammonemia

Hyponatremia

Hypoosmolality

Hemolysis/anemia

Acute renal failure

Death

Central nervous system

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Nausea/vomiting

Confusion/restlessness

Blindness

Twitches/seizures

Lethargy/paralysis

Dilated/nonreactive pupils

Coma

Death

TURP syndrome can occur as early as 15 minutes after surgery has started and as late as 24 hours after surgery. Patient complaints of dizziness, headache, nausea, chest or throat tightness, and shortness of breath are often early clinical signs. Then the patient becomes restless, confused, and starts to retch. Some patients complain of abdominal pain. The blood pressure often rises (both systolic and diastolic), and the heart rate decreases (Fig. 24.2). If not treated promptly, the patient becomes cyanotic and hypotensive and ultimately sustains cardiac arrest.

Occasionally, TURP syndrome manifests as neurologic signs. The patient becomes lethargic and then unconscious, and pupils dilate, reacting sluggishly to light. These signs may be followed by short episodes of tonic-clonic seizures and then coma lasting from minutes to hours.

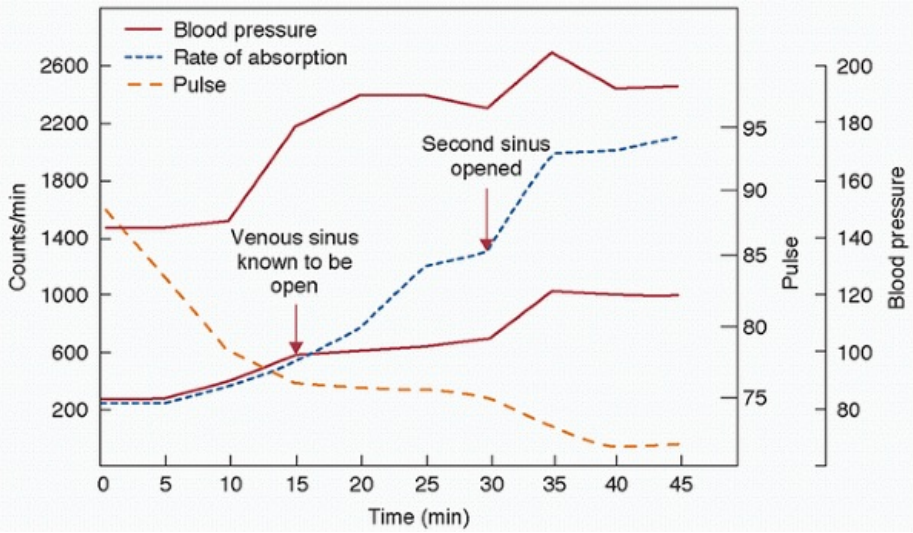


FIGURE 24.2 The blood pressure, heart rate, and absorption rate of radioactively tagged irrigation solution during transurethral resection of the prostate. (Modified from Taylor RO, Maxson ES, Carter FH, et al. Volumetric gravimetric and radioisotopic determination of fluid transfer in transurethral prostatectomy. *J Urol.* 1958;79:490-499, with permission.)

If the patient is under general anesthesia, the presenting signs of TURP syndrome are typically a rise and then a fall in blood pressure, decreasing oxygen saturation, and severe refractory bradycardia. The ECG may show nodal rhythm, ST-segment changes, U waves, and widening of the QRS complex. Recovery from general anesthesia is usually delayed.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438-446.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

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C.10. How can hyponatremia occur if the bladder irrigating fluid is not absorbed via the prostatic vessels?

If the complication of bladder perforation occurs, significant accumulation of irrigating fluid in the intraperitoneal or retroperitoneal space can occur, resulting in significant intravascular absorption of a hypotonic irrigating solution and ultimately hyponatremia syndrome.

Dorotta I, Basali A, Ritchey M, et al. Transurethral resection syndrome after bladder perforation. *Anesth Analg.* 2003;97:1536-1538.

C.11. How does the patient absorb irrigation solution during TURP? How much irrigation solution is typically absorbed?

The bladder irrigation solution enters the bloodstream directly through open prostatic venous sinuses created during monopolar and bipolar resection techniques, and it accumulates in the periprostatic and retroperitoneal spaces. The latter accumulation occurs primarily when the prostatic capsule is violated during surgery.

Reports in the literature suggest that as many as 8 L of irrigation solution can be absorbed by the patient during TURP. The average rate of absorption is 20 mL per minute and may reach 200 mL per minute; the average weight gain by the end of surgery is 2 kg (Fig. 24.3). A very thin resection “zone” combined with a coagulating benefit during laser TURP prevents significant opening of the prostatic venous sinuses and absorption of the irrigating solution.

Geavlete B, Multescu R, Dragutescu M, et al. Transurethral resection (TUR) in saline plasma vaporization of the prostate vs standard TUR of the prostate: ‘the better choice’ in benign prostatic hyperplasia? *BJU Int.* 2010;106(11):1695-1699.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

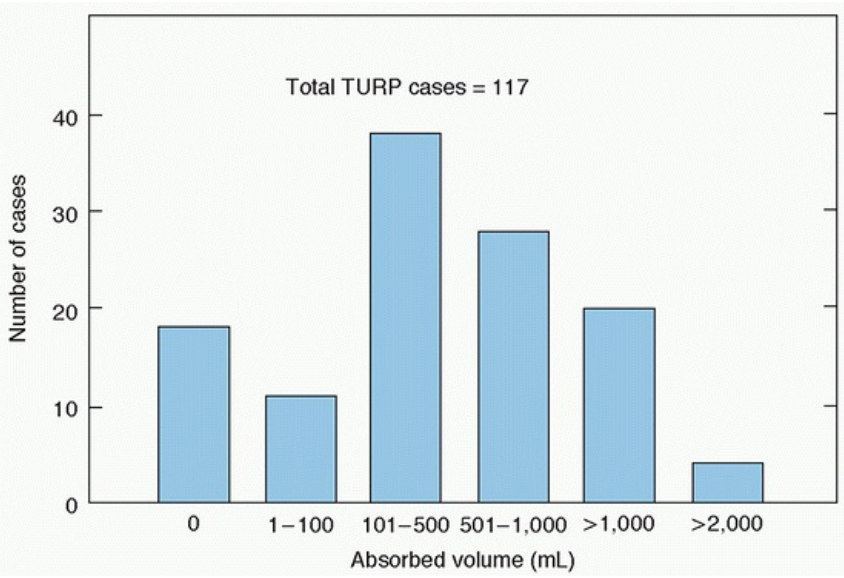


FIGURE 24.3 The volume of irrigation solution absorbed during transurethral resection of the prostate (TURP). (Modified from Madsen PO, Madsen RE. Clinical and experimental evaluation of different irrigating fluids for transurethral surgery. *Invest Urol.* 1965;3:122-129, with permission.)

C.12. How can one estimate the volume of irrigation solution absorbed during TURP?

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A practical method for estimating the absorbed volume of irrigation solution during TURP is based on the following equation:

$$\text{Volume absorbed} = \frac{\text{preoperative } [Na^+]}{\text{postoperative } [Na^+]} \times \text{extracellular fluid} - \text{extracellular fluid}$$

To use this equation, serum sodium level (Na^+) is determined at the beginning of surgery and again at the time when the volume absorbed is estimated. The extracellular fluid (ECF) volume is assumed to be 20% to 30% of body weight. For example, if the patient's preoperative body weight is 60 kg and the ECF is assumed to constitute 20% of the patient's body weight, then a decrease in serum sodium level from 140 to 100 mEq per L would suggest an absorption of 4.8 L:

140/100 × ECF - ECF = 1.4 ECF - ECF = 0.4 ECF = 0.4 × 60 × 20% = 4.8 L

Henderson DJ, Middleton RG. Coma from hyponatremia following transurethral resection of prostate. *Urology.* 1980;15:267-271.

Piros D, Fagerström T, Collins JW, et al. Glucose as a marker of fluid absorption in bipolar transurethral surgery. *Anesth Analg.* 2009;109:1850-1855.

C.13. What is the relation between the duration of surgery and the incidence of TURP syndrome?

Many believe that the duration of surgery is the most important determinant in the incidence of TURP syndrome. However, several studies report severe TURP syndrome occurring as early as 15 to 20 minutes after surgery has started. In general, a poor correlation has been observed between the duration of surgery and the amount of irrigation solution absorbed. In a large series, morbidity and mortality of patients undergoing TURP did not correlate with length of surgery, except when surgery lasted more than 150 minutes. Similarly, the incidence and severity of hyponatremia did not correlate with the duration of surgery.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.14. What factors increase the incidence of TURP syndrome?

TURP syndrome is more likely to occur if the prostatic gland is atypically large, the prostatic capsule is violated during surgery, or the hydrostatic pressure of the irrigation solution is excessively high. Large prostatic glands have rich venous networks that promote intravascular absorption of irrigation solution. The violation of the prostatic capsule during surgery promotes entry of irrigation solution into the periprostatic and retroperitoneal spaces. The hydrostatic pressure of the irrigation solution is an important determinant of the rate at which the patient will absorb the solution. This pressure depends primarily on the height of the irrigation solution pole. When the height of the pole exceeds 60 cm (˜2 ft), the absorption of irrigation solution is greatly enhanced. Also, an excessively distended bladder during surgery facilitates absorption.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438-446.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.15. What is the effect on cardiopulmonary, renal, and central nervous system (CNS) functions of excessive absorption of irrigation solution during TURP?

Excessive absorption of irrigation solution during TURP causes hypervolemia and hypertension and may induce angina and pulmonary edema (Fig. 24.4). It may also have an adverse effect on renal function. An inverse relation has been observed between the amount of irrigation solution absorbed during surgery and postoperative urinary output.

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Some patients with TURP syndrome exhibit neurologic signs resulting from water intoxication. They assume a decerebrate posture, exhibit clonus and positive Babinski reflex, and

eventually convulse and lapse into coma. Examination of the eyes reveals papilledema and dilated and sluggishly reacting pupils. The electroencephalogram shows low voltage bilaterally. The patients may remain in a coma from a few hours to several days.

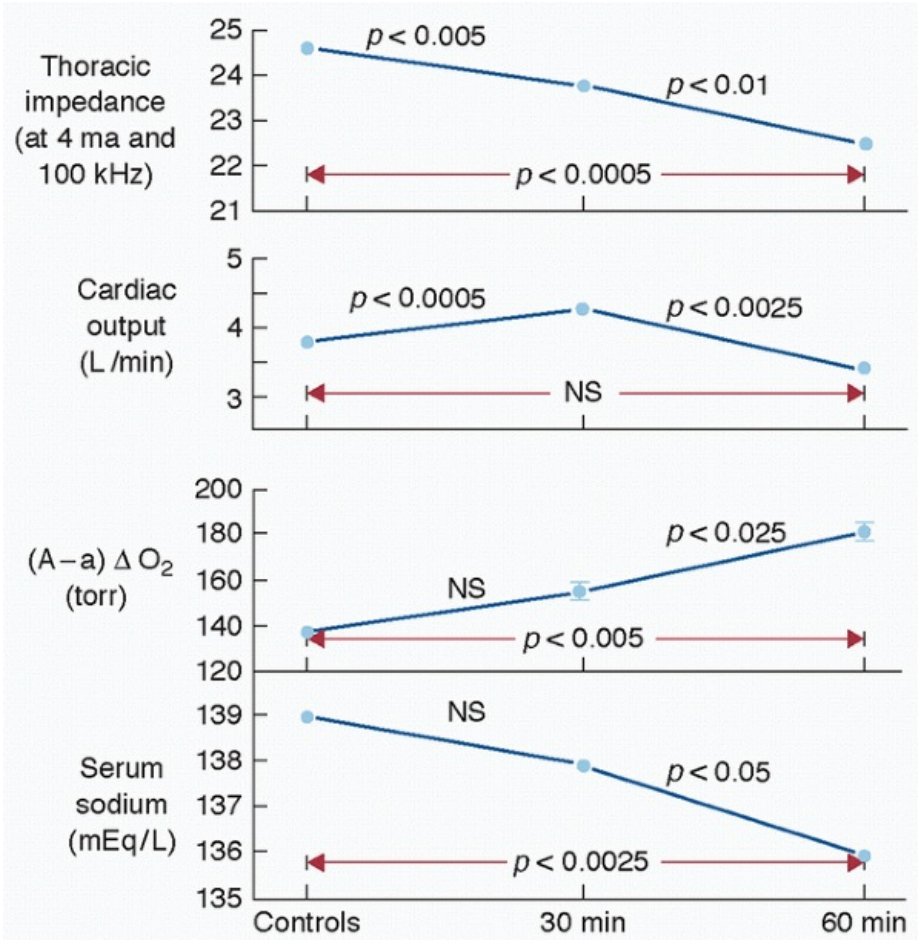


FIGURE 24.4 Mean changes in thoracic impedance, cardiac output, alveolar-arterial oxygen tension difference, and serum sodium level during transurethral resection of the prostate. NS, nonsignificant. (Modified from Casthely P, Ramanathan S, Chalon J, et al. Decreases in electric impedance during transurethral resection of the prostate: an index of early water intoxication. *J Urol.* 1981;125:347-349, with permission.)

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438-446.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.16. What causes CNS dysfunction in patients who have undergone TURP?

The crucial physiologic derangement of CNS function is not hyponatremia but acute hypoosmolality, which is predictable because the blood-brain barrier is essentially impermeable to sodium but freely permeable to water. Cerebral edema caused by acute hypoosmolality can increase intracranial pressure, which results in bradycardia and hypertension by the Cushing reflex. Furthermore, cerebral edema is not caused by decreased serum colloid oncotic pressure but by decreased osmolality. The hypervolemia and hyponatremia that often accompany TURP promote cerebral edema and this in turn raises intracranial pressure and induces neurologic symptoms. The rise in intracranial pressure is directly

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correlated to the gain in body weight during TURP.

Fujiwara A, Nakahira J, Sawai T, et al. Prediction of clinical manifestations of transurethral resection syndrome by preoperative ultrasonographic estimation of prostate weight. *BMC Urol.* 2014;14:67.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438-446.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.17. What is the physiologic role of sodium ions in the body? What is the effect of excessive absorption of irrigation solution on serum sodium level?

Sodium is a ubiquitous electrolyte that is essential for proper function of excitatory cells, particularly those of the heart and brain. Extreme reduction in serum sodium level alters brain, cardiac, and renal functions.

During monopolar TURP, serum sodium level typically falls 3 to 10 mEq per L. However, the correlation between the severity of hyponatremia and the amount of irrigation solution absorbed during surgery is inconsistent. The fall in serum sodium level apparently depends primarily on the rate at which the irrigation solution is absorbed rather than on the total amount absorbed.

Fujiwara A, Nakahira J, Sawai T, et al. Prediction of clinical manifestations of transurethral resection syndrome by preoperative ultrasonographic estimation of prostate weight. *BMC Urol.* 2014;14:67.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.18. What is the relation between serum sodium level and the incidence of neurologic symptoms in patients who have undergone TURP?

Acute severe hyponatremia is often associated with abnormal neurologic symptoms, and it can lead to irreversible brain damage. The neurologic signs may be accompanied by electroencephalogram abnormalities such as loss of α-wave activity and irregular discharge of high-amplitude slow-wave activity. However, the correlation between the severity of the hyponatremia and the incidence of neurologic symptoms is inconsistent because hyponatremia may not be the sole or even primary cause of the neurologic manifestations of TURP syndrome. The crucial derangement of CNS function is not hyponatremia but acute hyposmolarity. In some cases, moderate hyponatremia is associated with severe neurologic symptoms; in others, severe hyponatremia manifests no symptoms at all. Below 120 mEq per L, however, patients are almost always symptomatic. The primary factor governing the manifestation of symptoms is the rate at which the serum sodium level falls rather than the total fall itself; the faster the fall in serum sodium level, the greater the incidence of neurologic symptoms.

Blanshard H, Bennett D. TURP syndrome. In: Allman KG, McIndoe AK, Wilson IH, eds. *Emergencies in Anaesthesia.* Oxford: Oxford University Press; 2006:270-271.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.19. How does acute hyponatremia affect the cardiovascular system?

When serum sodium level falls to less than 120 mEq per L, signs of cardiovascular depression can occur. A decrease of less than 115 mEq per L causes bradycardia, widening of the QRS complex, ST-segment elevation, ventricular ectopic

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beats, and T-wave inversion. Patients with a serum sodium level of less than 110 mEq per L can develop respiratory and cardiac arrest.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.20. What prophylactic measures may reduce the incidence of TURP syndrome?

The incidence of TURP syndrome depends primarily on the surgeon's technical skills. However, if the patient is properly prepared before surgery and closely monitored during surgery, the incidence and severity of the syndrome can be reduced.

Fluid and electrolyte imbalance should be corrected preoperatively, and special attention should be paid to the serum sodium especially in traditional monopolar electrode TURP. Patients with preoperative CHF should be treated vigorously with diuretics and fluid restriction. A conservative surgical approach should be considered for critically ill patients. A simple canalization or balloon dilation of the urethra or a staged TURP is less likely to induce TURP syndrome.

The most important preventive measure during surgery is preservation of the prostatic capsule. Another preventive measure is restriction of the hydrostatic pressure of the irrigation solution to 60 cm H_2O. This can be accomplished by maintaining the height of the irrigation pole to 60 cm (˜2 ft) above patient level. Also, the bladder should not be allowed to overdistend and the duration of surgery should be restricted.

Serial serum sodium and osmolality are advisable in order to detect a decreasing trend. If clinical signs of TURP syndrome present, the surgeon should be informed and therapeutic measures immediately instituted. If serum sodium level approaches 120 mEq per L, surgery should be terminated as soon as possible.

Intravenous fluids should be cautiously administered during TURP. A microdrip is recommended particularly for patients with cardiac or renal disease. If regional anesthesia causes hypotension, a small dose of a vasoconstrictor is recommended to raise the blood pressure rather than rapid infusion of intravenous fluids.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

Watkins-Pitchford JM, Payne SR, Rennie CD, et al. Hyponatremia during transurethral resection—its practical prevention. *Br J Urol.* 1984;56:676-678.

C.21. What therapeutic measures are recommended for patients with TURP syndrome?

When symptoms of TURP syndrome appear, the following therapeutic measures are recommended:

- Terminate surgery as soon as possible.
- Administer furosemide, 20 to 40 mg intravenously. Although furosemide results in natriuresis, this effect is negligible relative to the desired acute diuresis and volume offloading of free water.
- Administer oxygen by nasal cannula or face mask to maintain oxygen saturation and consider intubation.
- Obtain arterial blood gas, serum osmolality, and sodium analysis.
- If the serum sodium level is abnormally low and clinical signs of hyponatremia are evident, intravenous administration of hypertonic saline (3% to 5%) may be recommended. The hypertonic solution should be given at a rate no faster than 100 mL per hour. In most cases, no more than 300 mL of saline is needed to correct the hyponatremia.
- If the patient develops seizures, a short-acting anticonvulsant such as diazepam (5 to 20 mg) or midazolam (2 to 10 mg) can be administered intravenously. If these drugs do not arrest the seizures, a barbiturate or phenytoin can be added. As a last resort, a muscle relaxant may also be used.
- If pulmonary edema or hypotension develops, invasive hemodynamic monitoring is recommended. This will serve as a

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guide for pharmacologic support and fluid administration.

- If significant blood loss is suspected, the administration of packed red blood cells should be considered. In general, intravenous fluids should be administered cautiously because of the propensity of these patients to develop pulmonary edema.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18:883-897. Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.22. Is normal saline administration always necessary to correct hyponatremia? Explain. What are the risks of rapidly correcting hyponatremia?

The administration of hypertonic saline to correct hyponatremia is not always necessary and sometimes can be detrimental. Unless the patient develops clinical signs of hyponatremia, saline administration is not recommended. Spontaneous or induced diuresis usually corrects the hyponatremia within a few hours.

Patients who have undergone TURP often sustain circulatory overloading during surgery; consequently, saline administration in these patients can induce pulmonary edema. In addition, rapid administration of hypertonic saline has been associated with central pontine

myelinolysis (osmotic demyelination syndrome)—a poorly understood and fatal neurologic complication.

To reduce the hazards of saline administration, serum osmolarity should be monitored and corrected aggressively only until symptoms substantially subside; then, hyponatremia should be corrected at a rate no faster than 1.5 mEq/L/hr.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438-446.

O'Donnell AM, Foo ITH. Anaesthesia for transurethral resection of the prostrate. *Contin Educ Anaesth Crit Care Pain.* 2009;9(3):92-96.

Rothenberg DM, Berns AS, Ivankovich AD. Isotonic hyponatremia following transurethral prostate resection. *J Clin Anesth.* 1990;2:48-53.

Sterns RH, Riggs JE, Schochet SS Jr. Osmotic demyelinization syndrome following correction of hyponatremia. *N Engl J Med.* 1986;314:1535-1542.

C.23. What are the toxic effects of glycine? Is there an antidote to glycine toxicity? What are the metabolic by-products of glycine?

Glycine is an inhibitory neurotransmitter similar to γ-aminobutyric acid in the spinal cord and brain. When absorbed by the patient in large amounts, glycine has direct toxic effects on the heart and retina. In patients who have undergone TURP with glycine absorption, it has been shown to cause an average decrease of 17.5% in cardiac output. In animal studies, the administration of the amino acid arginine reversed the myocardial depressing effect of glycine. The mechanism by which glycine depresses cardiac function and the mechanism by which arginine protects the heart is unknown.

Hyperglycinemia may cause transient visual disturbance (blindness) during TURP. However, glycine toxicity in patients who have undergone TURP is uncommon, probably because most of the absorbed glycine is retained in the periprostatic and retroperitoneal spaces, where access to the circulation is limited.

The most common metabolites of glycine are ammonia and glyoxylic and oxalic acids (Fig. 24.5). In some patients, excessive absorption of glycine during TURP leads to hyperammonemia. Hyperoxaluria could compromise renal function in patients with coexisting renal disease, which is often present in elderly patients undergoing TURP.

Glycine may cause encephalopathy and seizures through its ability to potentiate the effects of *N*-methyl-D-aspartate, an excitatory neurotransmitter. Magnesium exerts a negative control on the *N*-methyl-D-aspartate receptor, and

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the susceptibility to seizures. For this reason, a trial of magnesium therapy may be indicated in patients who develop seizures during TURP.

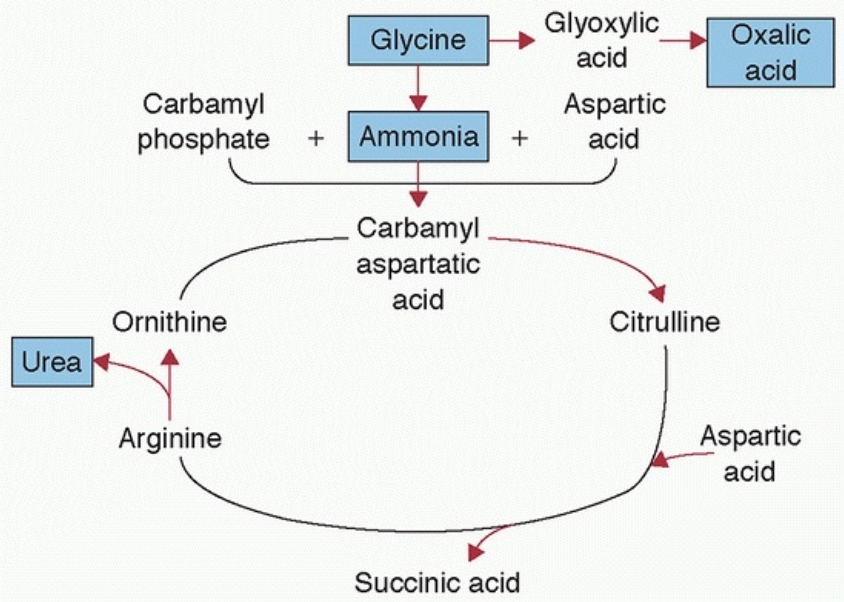


FIGURE 24.5 Metabolic pathways of glycine. (Modified from McGilvery RW, Goldstein GW. *Biochemistry: A Functional Approach.* 3rd ed. Philadelphia, PA: WB Saunders; 1983:584, with permission.)

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

Ovassapian A, Joshi CW, Brunner EA. Visual disturbances: an unusual symptom of transurethral prostatic resection reaction. *Anesthesiology.* 1982;57:332-334.

Wang JM, Wong KC, Creel DJ, et al. Effects of glycine on hemodynamic responses and visual evoked potentials in the dog. *Anesth Analg.* 1985;64:1071-1077.

C.24. What are the symptoms and clinical course of TURP-induced hyperammonemia?

The signs and symptoms of hyperammonemia usually appear within 1 hour of surgery. Typically, the patient becomes nauseated, vomits, and then becomes comatose. Blood ammonia level rises to more than 500 mmol per L. The patient remains comatose for 10 to 12 hours and eventually awakens when ammonia blood level decreases to less than 150 mmol per L. The hyperammonemia tends to linger postoperatively, probably because glycine absorption from the periprostatic space continues after surgery.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18:883-897. Roesch RP, Stoelting RK, Lingeman JE, et al. Ammonia toxicity resulting from glycine absorption during a transurethral resection of the prostate. *Anesthesiology.* 1983;58:577-579.

C.25. Why do some patients who have undergone TURP develop hyperammonemia and others do not? Is there a preventive treatment for hyperammonemia in these patients?

Because ammonia is metabolized primarily in the liver, it has been speculated that hyperammonemia after TURP is a

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result of liver dysfunction. However, liver dysfunction has not been found in these patients. Further, there is no evidence that patients with a known liver dysfunction are susceptible to hyperammonemia after TURP.

A more plausible explanation for the hyperammonemia is arginine deficiency. Normally, the ornithine cycle in the liver converts ammonia to urea (see Fig. 24.5). Arginine is an important intermediate product of this cycle. Patients who have undergone TURP while having arginine deficiency cannot detoxify the excess ammonia produced from glycine metabolism, and they therefore develop hyperammonemia. The time necessary to deplete the endogenous arginine stores may be as brief as 12 hours, which approximates the preoperative fasting time.

Several studies support this hypothesis. In dogs, the administration of arginine concurrently with glycine reduced the secretion of ammonia by the liver (Fig. 24.6). In humans, prophylactic administration of arginine or ornithine prevents hyperammonemia that otherwise follows rapid intravenous administration of glycine. Routine administration of arginine in patients undergoing TURP, however, is not recommended because they rarely develop hyperammonemia.

Fahey JL, Perry RS, McCoy PF. Blood ammonia elevation and toxicity from intravenous L-amino acid administration to dogs: the protection role of L-arginine. *Am J Physiol.* 1958;192:311-317.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438-446.

Nathans D, Fahey JL, Ship AG. Sites of origin and removal of blood ammonia formed during glycine infusion: effect of L-arginine. *J Lab Clin Med.* 1958;51:123-133.

Roesch RP, Stoelting RK, Lingeman JE, et al. Ammonia toxicity resulting from glycine absorption during a transurethral resection of the prostate. *Anesthesiology.* 1983;58:577-579.

C.26. What are the clinical characteristics, causes, and prognosis of TURP-related blindness?

Transient blindness is one of the more alarming complications of TURP. The patient complains of blurred vision and of seeing halos around objects. This can occur either during surgery or later in the recovery room. Although it is sometimes accompanied by other TURP-related complications, the blindness usually occurs as an isolated symptom. Examination of the eyes reveals dilated and unresponsive pupils. Postoperatively, TURP-related blindness gradually recedes and eyesight returns to normal within 8 to 48 hours of surgery.

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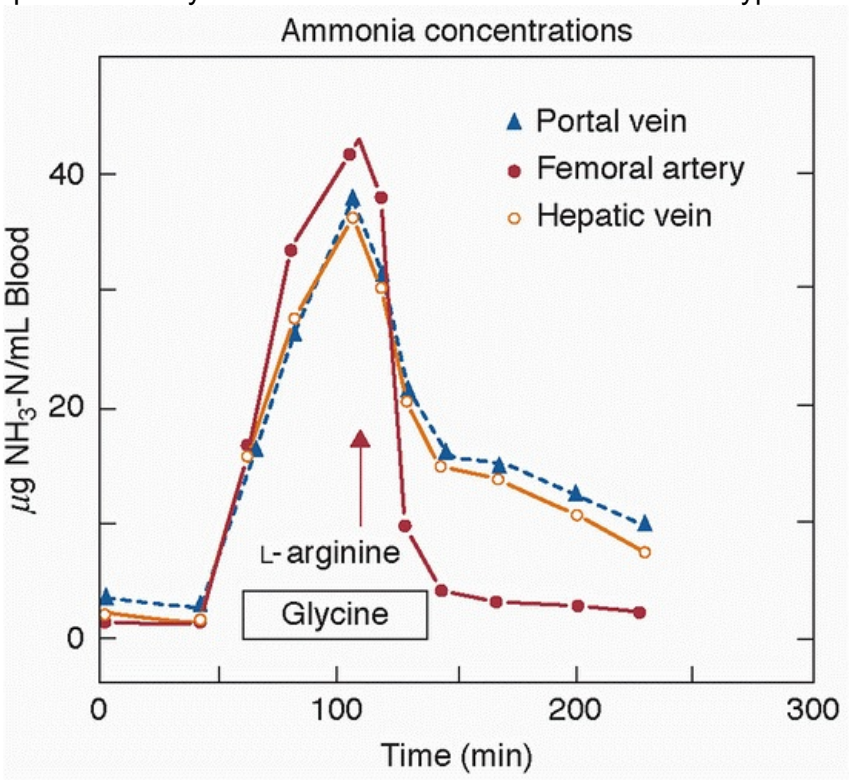


FIGURE 24.6 Ammonia blood levels during glycine administration in dogs before and after arginine supplementation. (Modified from Nathans D, Fahey JL, Ship AG. Sites of origin and removal of blood ammonia formed during glycine infusion: effect of L-arginine. *J Lab Clin Med.* 1958;51: 123-133, with permission.)

The cause of TURP-related blindness is unclear. The intraocular pressure and optic discs remain normal. In the past, edema of the cerebral optical cortex was suspected; however, the clinical signs of TURP-related blindness are consistent with retinal rather than cortical dysfunction. Unlike cortical blindness, TURP-related blindness allows perception of light and the blink reflex is preserved. TURP-related blindness is most likely caused by a toxic effect of glycine on the retina. This theory is supported by the fact that glycine is a known inhibitory neurotransmitter. In animals, glycine has been shown to inhibit neuronal visual pathways. Also, the severity of TURP-related blindness is directly related to glycine blood level. Postoperatively, vision gradually improves as the glycine blood level declines.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438-446.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

Ovassapian A, Joshi CW, Brunner EA. Visual disturbances: an unusual symptom of transurethral prostatic resection reaction. *Anesthesiology.* 1982;57:332-334.

C.27. What gynecologic procedure has been associated with a syndrome similar to TURP syndrome?

Hysteroscopy has been associated with symptoms not unlike those of TURP syndrome. The procedure involves visualization of the interior lining of the uterus for diagnostic purposes and, on occasion, for transcervical resection of the endometrium or submucous myomectomy. The latter often requires electrical cauterization. As with TURP, hysteroscopy requires irrigation with nonionic isotonic solutions. Commonly used solutions contain either glucose or glycine. Side effects such as hyponatremia, hyperglycemia, circulatory overloading, and coagulopathy have been reported.

Carson SA, Hubert GD, Schriock ED, et al. Hyperglycemia and hyponatremia during operative hysteroscopy with 5% dextrose in water distention. *Fertil Steril.* 1989;51:341-343.

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Goldenberg M, Zolti M, Seidman DS, et al. Transient blood oxygen desaturation, hypercapnia, and coagulopathy after operative hysteroscopy with glycine used as the distending medium. *Am J Obstet Gynecol.* 1994;170:25-29.

Hahn RG. Fluid absorption in endoscopic surgery. *Br J Anaesth.* 2006;96:8-20.

C.28. What are the causes of excessive bleeding during TURP?

Patients undergoing TURP commonly bleed perioperatively. One possible cause is dilutional thrombocytopenia resulting from excessive absorption of irrigation solution. Another possible cause is local release of fibrinolytic agents (plasminogen and urokinase) from the mucosa of the lower urinary tract. During and immediately after TURP, these agents cause local fibrinolysis and promote bleeding from the raw surfaces of the prostatic gland. The existence of a local fibrinolytic mechanism is supported by the observation that prophylactic administration of ε-aminocaproic acid (an antifibrinolytic agent) reduces bleeding from the prostatic bed.

Systemic coagulopathy can also occur during TURP. Contrary to common misconception, the coagulopathy is caused by disseminated intravascular coagulation (DIC) rather than by primary fibrinolysis. Characteristically, the platelet count and fibrinogen blood level are abnormally low. At autopsy, multiple microthrombi are observed in various parts of the body. The high level of fibrin-degradation products found in the blood of these patients is caused by secondary fibrinolysis, which commonly accompanies DIC.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

Smith RB, Riach P, Kaufman JJ. Epsilon aminocaproic acid and the control of post-prostatectomy bleeding: a prospective double-blind study. *J Urol.* 1984;131:1093-1095.

C.29. What triggers disseminated intravascular coagulopathy in patients undergoing TURP? How would you treat it?

DIC is triggered during TURP by prostatic particles rich in thromboplastin that enters the bloodstream during surgery. The recommended treatment for DIC is replacement of blood loss and administration of platelets, cryoprecipitates, and fresh frozen plasma. Heparin administration is controversial.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18:883-897.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.30. What are the causes, signs, symptoms, and treatment of bladder perforation during TURP?

The incidence of bladder perforation during TURP is approximately 1% and stems from trauma by surgical instrumentation, overdistention of the bladder, and, rarely, explosion of traces of hydrogen gas inside the bladder.

An early sign of bladder perforation is a sudden decrease in the return of irrigation solution from the bladder. This sign often goes unnoticed until a significant amount of irrigation solution accumulates in the abdomen, causing abdominal distress. Other clinical signs are hypotension, followed by hypertension and nausea. Reflex-type movements of the limbs have been observed under both general and regional anesthesia. When the perforation is intraperitoneal, symptoms develop faster and include severe shoulder pain caused by diaphragmatic irritation.

Diagnosis of bladder perforation is confirmed by cystourethrography. Treatment is immediate suprapubic cystotomy.

Hansen RI, Iversen P. Bladder explosion during uninterrupted transurethral resection of the prostate: a case report and an experimental model. *Scand J Urol Nephrol.* 1979;13:211-212.

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Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

C.31. What are the causes, signs, symptoms, and preventive measures for bladder explosion during TURP?

A rare but extremely dangerous complication of TURP is gas explosion inside the bladder during surgery. Various explosive gases, particularly hydrogen, are generated by the cauterization of prostatic or bladder tissue during TURP. The explosion is triggered by the hot metal

loop of the resectoscope. After a loud thump, the patient complains of sudden abdominal pain. This is accompanied by an abrupt decline in the return of irrigation solution. The concentration of oxygen in the bladder is usually too low to support combustion or explosion. However, if air is allowed to enter the irrigation system during surgery, oxygen concentration in the bladder will rise, and this in turn may trigger an explosion.

Strict precautions should be taken to prevent entry of air into the bladder during TURP. If air is observed in the bladder at the beginning of surgery, it must be evacuated before cauterization starts. The bladder should be emptied regularly in order to avoid accumulation of explosive gases during surgery.

Hansen RI, Iversen P. Bladder explosion during uninterrupted transurethral resection of the prostate: a case report and an experimental model. *Scand J Urol Nephrol.* 1979;13:211-212.

C.32. What are the causes of hypotension during TURP?

The more common causes of hypotension during TURP are circulatory overloading with CHF, MI or myocardial ischemia, severe anemia resulting from blood loss, and severe hyponatremia and water intoxication.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

D. Postoperative Management

D.1. What is the source of postoperative bacteremia in patients who have undergone TURP? What factors increase the incidence of bacteremia?

The prostatic gland often harbors large amounts of various bacteria. TURP facilitates the entry of these bacteria into the bloodstream, leading to postoperative bacteremia. Also, a preoperative indwelling catheter promotes bacterial growth in the urethra. Approximately 30% of patients undergoing TURP have infected urine preoperatively, and half of them sustain bacteremia postoperatively.

Surgical disruption of the prostatic venous sinuses and excessive hydrostatic pressure of the irrigation solution facilitate the entry of bacteria into the bloodstream.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

D.2. What are the signs of post-TURP septicemia? What preventive measures are generally recommended?

The signs of septicemia usually appear postoperatively in the postanesthesia care unit. They include fever, chills, low blood pressure, and tachycardia.

Antibiotics administered prophylactically before TURP do not sterilize the urine because they do not easily penetrate the prostatic gland. Nevertheless, the preoperative administration of antibiotics is recommended to render the bloodstream hostile to bacteria. The prophylactic administration of antibiotics in patients undergoing TURP is particularly important

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because of the grave prognosis of septicemia in these patients.

If sepsis is suspected postoperatively in a patient who has undergone TURP, broadspectrum antibiotics should be started immediately without waiting for blood culture results.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

D.3. What bacteria-related cause may possibly lead to sudden postoperative shock in patients who have undergone TURP?

Occasionally, patients who have undergone TURP develop postoperatively a short episode of hypotension, severe chills, and fever. However, these symptoms persist only a few hours, and then the patient recovers uneventfully. The cause of these symptoms is not clear; however, absorption of bacterial endotoxins has been suspected. Experimentally,

the administration of bacterial endotoxins in humans induced symptoms similar to those described.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

D.4. Is postoperative hypothermia a risk factor for myocardial ischemia?

Yes. Unexpected hypothermia is associated with a significantly higher incidence of postoperative myocardial ischemia. Therefore, it is important to maintain normothermia during the perioperative period. (See section D.4 in Chapter 14.)

D.5. How would you diagnose perioperative MI?

An intraoperative MI can be totally silent, or the anesthesiologist may become aware of it by a sudden decrease in blood pressure. This sudden decrease in blood pressure may be accompanied by tachycardia, which is indistinguishable from the hypovolemic hypotension resulting from acute blood loss.

The ECG is a good monitor of the adequacy of coronary circulation. Only the appearance of Q waves more than 0.03 seconds in width is definitively diagnostic of MI. However, the Q waves usually appear postoperatively, not intraoperatively. Postoperative measurements of the myocardial isoenzymes of creatine phosphokinase may confirm the diagnosis. Cardiacspecific enzyme elevations such as troponin I (cTn I), or troponin T (cTn T), are currently the standard of care for biochemical diagnosis of a perioperative MI because they demonstrate sensitivity and tissue specificity superior to other available biomarkers. (See section D.5 in Chapter 14.)

E. Comparing Monopolar, Bipolar, and Laser TURP

E.1. What differentiates monopolar from bipolar TURP?

Monopolar TURP uses high energy, which allows a fast cutting technique of prostatic tissue with minimal coagulation in the process. The body is the conduit of the energy dispersed from the monopolar electrode to complete the electrical circuit to a large-surface skin grounding pad placed on the patient. It also requires the use of an electrolyte-free bladder irrigating fluid. In bipolar TURP, the electrical circuit is completely contained within the resectoscope. This prevents energy from traveling through the body. Instead, the energy remains confined to the site of prostatic resection and is returned via the second limb of the bipolar resectoscope. With the bipolar electrode, less bleeding occurs at the prostatic tissue site and normal saline can be used as the bladder irrigating fluid.

Issa MM. Technological advances in transurethral resection of the prostate: bipolar versus monopolar TURP. *J Endourol.* 2008;22:1587-1595.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2217-2243.

O'Hara J. Anesthesia for select urologic procedures. In: *ASA Refresher Courses in Anesthesiology.* 2011;39(1):115-119.

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E.2. Are decreased morbidity and mortality associated more closely with monopolar TURP or with bipolar TURP?

In a meta-analysis that reviewed the safety of monopolar versus bipolar TURP in a small number of TURP patients (1,802), a significant benefit was reported in the bipolar group in overall complication rate, need for transfusion, and the absence of TURP syndrome. Recent randomized controlled trials have confirmed this.

Chen Q, Zhang L, Fan QL, et al. Bipolar transurethral resection in saline vs traditional monopolar resection of the prostate: results of a randomized trial with a 2-year follow-up. *BJU Int.* 2010;106(9):1339-1343.

Issa MM. Technological advances in transurethral resection of the prostate: bipolar versus monopolar TURP. *J Endourol.* 2008;22:1587-1595.

Reich O, Gratzke C, Bachmann A, et al. Morbidity, mortality, and early outcome of transurethral resection of the prostrate: a prospective multicenter evaluation of 10,654 patients. *J Urol.* 2008;180:246-249.

E.3. What differentiates the technologies for laser TURP?

Laser prostatectomy has generated renewed interest among urologists, and it is being used in several centers. It is challenging monopolar TURP as an alternative TURP technique. Holmium yttrium-aluminum-garnet (YAG), photoselective high-powered potassium titanyl phosphate (KTP; also known as the GreenLight laser), and GreenLight High Performance System (HPS) lasers are the three most recent systems used in TURP. The YAG laser wavelength is highly absorbed by water, which limits tissue cutting penetration. The KTP and HPS lasers have a wavelength absorbed by oxyhemoglobin and blood-rich tissue, which vaporizes a very thin prostatic tissue zone. Both techniques create a coagulation zone during resection, which minimizes bleeding and irrigating fluid absorption. There are five advantages of laser TURP: (1) It uses sterile water or normal saline as the irrigating bladder solution; (2) it minimizes the absorption of irrigating fluid; (3) it minimizes or altogether eliminates TURP syndrome; (4) it produces significantly less bleeding, which allows the procedure to be performed on an anticoagulated patient; and (5) it de-emphasizes regional anesthesia as the preferred anesthetic technique.

Geavlete B, Multescu R, Dragutescu M, et al. Transurethral resection (TUR) in saline plasma vaporization of the prostate vs standard TUR of the prostate: ‘the better choice’ in benign prostatic hyperplasia? *BJU Int.* 2010;106(11):1695-1699.

Hanson RA, Zornow MH, Conlin MJ, et al. Laser resection of the prostate: implications for anesthesia. *Anesth Analg.* 2007;105:475-479.

Tan AH, Gilling PJ. Holmium laser prostatectomy: current techniques. *Urology.* 2002;60:152-156.

Wosnitzer MS, Rutman MP. KTP/LBO laser vaporization of the prostate. *Urol Clin North Am.* 2009;36:471-483.

F. Are There Preferred Anesthetic and Preferred Surgical TURP Techniques for This Patient?

This 79-year-old man needing TURP has a history of ICD, MI, and recommendation to avoid interruption of antiplatelet therapy due to cardiac stents. With an anticoagulated patient, regional anesthesia would be avoided. This leaves the choice of general anesthesia with consideration of intra-arterial blood pressure monitoring. The advantages of laser TURP would include minimization of prostatic tissue bleeding and lowering the risk of TURP syndrome.

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Chapter 25
Kidney Transplant

Panchali Dhar
Peter Fleischut
Fun-Sun F. Yao

A 50-year-old man with rapid onset of end-stage renal disease (ESRD) prefers not to start hemodialysis. He would like to have an organ from a living related donor, but other options include expanded criteria donors or a paired donor exchange program.

A. Medical Disease and Differential Diagnosis

1. What are causes of chronic renal disease that can progress to renal failure?
2. How is chronic kidney disease (CKD) diagnosed?
3. What are the indications for dialysis?
4. What are the common clinical manifestations of ESRD?
5. What electrolyte imbalances occur in patients with impaired renal function, and how are they treated?
6. How is metabolic acidosis managed in chronic renal failure?
7. Are patients with renal disease at increased risk of cardiovascular disease?
8. When is the best time to receive a kidney transplant?
9. How are immunosuppressive drugs managed in kidney transplant recipients?
10. Who is an expanded criteria kidney donor?
11. What is donation after circulatory death?
12. What is a living donor transplant program?
13. What is a paired donor exchange transplant program?
14. What are some barriers to receiving a kidney transplant?
15. What surgical techniques are available for donor nephrectomy?
16. How is a donor kidney preserved?
17. Describe the operative procedure of kidney transplantation.

B. Preoperative Evaluation and Preparation

1. What preoperative workup would you order for a recipient?
2. How does the presence of obesity affect the outcome of a transplanted kidney?
3. How are routine medications and immunosuppressive medications managed in the perioperative period?

C. Intraoperative Management

1. Are a central venous pressure (CVP) monitoring line, an arterial line, and a pulmonary artery catheter required for the transplant procedure?
2. What type of intravenous fluid should be used during surgery?
3. How would you conduct the anesthesia induction?

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4. Is succinylcholine contraindicated in renal failure patients?
5. How are the nondepolarizing muscle relaxants affected by renal failure?
6. How would you maintain anesthesia during the case?
7. What are the effects of inhalation anesthetics on renal blood flow (RBF), glomerular filtration, and urine output?
8. What are the potential nephrotoxic effects of inhalation anesthetics? What are the nephrotoxic metabolites of inhalation anesthetics?
9. How does renal failure affect the pharmacology of opioids?

D. Postoperative Management

1. How is the diagnosis of transplant rejection made?
2. What are immunosuppressive agents and how do they affect anesthetic care?

A. Medical Disease and Differential Diagnosis

A.1. What are causes of chronic renal disease that can progress to renal failure?

The most common etiologies of renal disease leading to kidney transplant are:

- Diabetes, 31%
- Chronic glomerulonephritis, 28%
- Polycystic kidney disease, 12%
- Hypertension, 9%
- Systemic lupus erythematosus, 3%
- Interstitial nephritis, 3%

CKD has many potential causes that differ among the world populations. In developed countries, age, hypertension, cardiovascular disease, diabetes, increased body mass index (BMI), and smoking are associated with CKD. In the developing world, causes of kidney failure include infections due to bacteria, viruses, and parasites.

The global increase in CKD parallels the obesity epidemic. Obesity has been associated with a secondary focal segmental glomerulosclerosis coined obesity-related glomerulopathy (ORG). The accumulation of lipid in the cellular structure of the kidney is associated with structural and functional changes.

In recent years, Central America, Egypt, India, and Sri Lanka have reported a high prevalence of CKD of unknown etiology in agricultural communities, predominantly among male farmworkers. The dominant histopathologic diagnosis is chronic tubulointerstitial nephritis. There are associations reported with agricultural work, agrochemical exposure, dehydration, hypertension, homemade alcohol use, and family history of CKD.

Almaguer M, Herrera R, Orantes CM. Chronic kidney disease of unknown etiology in agricultural communities. *MEDICC Rev.* 2014;16(2):9-15.

de Vries AP, Ruggenenti P, Ruan XZ, et al. Fatty kidney: emerging role of ectopic lipid in obesity-related renal disease. *Lancet Diabetes Endocrinol.* 2014;2(5):417-426.

A.2. How is chronic kidney disease (CKD) diagnosed?

CKD is defined as abnormalities of kidney structure or function that is present for more than 3 months, with implications for health. It is not dependent on the etiology leading to deteriorated kidney function.

The criteria for CKD include either of the following present for more than 3 months:

Markers of kidney damage (one or more)

- Albuminuria

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- Urine sediment abnormalities
- Electrolyte and other abnormalities due to tubular disorders

- Abnormalities detected by histology
- Structural abnormalities detected by imaging
- History of kidney transplantation
- Glomerular filtration rate (GFR) less than 60 mL/min/1.73 m^2

The Modification of Diet in Renal Disease (MDRD) formula is used to estimate GFR and the progression of CKD. ESRD is established when GFR is less than 15 mL/min/1.73 m^2.

GFR = 175 × (standardized SCr)$^{-1.154}$ × (age)$^{-0.203}$ × 0.7429 (if female) or 1.212 (if African American)

SCr is the serum creatinine (milligrams per deciliter). Among individuals with established CKD, progression is based on estimation of GFR and level of albuminuria.

KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl.* 2012;3(1):1-163.

A.3. What are the indications for dialysis?

Early start of dialysis is initiated when GFR reaches ≤10 mL/min/1.73 m^2 in a patient without diabetes or ≤15 mL/min/1.73 m^2 in a patient with diabetes. Recent data indicate that the mortality while on dialysis may be higher with an early start and that there is no significant benefit in terms of quality of life. Some nephrologists support initiating dialysis at a lower GFR (<7.0 mL/min/1.73 m^2) provided that patients are given careful clinical management, and at an even lower rate (<5 mL/min/1.73 m^2) in selected elderly patients given a supplemented very low protein diet with careful management of the nutritional status, fluid and electrolyte balance, body weight, mineral metabolism, anemia, and blood pressure.

Patients with uremic symptoms (e.g., anorexia, vomiting, weight loss, pericarditis, and pleuritis) or fluid overload should be started on dialysis even if GFR is not at critically low levels. Other indications for dialysis in CKD include hyperkalemia that causes electrocardiogram (ECG) changes or that is persistent (K^+ >6 mEq per L), heart failure poorly controlled with drugs, and metabolic acidosis that is difficult to control.

Cooper BA, Branley P, Bulfone L, et al. A randomized, controlled trial of early versus late initiation of dialysis. *N Engl J Med.* 2010;363(7):609-619.

Rosansky S, Glassock RJ, Clark WF. Early start of dialysis: a critical review. *Clin J Am Soc Nephrol.* 2011;6(5):1222-1228.

A.4. What are the common clinical manifestations of ESRD?

The common problems related to ESRD are the following:

- Electrolytes: volume expansion, hyponatremia, hyperkalemia, metabolic acidosis, hyperuricemia, hyperphosphatemia, hypocalcemia
- Gastrointestinal: gastroparesis, nausea, vomiting, pancreatitis, anorexia, uremic gastroenteritis, peptic ulcer disease, gastrointestinal bleeding
- Cardiovascular: accelerated atherosclerosis, systemic hypertension, left ventricular hypertrophy, congestive heart failure, pulmonary edema, cardiomyopathy, pericarditis, hyperdynamic circulation
- Hematologic: anemia, B- and T-cell dysfunction, qualitative platelet dysfunction, bleeding diathesis
- Musculoskeletal: muscle weakness, uremic osteodystrophy (osteomalacia, osteosclerosis, osteitis fibrosa cystica)
- Neurologic: encephalopathy, loss of memory, seizures, peripheral neuropathy, autonomic dysfunction (postural

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hypotension), myoclonus, asterixis, dialysis disequilibrium (dehydration, weakness, nausea and vomiting, hypotension, and occasionally convulsion and coma)

- Endocrine: vitamin D deficiency, secondary hyperparathyroidism, carbohydrate intolerance, hypertriglyceridemia

Pain is extremely common in ESRD and can result from renal and nonrenal etiologies. In a prospective study of 205 hemodialysis patients, musculoskeletal pain was most common (63.1%), followed by dialysis-associated pain (13.6%), peripheral neuropathy (12.6%), and peripheral vascular disease claudication pain (9.7%). Polycystic kidney disease can cause chronic abdominal pain. Fentanyl and methadone are considered the safest opioids for use in patients with ESRD. Secondary hyperparathyroidism often results in bone pain.

O'Connor NR, Corcoran AM. End-stage renal disease: symptom management and advance care planning. *Am Fam Physician.* 2012;85(7):705-710.

A.5. What electrolyte imbalances occur in patients with impaired renal function, and how are they treated?

Chronic renal insufficiency and ESRD are associated with abnormalities in sodium (Na), potassium, calcium, magnesium balance, and metabolic acidosis.

Na and water (H_2O) balance are closely related. The kidney has its own inherent circadian rhythm involved in the transcription genes for renal Na excretion and blood pressure control. This function is impaired in renal disease. In patients with chronic renal failure, the total body content of Na and H_2O may be increased. This can be due to glomerular disease promoting Na retention or excessive ingestion of Na leading to extracellular fluid (ECF) expansion. The ECF expansion and hyperosmolarity contributes to hypertension. Nonanuric patients may be treated with loop diuretics and salt restriction.

The renal mechanisms for conserving Na and H_2O are impaired in ESRD. Urine in nonoliguric patients is isosthenuric. This means the usual indices of prerenal azotemia (high urine osmolality, low urine Na, and low fractional excretion of sodium [FENa]) are not applicable. If additional fluid loss (vomiting, fever) is imposed, such patients become severely volumedepleted. These patients have to be hydrated carefully with normal saline.

Hyperkalemia rarely occurs in patients with a GFR greater than 25 mL/min/1.73 m^2 in the absence of an endogenous or exogenous potassium load. Patients are usually chronically hyperkalemic. Severe hyperkalemia increases cardiac and skeletal muscle excitability. The earliest changes begin with levels above 6.5 mEq per L. The ECG shows peaked T waves, flattened P waves, lengthened PR interval, disappearance of P waves, and a widened QRS complex that can progress to a “sine wave,” ventricular asystole, or ventricular fibrillation. Muscle weakness can cause respiratory failure. Membrane excitability is more dependent on the rate of increase in potassium than on potassium concentration per se. The treatment of hyperkalemia includes a combination of insulin, glucose, loop diuretics (nonanuric), sodium bicarbonate, calcium, and magnesium (Table 25.1). The anesthesiologist may also institute hyperventilation in mechanically ventilated patients. Hemodialysis or peritoneal dialysis is the definitive treatment for severe hyperkalemia.

Magnesium imbalance can accompany chronic renal failure. High blood magnesium levels cause dose-dependent neuromuscular toxicity and increased sensitivity to depolarizing and nondepolarizing neuromuscular blockers. Bradycardia, hypotension, and heart block are due to the calcium channel-blocking effects of magnesium. The acute toxicity can be antagonized by intravenous infusion of calcium. Conversely, decreased dietary intake and impaired intestinal absorption can lead to hypomagnesemia. Magnesium deficiency has been related to progression of atherosclerosis and low parathyroid hormone (PTH) levels.

Phosphate retention occurs when GFR begins to decline. Retained phosphate promotes secondary hyperparathyroidism by lowering ionized plasma calcium levels, decreasing renal formation of calcitriol (1,25 dihydroxyvitamin D), and stimulating PTH gene expression.

Ionized and protein-bound calcium levels are lower in uremic patients. This is the result of hyperphosphatemia and reduced gastrointestinal absorption secondary to the decreased production of vitamin D.

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TABLE 25.1 Drug Treatment for Hyperkalemia

DRUG	DOSE
Calcium chloride	5 mL of 10% solution IV over 2 min (monitor for bradycardia)
Calcium gluconate	10 mL of 10% solution IV over 2 min (monitor for bradycardia)
Insulin	5-10 units regular insulin with 1-2 amps $D_{50}W$ IV bolus
Sodium bicarbonate	1 mEq/kg slow IV push or continuous drip; not to exceed 50-100 mEq
β-Agonists (albuterol)	2.5 mg mixed with 3 mL isotonic saline through nebulizer every 20 min as tolerated
Diuretic (furosemide)	20-40 mg IV push
Magnesium	1-2 g IV over 30-60 sec; repeat every 5-15 min as required or 3-10 mg/min IV infusion

Kanbay M, Goldsmith D, Uyar ME, et al. Magnesium in chronic kidney disease: challenges and opportunities. *Blood Purif.* 2010;29(3):280-292.

Kovesdy CP. Management of hyperkalaemia in chronic kidney disease. *Nat Rev Nephrol.* 2014;10(11):653-662.

Malberti F. Hyperphosphatasemia: treatment options. *Drugs.* 2013;73(7):673-688.

Nikolaeva S, Pradervand S, Centeno G, et al. The circadian clock modulates renal sodium handling. *J Am Soc Nephrol.* 2012;23(6):1019-1026.

A.6. How is metabolic acidosis managed in chronic renal failure?

A mild-to-moderate acidosis is commonly noted when the GFR decreases to less than 20% to 25% of normal. The decreased renal mass results in decreased NH_4^+ production and excretion of proton load. The plasma bicarbonate concentration ranges between 12 and 22 mEq per L, and blood pH remains greater than 7.20. This does not routinely require correction. It may gradually evolve into a high anion gap acidosis when the GFR is below 20 mL/min/1.73 m^2. Some patients with ESRD maintain close to normal acid-base parameters even when renal function is severely compromised. However, when exposed to an increased dietary acid load, these patients may have decreased ability to increase bicarbonate generation.

The correction of acidosis by oral sodium bicarbonate or a diet rich in fruits and vegetables can attenuate rate of decline of renal function.

Goraya N, Wesson DE. Does correction of metabolic acidosis slow chronic kidney disease progression? *Curr Opin Nephrol Hypertens.* 2013;22(2):193-197.

Loniewski I. Combining a fruit and vegetable diet with sodium bicarbonate supplementation seems the best dietary option for chronic kidney disease patients. *Kidney Int.* 2012;82(8):937.

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A.7. Are patients with renal disease at increased risk of cardiovascular disease?

ESRD is associated with an increased incidence and prevalence of a wide range of cardiovascular morbidities including hypertension, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, sudden cardiac death, pulmonary hypertension, and valvular heart disease.

Extensive vascular calcification contributes to early onset cardiovascular disease and cardiovascular mortality. In addition to traditional cardiovascular risks, risk factors specific to CKD such as phosphate retention, hypercalcemia, history of dialysis, high-dose vitamin D therapy, and deficiency of calcification inhibitors promote arterial calcification. There is no specific therapy to reverse vascular calcification, but statin therapy is associated with decreased cardiovascular death. Additional measures such as reduction of calcium phosphate load, using non-calcium-containing phosphate binders, and moderate doses of active vitamin D may attenuate arterial hardening.

The rate of sudden cardiac death increases as the stage of CKD increases and could be responsible for 60% of cardiac deaths in patients undergoing dialysis. The uremic load results in cardiac fibrosis and in left ventricular systolic and diastolic dysfunction. The occurrence of conduction abnormalities and arrhythmias is exacerbated by electrolyte shifts, diabetes, and autonomic neuropathy. Cardioverter-defibrillator implantation decreases the risk of sudden death in patients with CKD.

Hypertension has been reported to occur in 85% to 95% of patients with CKD (stages 3 to 5). The relationship between hypertension and CKD is cyclic in nature. Uncontrolled hypertension is a risk factor for developing CKD and leads to a more rapid progression of CKD. In turn, renal disease exacerbates uncontrolled hypertension due to volume expansion and increased systemic vascular resistance. An imbalanced autonomic system results in an exaggerated sympathetic drive with a loss of vagal tone. Autonomic neuropathy creates a setting for silent myocardial ischemia.

Correction of the uremic state and improved GFR after kidney transplant may decrease the incidence and severity of cardiovascular complications.

Botdorf J, Chaudhary K, Whaley-Connell A. Hypertension in cardiovascular and kidney disease. *Cardiorenal Med.* 2011;1:183-192.

Disthabanchong S. Vascular calcification in chronic kidney disease: pathogenesis and clinical implication. *World J Nephrol.* 2012;1(2):43-53.

Glicklich D, Vohra P. Cardiovascular risk assessment before and after kidney transplantation. *Cardiol Rev.* 2014;22(4):153-162.

Shamseddin MK, Parfrey PS. Sudden cardiac death in chronic kidney disease: epidemiology and prevention. *Nat Rev Nephrol.* 2011;7(3):145-154.

A.8. When is the best time to receive a kidney transplant?

Studies show that survival of a transplanted kidney is incrementally worse if the recipient has been on long-term dialysis. The best outcomes are seen for patients who are preemptively transplanted before dialysis is initiated. However, renal failure in some patients is slowly progressive so it is not practical to perform a transplant months or even years before it is needed. Also, there is a small fraction of patients diagnosed with “end-stage” kidney disease that regain kidney function. For example, patients with kidney injury from malignant hypertension may regain kidney function weeks or even months after hypertension control is established.

In general, a patient is a candidate for a kidney transplant if the estimated glomerular filtration rate (eGFR) is 20 mL/min/1.73 m^2 or less. The rate of progression to ESRD is also important. In diabetics, renal failure can develop rapidly. If it is obvious the patient will eventually require dialysis, and a living donor is available now, transplant is practical and cost-effective option.

Preparation for a transplant candidate can take several months. It involves thorough medical evaluation, with optimization of cardiac and pulmonary status. The workup for potential living donors also takes several months.

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Link DK, Saxena R. The right patient, the right treatment, the right access and the right time. *Adv Chronic Kidney Dis.* 2014;21(4):360-364.

Taal MW, Chertow GM, Marsden PA, et al, eds. *Brenner and Rector's The Kidney.* 9th ed. Philadelphia, PA: Saunders; 2012:2495-2514.

A.9. How are immunosuppressive drugs managed in kidney transplant recipients?

In order to decrease the incidence of graft rejection, several regimens of immunosuppressive agents have been devised. Centers throughout the world may use different combinations of these drugs, but the basic idea behind their use is to prevent acute and chronic T-cell alloimmune rejection. The regimens are separated into the induction phase and then a long-term maintenance phase. Four classes of immunosuppressive medications are used: corticosteroids, calcineurin inhibitors (cyclosporine and tacrolimus), antimetabolites (mycophenolate mofetil, mycophenolate sodium, and azathioprine), and the target-of-rapamycin (TOR) inhibitor (sirolimus). The maintenance phase involves a combination of two or three of these drugs, each from a separate class.

Immunosuppressant therapy is started in the immediate preoperative period. In the intraoperative period, induction therapy is targeted to eliminate lymphoid cells that may cause acute rejection of the graft. An induction agent may be withheld if immediate graft function occurs from a living donor kidney. After surgery, maintenance therapy is begun for the life of the recipient. Although lifelong immunosuppression helps prevent rejection of the allograft, it also increases the risk of malignancy and infectious diseases. The regimens may not prevent the slow deterioration associated with chronic graft rejection.

In an effort to reduce the long-term toxicities of immunosuppressant drugs, corticosteroid-and calcineurin inhibitor (CNI)-sparing protocols have become popular in managing kidney transplant patients. This is because the long-term use of steroids contributes to cardiovascular disease and/or infectious disease complications.

CNIs prevent acute rejection but are associated with reduced long-term allograft function. Protocols with agents such as mycophenolate mofetil, mycophenolate sodium, sirolimus, everolimus, and belatacept allow discontinuation of CNI within 6 months or avoid the CNIs.

Helal I, Chan L. Steroid and calcineurin inhibitor-sparing protocols in kidney transplantation. *Transplant Proc.* 2011;43(2):472-477.

A.10. Who is an expanded criteria kidney donor?

There are an increasing number of persons awaiting a kidney transplant. The standard donor is aged 5 to 49 years, nonhypertensive, whose cause of death was not cerebrovascular accident, and whose creatinine was less than or equal to 1.5 mg per dL.

The term “expanded criteria donor” (ECD) is a term that has been introduced as a part of an effort to increase the use of kidneys that might otherwise have been discarded and to minimize the length of cold ischemia to which they are subjected. An ECD is a deceased donor who is either:

- Age 60 years or older
- Age 50 to 59 years meeting two or more of the following criteria:
  1. History of hypertension
  2. Death from cardiovascular accident
  3. Serum creatinine ≥ 1.5 mg per dL

ECD kidneys account for approximately 15% of deceased donor kidneys. Patient survival is similar to standard criteria organs in the short term but lower after 5 or more years in the ECD kidneys. The grafts are evaluated histologically before implantation. ECD kidneys are offered only to patients willing to accept them. Oftentimes, this decision must be made within 2 hours. This has increased the number of transplants anesthesiologists encounter. It is not recommended that patients younger than 40 years or a person scheduled for retransplantation receive an ECD kidney. Patients 40 years or

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older, either with diabetic nephropathy or nondiabetic disease, and a long expected waiting time have survival benefit after receiving an ECD kidney than remaining on dialysis.

Lionaki S, Kapsia H, Makropoulos I, et al. Kidney transplantation outcomes from expanded criteria donors, standard criteria donors or living donors older than 60 years. *Ren Fail.* 2014;36(4): 526-533.

A.11. What is donation after circulatory death?

Donation after circulatory death (DCD) has opened new perspectives in the donor pool. DCD refers to kidney donation from patients with brain injuries who do not meet the criteria for brain death and who experience cardiopulmonary arrest after withdrawal of ventilatory support. This criterion does increase the number of organs available, but DCD kidneys do have a 5.73-fold increase in the incidence of delayed graft function and a higher primary nonfunction rate compared to donation after brain death. DCD kidneys also have a higher rate of discard and retrieval-associated injury. The long-term graft function is equivalent between brain death and cardiac death donors. Renal preservation fluid is delivered either with rapid laparotomy and direct aortic cannulation or using an intra-aortic catheter placed via the femoral artery.

Rapid laparotomy is associated with lower kidney discard rate, shorter warm ischemia times, and higher graft survival rates. Newer preservation strategies using extracorporeal membrane oxygenation (ECMO) are under study to develop uniform guidelines for procurement.

Akoh JA. Kidney donation after cardiac death. *World J Nephrol.* 2012;1(3):79-91. Morrissey PE, Monaco AP. Donation after circulatory death: current practices, ongoing challenges, and potential improvements. *Transplantation.* 2014;97(3):258-264.

Neyrinck A, Van Raemdonck D, Monbaliu D. Donation after circulatory death: current status. *Curr Opin Anaesthesiol.* 2013;26(3):382-390.

A.12. What is a living donor transplant program?

A living donor transplant program allows recipient and donor surgery to be scheduled simultaneously. It offers the advantage of minimal organ preservation time. The total ischemia time from removal of the kidney from the donor to the restoration of blood flow in the recipient can be less than 1 hour. A short preservation time allows immediate graft function, high-volume urine output, and initiation of creatinine clearance.

A large number of recipients have preformed antibodies to potential living donors. These antibodies are the result of exposure to foreign antigens by blood transfusions, prior transplantation, or pregnancy. As a result, the recipients have positive crossmatches against living donor tissue antigens. There are preoperative measures that can facilitate the transplant to occur. One such regimen involves the combination of plasmapheresis and low-dose intravenous immunoglobulin with or without rituximab (a B-cell depleter) administered to a positive crossmatch and/or highly sensitized recipient. The living donor transplant is conducted when the crossmatch converts to negative. The recipient usually has to undergo additional plasmapheresis treatments and immunoglobulin infusions postoperatively.

Jin MK, Cho JH, Kwon O, et al. Successful kidney transplantation after desensitization using plasmapheresis, low-dose intravenous immunoglobulin, and rituximab in highly sensitized patients: a single-center experience. *Transplant Proc.* 2012;44(1):200-203.

Tong A, Chapman JR, Wong G, et al. Living kidney donor assessment: challenges, uncertainties and controversies among transplant nephrologists and surgeons. *Am J Transplant.* 2013;13(11):2912-2923.

A.13. What is a paired donor exchange transplant program?

This program is sometimes referred to as a “kidney swap.” For example, one incompatible donor-candidate pair is matched to another pair with a complementary incompatibility, such that the donor from one pair gives an organ to a compatible candidate in the other pair and vice versa. Each kidney paired donation (KPD) has developed its own features to accommodate local needs. Reasons for participating in KPD include blood group incompatibility, sensitization

of the recipient against the donor, the potential for improvement in transplant quality (e.g., age difference or graft size), and tissue compatibility. Sophisticated algorithms allow simultaneous two-way, three-way, or four-way exchanges or nonsimultaneous chains of transplants over the course of months.

There are many benefits to a paired donor exchange program:

- It expands the pool of donors.
- By using ABO-compatible but nonidentical donors, transplants can be performed at individual centers without requiring large sharing networks.
- Type O recipients with incompatible donors are likely to be the primary beneficiary of exchange programs.
- These programs reflect a paradigm shift for live donation, converting a private resource (the donor) to a shared one.
- Both donors and recipients are more willing to participate if their intended recipient, or donor is enthusiastic about participating.

Chkhotua A. Paired kidney donation: outcomes, limitations, and future perspectives. *Transplant Proc.* 2012;44(6):1790-1792.

Mierzejewska B, Durlik M, Lisik W, et al. Current approaches in national kidney paired donation programs. *Ann Transplant.* 2013;18:112-124.

A.14. What are some barriers to receiving a kidney transplant?

Absolute contraindications to kidney transplant include life-threatening infections, active malignancy, unstable cardiovascular disease, AIDS, and behavior that would result in nonadherence to immunosuppressive regimens. Old age is not a contraindication to transplant. A living donor transplant is often the best option for an older patient. However, a patient who has a life expectancy of less than 2 years due to comorbidities should not undergo transplantation.

Recipient with HIV infection is not a contraindication to acquiring a kidney. The U.S. Congress passed a law called the HIV Organ Policy Equity (HOPE) Act. This law ended a federal ban on transplantation of organs from deceased HIV-infected donors to HIV-infected recipients. The new policy will expand the number of donor organs available for transplantation into HIV-positive patients. The potential recipient should be clinically stable on highly active antiretroviral therapy (HAART), with an undetectable viral load, and a CD4 count ≥200 cells per μL.

Because the incidence of obesity has increased in the general population, more obese patients are referred for kidney transplantation. Obese patients have increased risk for delayed graft failure. Diet and/or bariatric surgery are beneficial for patients with a BMI of 40 kg per m^2 or more prior to transplant. Improvements in postoperative management have resulted in similar graft survival and mortality in obese patients compared to nonobese patients.

Many patients on dialysis are infected with hepatitis B and/or hepatitis C. Currently, chronic hepatitis B is treated with interferon-α-2a or interferon-α-2b and lamivudine. Antiviral treatment with interferon is contraindicated after transplantation due to the risk of rejection, so treatment is recommended before transplant. Unlike interferon, lamivudine is a safe and effective antiviral hepatitis B virus (HBV) treatment both before and after renal transplantation. New treatment strategies with oral nucleotide NS5B polymerase inhibitors (sofosbuvir) are revolutionizing therapy for hepatitis C virus (HCV). A recipient infected with HCV may accept an organ from an HCV-positive donor. Established HBV or HCV with cirrhosis and active viral infection is a relative contraindication to renal transplant.

Bahde R, Vowinkel T, Unser J, et al. Prognostic factors for kidney allograft survival in the Eurotransplant Senior Program. *Ann Transplant.* 2014;19:201-209.

Burra P, Rodríguez-Castro KI, Marchini F, et al. Hepatitis C virus infection in end-stage renal disease and kidney transplantation. *Transpl Int.* 2014;27(9):877-891.

Malani PN. New law allows organ transplants from deceased HIV-infected donors to HIV-infected recipients. *JAMA.* 2013;310(23):2492-2493.

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Nicoletto BB, Fonseca NK, Manfro RC, et al. Effects of obesity on kidney transplantation outcomes: a systematic review and meta-analysis. *Transplantation.* 2014;98(2):167-176.

A.15. What surgical techniques are available for donor nephrectomy?

The standard techniques for donor nephrectomy (DN) are open surgery, laparoscopic, and hand-assisted laparoscopic DN. Laparoscopic living-donor nephrectomy (LLDN) has increased in popularity. In some centers, it has replaced open DN as the standard technique. Laparoscopic DN results in less blood loss, reduced operative time, and shorter hospital stay than open DN. Hand-assisted laparoscopic DN has the potential to decrease warm ischemia time for renal allografts. Donors managed laparoscopically have fewer complications, significantly less wound-related morbidity, and less delayed graft function than patients who undergo open DN.

Robotic nephrectomy offers several advantages compared to standard laparoscopic approaches. In particular, a robotic system restores the three-dimensional vision lost in the laparoscopic approach and enhances the ability of the surgeon to perform complex tasks.

Laparoendoscopic single-site surgery (LESS) uses one extraction site to place all ports to minimize the invasiveness of the planned procedure. A hybrid technique uses one periumbilical access and extraction site and an additional 2-mm needlescopic port. A robot can be used to aid in the surgery.

Caso JR. Minimally invasive donor nephrectomy: innovations. *Curr Urol Rep.* 2014;15(1):378.

Giacomoni A, Di Sandro S, Lauterio A, et al. Evolution of robotic nephrectomy for living donation: from handassisted to totally robotic technique. *Int J Med Robot.* 2014;10(3):286-293.

A.16. How is a donor kidney preserved?

Currently, static cold storage and hypothermic pulsatile machine perfusion are the two methods used to preserve donor kidneys. The benefit of one method over the other remains debated.

In static cold storage, the kidney is flushed, cooled with one of several cold preservation solutions, and transported on ice. In hypothermic machine perfusion, after an initial washout of blood, the kidney is connected to a perfusion device, and a solution is pumped continuously through the organ at temperatures between 1°C and 10°C until the moment of graft placement.

Preservation solutions are agents that do not readily permeate the cell membrane and have an electrolyte composition similar to the intracellular environment (low sodium, high potassium), thus preventing loss of cellular potassium. The organ-preserving cold storage interval is called cold ischemia time (CIT). It extends from the initiation of cold preservation of donor organs to restoration of warm circulation in the organ recipient. In general, kidneys with a CIT over 24 hours or more are susceptible to delayed graft function. Delayed graft function means a requirement for dialysis in the first week after receiving a transplant.

As more suboptimal donor kidneys are utilized, machine perfusion has regained clinical interest. Hypothermic machine perfusion reduces delayed graft function compared with static cold. There is no difference in primary nonfunction, acute rejection, long-term renal function, or patient survival between the two methods.

Kidneys from living donors are easier to handle. The organ is flushed with preservation solution or iced Ringer's lactate solution containing heparin and mannitol. The ischemic time during implantation is usually 20 to 30 minutes because the transplant operation takes place immediately. Some practices place the living donor kidney in a pulsatile preservation machine that maintains organ viability for longer periods of time. The influence of improved immunosuppression, lower CIT have contributed to the recent improvements in graft function and survival.

Bathini V, McGregor T, McAlister VC, et al. Renal perfusion pump vs cold storage for donation after cardiac death kidneys: a systematic review. *J Urol.* 2013;189(6):2214-2220.

O'Callaghan JM, Morgan RD, Knight SR, et al. Systematic review and meta-analysis of hypothermic machine perfusion versus static cold storage of kidney allografts on transplant outcomes. *Br J Surg.* 2013;100(8):991-1001.

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A.17. Describe the operative procedure of kidney transplantation.

Prior to the induction of anesthesia, a large-bore peripheral intravenous line (18- or 16-gauge) is required. Following induction of anesthesia, a triple-lumen central line maybe placed either in the internal jugular or subclavian route. A Foley catheter is placed in the bladder, and the bladder is irrigated with an antibiotic solution. Fluids are infused liberally through the central line and intravenous line. An arterial line may also be placed depending on the patient's underlying clinical status.

A kidney is harvested from a living donor using a left-flank laparoscopic approach. Harvesting of the left kidney is favored because the left renal vein is longer. New surgical techniques allow preservation of longer arterial length on the harvested kidney. Longer vessel preservation facilitates a right kidney donation.

The donor kidney is placed in either the right or left iliac fossa. The right kidney is usually placed in the left groin and vice versa. The renal artery of the donor kidney is connected to the external or internal iliac artery in the recipient. The renal vein of the donor kidney is connected to the external iliac vein in the recipient. Occasionally, a donor kidney has multiple renal arteries. This is addressed using primary or secondary anastomosis. A multiple-artery donor kidney has a longer operative and ischemic time than a kidney with a single artery. In the event that the recipient weighs less than 20 kg, the kidney is placed intra-abdominally posterior to the right colon. Urinary continuity is restored by placing the distal ureter into the bladder through a tunnel without opening the bladder.

In deceased donor kidney transplant, prior to the release of the arterial clamp and following completion of the anastomosis, an intra-arterial injection of verapamil or papaverine may be given by direct push into the renal artery to prevent arterial vasospasm.

In dual kidney transplantation, two kidneys from a donor are placed into one recipient. It is a reflection of donor shortage and reluctance to discard potentially functional organs. Such kidneys have usually been refused for single kidney transplantation. The criteria extends to very old (>60 years) or very young (<3 years) donors. The kidneys are transplanted en bloc. The donor aorta and vena cava are anastomosed to the external iliac artery and vein of the recipient. A dual kidney transplant procedure is of longer duration and involves more third spacing, greater volume requirements, and blood loss.

Chedid MF, Muthu C, Nyberg SL, et al. Living donor kidney transplantation using laparoscopically procured multiple renal artery kidneys and right kidneys. *J Am Coll Surg.* 2013;217(1):144-152.

Laftavi MR, Stephan R, Feng L, et al. Dual kidney transplants from very old or very young donors: long-term outcomes and complications. *Transplant Proc.* 2011;43(2):507-511.

B. Preoperative Evaluation and Preparation

B.1. What preoperative workup would you order for a recipient?

The transplant recipient should have routine systemic tests such as ECG, chest radiograph, blood counts, platelet count, electrolytes, serum glucose, blood urea nitrogen, creatinine concentration, prothrombin time, partial thromboplastin time, liver function enzymes (aspartate aminotransferase [AST], alanine aminotransferase [ALT]), bilirubin, and albumin.

Medical treatment for coronary artery disease is recommended where indicated by the cardiologist. Because cardiac disease is prevalent in the patient population, a thorough cardiac evaluation is recommended. Patients should have a cardiac stress test performed if (1) they are more than 49 years old; (2) they have diabetes mellitus; (3) they have an abnormal ECG showing changes suggestive of ischemia or previous myocardial infarction, a new left bundle branch block, or diagnostic Q-wave changes in two contiguous leads; and (4) if they have a history of ischemic heart disease, peripheral vascular disease, or ischemic cerebrovascular disease. Patients who are unable to undergo an exercise stress test should have dipyridamolethallium imaging or dobutamine stress echocardiography. If possible, stress testing should be performed without concurrent β-blocker therapy. Patients with a positive stress test should be further evaluated with coronary angiography. In addition, high-risk patients such as those with known coronary artery disease, congestive heart failure, or previous myocardial infarction should also undergo cardiac catheterization. Preemptive coronary revascularization with stent or coronary artery bypass grafting (CABG) is associated with improved cardiac event-free survival rate.

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Dialysis, if indicated, is done within 24 hours of the operation. It is best to avoid overzealous ultrafiltration as expanded filling pressures are desired. A urinalysis and urine culture should be performed on all urinating patients. Dialysis-related problems such as dialysis dementia, disequilibrium syndrome after dialysis (cerebral edema), hypovolemia (hypotension after anesthetic induction following recent dialysis), peritonitis (peritoneal dialysis), and systemic anticoagulation (after dialysis) should be evaluated. It is important to know the time of the last dialysis. The dialysis records should be reviewed for pre- and postdialysis body weight. The goal of dialysis is clearance rather than fluid removal. Patients should be above dry weight. The loss of more than 2 kg during dialysis suggests intravascular volume depletion, which may result in severe hypotension during or after anesthetic induction.

Kumar N, Baker CS, Chan K, et al. Cardiac survival after pre-emptive coronary angiography in transplant patients and those awaiting transplantation. *Clin J Am Soc Nephrol.* 2011;6(8):1912-1919.

B.2. How does the presence of obesity affect the outcome of a transplanted kidney?

The benefit of renal transplantation in obese patients is controversial, with many centers setting upper limits on BMI in consideration for listing patients for transplant. High BMI at transplant is associated with increased risk of wound and surgical site infections, delayed graft function, acute rejection episodes, and graft loss. Prospective evaluations of the impact of targeted risk modification such as dietary changes, and monitored exercise programs are being investigated at this time. Bariatric surgery is both safe and effective in patients with

CKD and ESRD. A sleeve gastrectomy improves eligibility for transplant based on BMI and does not affect postoperative immunosuppressant dosing regimens. All patients presenting for kidney transplant should be considered to have full stomachs, regardless of the period of preoperative fasting.

Lentine KL, Delos Santos R, Axelrod D, et al. Obesity and kidney transplant candidates: how big is too big for transplantation? *Am J Nephrol.* 2012;36(6):575-586.

Pham PT, Danovitch GM, Pham PC. Kidney transplantation in the obese transplant candidates: to transplant or not to transplant? *Semin Dial.* 2013;26(5):568-577.

B.3. How are routine medications and immunosuppressive medications managed in the perioperative period?

Patients awaiting transplant often have comorbidities such as hypertension and diabetes. Antihypertensive drugs should be continued until the time of surgery. There are no rigorous studies in the transplant population regarding the protective value of β-blockers. It is recommended that β-blockade be continued to reduce the risk of myocardial infarction. Medications such as angiotensin-converting enzyme inhibitor (ACE-I) and angiotensin II receptor blocker (ARB) should be omitted because of the risk of severe and refractory intraoperative hypotension. In spite of careful antihypertensive therapy, patient hemodynamics may still remain labile during induction, laryngoscopy, intubation, and extubation.

Oral hypoglycemic agents should be held on the morning of surgery. An aspart insulin sliding scale can be used to manage patients on insulin. The sliding scale may be used intraoperatively if high blood glucose levels are measured. Antibiotic prophylaxis for infectious complications includes a first-generation cephalosporin (cefazolin 2 g 30 minutes preoperatively), or if penicillin-allergic, vancomycin (1 g intravenously).

Anxiolytics should be titrated carefully because these patients may have increased sensitivity to premedication drugs. For example, diazepam is highly bound to albumin, but with decreased albumin levels, the effect of the drug is increased. Midazolam is water-soluble, less affected by albumin levels, and useful prior to induction.

Prior to entering the operating room, patients are given intravenous methylprednisolone (Solu-Medrol) and mycophenolate mofetil (CellCept). Diphenhydramine and acetaminophen should be given before the rabbit antithymocyte globulin (Thymoglobulin) is infused intraoperatively. Under specific circumstances, basiliximab (Simulect) is substituted for Thymoglobulin. This is practiced if the patient has history of reaction to Thymoglobulin or is a perfect match to the donor kidney. No prophylactic premedication is required with basiliximab. Rituximab and plasmapheresis followed by intravenous immunoglobulin are incorporated into the regimens of those patients with a positive crossmatch. A steroid-sparing regimen includes intraoperative methylprednisolone which is tapered over 4 days. Patients go home taking only

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tacrolimus (Prograf) and mycophenolate mofetil (CellCept). In the steroid protocol, patients are continued on prednisone.

Spiro MD, Eilers H. Intraoperative care of the transplant patient. *Anesthesiol Clin.* 2013;31(4):705-721.

C. Intraoperative Management

C.1. Are a central venous pressure (CVP) monitoring line, an arterial line, and a pulmonary artery catheter required for the transplant procedure?

Adequate hydration is an important part of the anesthetic management in renal transplant. Measuring the CVP is not an absolute requirement. External jugular venous pressure has been used as an alternative to CVP monitoring. The CVP or pulmonary artery pressure (only in patients with left ventricular dysfunction) can be used to guide fluid therapy. Adequate hemodialysis should be performed within 48 hours of surgery. These postdialysis patients have intravascular volume depletion. To decrease the incidence of postoperative acute tubular necrosis (ATN), a liberal hydration policy is employed intraoperatively. Hydration guided by CVP monitoring has been shown to maintain stable hemodynamics and promote diuresis.

The systolic blood pressure is maintained between 130 and 160 mm Hg, and the CVP is maintained between 12 and 14 mm Hg. Maintaining adequate CVP is especially important in pediatric recipients because reperfusion of an adult-size kidney graft may divert a significant amount of their own blood volume. CVP may decline 1 to 2 hours after revascularization despite aggressive fluid management in the operating room. The decline in CVP is similar in recipients of both cadaveric and living related donor kidneys. It may decline 25% to 50 % below the CVP measured in the operating room at reperfusion of the transplanted kidney. The reason for the decline is not clear but may be multifactorial such as redistribution of fluids, changes in vascular permeability, or increased nitric oxide levels. This is why postoperative hydration is an essential factor in maintaining renal function. Increased hydration likely works by atrial distension and the subsequent release of atrial natriuretic peptide and increased renal perfusion. The patient should receive an equal amount of fluid replacing the urine output. This approximates to 1 L per hour.

An arterial line is not absolutely required for the transplant procedure. It should be placed if a patient has an advanced comorbid condition that requires close monitoring of blood pressure or acid-base status. Oftentimes, placement of an intra-arterial line is difficult because many recipients have poor arterial access secondary to diabetes, peripheral vascular disease, arteriovenous fistulas, and shunts. Major swings in blood pressure may occur, with hypotension (49.6%) being more likely than hypertension (26.8%). Administration of induction drugs and maintenance agents should be titrated carefully. The main utility of instantaneous blood pressure reading is toward the end of the procedure. Hypotension may occur after unclamping of the iliac vessels and/or from partial systemic absorption of the vasodilator (verapamil or papaverine) injected by the surgeon into the graft vessels. Hypotension must be avoided during this period because it can lead to delayed graft function and/or renal vein thrombosis.

A pulmonary artery catheter is not routinely placed for kidney transplantation. Patients with severe comorbid conditions, such as symptomatic coronary artery disease, left ventricular dysfunction, congestive heart failure, valvular heart disease, or severe chronic obstructive pulmonary disease can be monitored precisely with a pulmonary artery catheter. A transesophageal echocardiography can help determine if hypotension is caused by hypovolemia or myocardial dysfunction.

Othman MM, Ismael AZ, Hammouda GE. The impact of timing of maximal crystalloid hydration on early graft function during kidney transplantation. *Anesth Analg.* 2010;110(5):1440-1446.

Trzebicki J, Flakiewicz E, Nowakowski P, et al. Is external jugular venous pressure a good predictor of volume status in kidney graft recipients? *Transplant Proc.* 2009;41(8):3033-3035.

C.2. What type of intravenous fluid should be used during surgery?

The administration of normal saline and normal saline-based fluids (5% albumin) is the standard of care for fluid management in patients undergoing renal transplant surgery. This practice is primarily based on avoidance of potassium-containing fluids which can contribute to intraoperative hyperkalemia. One study suggests a higher risk of acidosis when using normal saline solutions versus lactated Ringer's solution. The typical fluid requirement for a

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70-kg adult is about 3,000 to 4,000 mL. In addition, 500 mL of 5% albumin is given. The recipient's blood is usually typed and screened, but blood loss is minimal, so transfusion is unlikely. The anesthesiologist should attempt to maintain a systolic blood pressure range of 130 to 160 mm Hg, CVP between 10 and 14 cm H_2O, and/or mean pulmonary artery pressure of 18 to 20 mm Hg.

The intravenous administration of adequate volumes of fluid is associated with earlier onset of graft function, lower postoperative serum creatinine, higher postoperative creatinine clearance, reduced incidence of delayed graft function, and improved graft survival.

Khajavi MR, Etezadi F, Moharari RS, et al. Effects of normal saline vs. lactated ringer's during renal transplantation. *Ren Fail.* 2008;30(5):535-539.

Othman MM, Ismael AZ, Hammouda GE. The impact of timing of maximal crystalloid hydration on early graft function during kidney transplantation. *Anesth Analg.* 2010;110(5):1440-1446.

C.3. How would you conduct the anesthesia induction?

The circumstances for renal transplant can vary between a scheduled or emergent procedure. Living donor transplants are scheduled surgical cases. Patients receiving cadaver kidneys may learn of the surgical procedure under short notice. Standard anesthesia monitors are required prior to induction. The central venous line and/or arterial line are usually placed after induction.

The induction of general anesthesia and intubation of the trachea can be safely accomplished with several of the commonly used drugs. The induction drugs should be given slowly to minimize the chance of drug-induced hypotension. Regardless of blood volume status, these patients often respond induction of anesthesia as if they were hypovolemic. The sympathetic nervous system response may be attenuated by antihypertensive therapy or diabetic autonomic neuropathy. A blunted sympathetic response impairs compensatory peripheral vasoconstriction. In addition, the central nervous system (CNS) may exhibit an increased sensitivity to the induction drugs. Low serum protein and albumin levels can increase the level of unbound drug crossing the blood-brain barrier into CNS receptors. Uremia can also disrupt the blood-brain barrier. The dose of induction agent may need to be adjusted based on volume status, acidic pH, and comorbidities. Propofol, thiopental, or etomidate can be used in routine circumstances. A reduced induction dose of propofol or thiopental may be considered because lower plasma protein levels and postdialysis hypovolemia can exaggerate their cardiodepressant effects. Of note, an animal study model has noted reduced ischemia/reperfusion injury with the use of propofol anesthesia. Ketamine pharmacokinetics is not significantly altered by renal disease, but its hypertensive effects make it undesirable in patients with underlying hypertension. Etomidate is well tolerated and preserves hemodynamic stability.

Large fluctuations in blood pressure and heart rate may occur in patients with preexisting hypertension during intubation. Underlying coronary artery disease is a major consideration. Opioids can blunt the response to laryngoscopy. Fentanyl in moderate doses (5 μg per kg) can be used, but there is a small risk of hypotension after induction and lack of stimulation. Remifentanil is also effective for heart rate control. A short-acting β-blocker such as esmolol (0.5 to 1.0 mg per kg) can blunt the response to intubation.

A number of neuromuscular-blocking agents can be used to facilitate tracheal intubation. Patients with uremia and diabetes may have gastroparesis. Pretreatment with a clear, nonparticulate antacid such as 30 mL of sodium citrate raises gastric pH. A rapid sequence induction with cricoid pressure using either succinylcholine or rocuronium may be required to prevent reflux and aspiration. Succinylcholine can be used safely as potassium release is not exaggerated in patients with chronic renal failure. If the preoperative potassium is in the high normal range or if there is underlying metabolic acidosis, the additional increase of 0.5 to 1.0 mEq per L should be considered. When choosing a nondepolarizing agent for maintenance, it is better to use ones that are independent of renal clearance mechanisms (cisatracurium, atracurium).

Schmid S, Jungwirth B. Anaesthesia for renal transplant surgery: an update. *Eur J Anaesthesiol.* 2012;29(12): 552-558.

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C.4. Is succinylcholine contraindicated in renal failure patients?

Normally, succinylcholine causes an increase in serum potassium of 0.5 to 1.0 mEq per L within 3 to 5 minutes after intravenous administration, and lasts less than 10 to 15 minutes. Succinylcholine can be used safely in patients with chronic renal failure if the potassium concentration is less than 5.5 mEq per L and repeated doses are avoided. Potassium flux after administration of succinylcholine in patients with renal failure does not differ from normal patients. Plasma cholinesterase activity has been reported to be below normal in more than 20% of ESRD patients whether they are receiving any form of dialysis. Values are rarely so low that they cause a prolonged block.

Miller RD, Cohen NH, Eriksson LI, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier/Churchill-Livingstone; 2015:958-994, 2262-2291.

TABLE 25.2 Pharmacokinetics of Neuromuscular-Blocking Agents in Normal versus Anephric Patients

DRUG	RENAL EXCRETION (%)	NORMAL $t_{1/2}$ (min)	ANEPHRIC $t_{1/2}$ (min)
Pancuronium	85	132	258
Rocuronium	10	42	58
Vecuronium	40-50	54	84
Atracurium	10-40	18	24
Cisatracurium	16	34	No effect
Mivacurium	<5%	1.8	3.6
Succinylcholine	<25%	1	1

C.5. How are the nondepolarizing muscle relaxants affected by renal failure?

Table 25.2 notes the commonly used nondepolarizing agents and how they are affected by renal failure. The prolonged duration of action to nondepolarizing agents is primarily due to slow renal clearance. Cisatracurium mainly undergo Hoffman elimination that is not altered in patients with CKD. Renal failure may delay clearance of laudanosine, the principal metabolite of cisatracurium. Laudanosine does not have effect at the neuromuscular junction but at high plasma levels may act as a CNS stimulant. The long-acting muscle relaxant such as pancuronium is not suitable for use as the kidneys excrete most of the drug and its metabolite. The prolonged effect of a nondepolarizing agent may not be apparent after a single small dose. After a small dose, the termination of action is by redistribution rather than elimination. It is only after a single large dose, repeated dosing, or prolonged infusion that the increased elimination half-life becomes clinically apparent. It has also been shown that there are large differences in pharmacokinetics with renal failure patients receiving rocuronium. Maintenance doses for patients with decreased renal function should be smaller, and the interval between doses should be increased. Monitoring of neuromuscular blockade with a nerve stimulator is recommended.

Miller RD, Cohen NH, Eriksson LI, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier/Churchill-Livingstone; 2015:958-994, 2262-2291.

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Staals LM, de Boer HD, van Egmond J, et al. Reversal of rocuronium-induced neuromuscular block by sugammadex is independent of renal perfusion in anesthetized cats. *J Anaesth.* 2011;25(2):241-246.

Staals LM, Snoeck MM, Driessen JJ, et al. Reduced clearance of rocuronium and sugammadex in patients with severe to end-stage renal failure: a pharmacokinetic study. *Br J Anaesth.* 2010;104(1):31-39.

C.6. How would you maintain anesthesia during the case?

General anesthesia is the preferred technique for kidney transplantation. Volatile agents, opioids, and a muscle relaxant are required to provide optimal operating conditions.

The choice of inhaled anesthetic includes desflurane and isoflurane. Sevoflurane may be avoided because the metabolism of sevoflurane has been implicated in renal toxicity due to production of fluoride and compound A. Desflurane and isoflurane do not have any nephrotoxic potential secondary to fluoride accumulation.

Opioids such as fentanyl, sufentanil, alfentanil, and remifentanil can be used during the procedure. Morphine and meperidine have metabolites that depend on renal clearance and can accumulate. A muscle relaxant that is not dependent on renal clearance such as cisatracurium should be used.

Hypotension may occur after unclamping the iliac vessels and reperfusion of the graft. It is important to maintain the blood pressure because renal function is critically dependent on adequate perfusion. It is critical that the patient is adequately hydrated throughout surgery in preparation for reperfusion of the graft. Close monitoring of the CVP and lightening the level of anesthesia during hemodynamic instability can prevent hypotension. Vasopressors with α-agonist action should be avoided because they can comprise blood flow to the transplanted

organ. Additional fluid may be required to maintain blood pressure and replace urine output. Furosemide or mannitol can enhance urine output. Loop diuretics block the Na/K channels in the thin ascending loop of Henle. This prevents reabsorption of electrolytes in this part of the nephron. The high-osmolar fluid then prevents reabsorption of water in the distal tubule. A large volume of fluid with high electrolyte content is excreted. Mannitol is freely filtered in the glomerulus but not reabsorbed. It causes osmotic expansion of urine volume.

The estimated blood loss during the case ranges between 200 and 500 mL. In some cases, greater blood loss may require transfusion of packed red blood cells. Packed red blood cells should be cytomegalovirus-negative. At the end of surgery, patients can be given reversal agents and extubated promptly. Patients are then transferred to the postanesthesia care unit (PACU) for continued monitoring of urine output and electrolytes.

Morris P, Knechtle SJ. *Kidney Transplantation: Principles and Practice.* 7th ed. Philadelphia, PA: Saunders Elsevier; 2014.

Spiro MD, Eilers H. Intraoperative care of the transplant patient. *Anesthesiol Clin.* 2013;31(4):705-721.

C.7. What are the effects of inhalation anesthetics on renal blood flow (RBF), glomerular filtration, and urine output?

All volatile anesthetics produce a dose-related transient and reversible decrease in RBF, GFR, urine output, and the urinary excretion of sodium. This is primarily in response to a decline in systemic blood pressure and cardiac output. Reduced RBF, loss of renal autoregulation, and neurohumoral and neuroendocrine factors also contribute. Specific differences among the agents on renal function are to be noted. Desflurane and sevoflurane are two most frequently used inhalational anesthetics. Desflurane has demonstrated better hepatic and renal function tests after surgery when compared to sevoflurane.

Ko JS, Gwak MS, Choi SJ, et al. The effects of desflurane and sevoflurane on hepatic and renal functions after right hepatectomy in living donors. *Transpl Int.* 2010;23(7):736-744.

Miller RD, Cohen NH, Eriksson LI, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier/Churchill-Livingstone; 2015:958-994, 2262-2291.

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C.8. What are the potential nephrotoxic effects of inhalation anesthetics? What are the nephrotoxic metabolites of inhalation anesthetics?

Fluoride-induced nephrotoxicity is a potential hazard following metabolism of volatile anesthetics. Desflurane (0.02%), isoflurane (0.2%), enflurane (2%), sevoflurane (2% to 3%), and halothane (12% to 20%) are metabolized in the body (rule of 2). When serum inorganic fluoride reaches 50 to 80 mmol per L, subclinical renal toxicity (laboratory abnormalities) occurs. Clinical nephrotoxicity usually becomes apparent when the serum fluoride level is more than 80 mmol per L. The high-output renal failure is dose-related and characterized by vasopressin-resistant polyuria, hypernatremia, serum hyperosmolarity, increased serum urea nitrogen, and inorganic fluoride concentration. Despite the potential for relatively high plasma levels of fluoride after long exposure to newer anesthetics, the minimal amount of sevoflurane and enflurane renal defluorination may explain the relative absence of serious renal concentrating defects with these anesthetics. Although the conventional measurements of renal function (blood urea nitrogen, creatinine) are not altered, evidence shows transient impairment of renal concentrating ability and renal tubular injury in patients receiving sevoflurane or enflurane. Nevertheless, it has not been confirmed whether administration of sevoflurane in patients with preexisting renal disease could further deteriorate renal function. Fluoride levels after isoflurane and halothane increase by 3 to 5 μM per L and 1 to 2 μM per L, respectively. These agents do not pose a risk for nephrotoxicity. Desflurane is resistant to biodegradation because fluorine is the only halogen in the desflurane molecule. Mean inorganic fluoride concentration after 1 minimum alveolar concentration (MAC) hour exposure to desflurane is less than 1 μmol per L. Prolonged exposure to desflurane (7.0 MAC hours) has been associated with normal renal function in patients without renal disease. Neither desflurane nor isoflurane lead to a deterioration of creatinine clearance in patients with preexisting renal impairment.

Sodium or barium hydroxide lime absorbents react with sevoflurane, resulting in a byproduct called *compound A.* The nephrotoxic potential of compound A has been noted in animals and is inconclusive in human studies. The concentrations that occur in humans are far below the nephrotoxic levels in animals. A fresh gas flow of 1 L per minute or higher is recommended to minimize the accumulation of compound A in the breathing circuit. Lowflow sevoflurane (1 L per minute) has been used on many occasions with no effect on renal function. Carbon dioxide absorbents that contain calcium hydroxide and calcium chloride do not result in compound A formation when exposed to sevoflurane. The U.S. Food and Drug Administration (FDA) recommends the use of sevoflurane with fresh gas flow rates at least 1 L per minute for exposures up to 1 hour and at least 2 L per minute for exposures greater than 1 hour. Nevertheless, it is important to note that other countries have not recommended such limitations on the clinical use of sevoflurane and problems have not been noted.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia.* 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:438-439, 1356.

Frink EJ Jr, Malan TP Jr, Isner RJ, et al. Renal concentrating function with prolonged sevoflurane or enflurane anesthesia in volunteers. *Anesthesiology.* 1994;80:1019-1025.

Gentz BA, Malan TP Jr. Renal toxicity of sevoflurane: a storm in a teacup? *Drugs.* 2001;61:2155-2162. Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease.* 6th ed. Philadelphia, PA: Churchill Livingstone; 2012:338.

Litz RJ, Hübler M, Lorenz W, et al. Renal response to desflurane and isoflurane in patients with renal insufficiency. *Anesthesiology.* 2002;97:1133-1136.

C.9. How does renal failure affect the pharmacology of opioids?

The effect of renal failure on individual opioids varies, so one must consider the effect of renal failure on drug metabolites as well as the parent compound.

Morphine is metabolized in the liver to morphine-6-glucuronide (M6G) (10%), morphine-3-glucuronide (M3G) (55%), and normorphine (4%), all of which are excreted by the kidneys, along with about 10% of the parent compound, in subjects with normal renal function. M6G has been reported to mediate CNS and respiratory depression when it accumulates in renal failure.

Meperidine is metabolized in the liver to normeperidine, also excreted by the kidneys. Accumulation of this metabolite may

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lead to excitatory CNS effects such as convulsions.

Fentanyl is metabolized by the liver, with only 7% excreted unchanged in the urine. Fentanyl is suitable for use during surgery and is safe in the short term. There are reports of the parent compound accumulating during renal failure, but clinical experience is that there are no adverse effects. However, if being used long term in renal failure patients, the pharmacodynamic effects should be monitored carefully.

Alfentanil metabolism occurs by inducible cytochrome c enzymes in the liver, making it suitable for renal failure patients. The clearance and half-life of sufentanil and alfentanil are not significantly different in patients with reduced renal function.

Remifentanil is metabolized by blood and tissue esterases. The principle metabolite of remifentanil (GR90291) is eliminated by the kidney. The reduced renal elimination of this metabolite is not of clinical significance because the potency is 1 in 4,000 of the parent compound.

Nayak-Rao S. Achieving effective pain relief in patients with chronic kidney disease: a review of analgesics in renal failure. *J Nephrol.* 2011;24(1):35-40.

Niscola P, Scaramucci L, Vischini G, et al. The use of major analgesics in patients with renal dysfunction. *Curr Drug Targets.* 2010;11(6):752-758.

D. Postoperative Management

D.1. How is the diagnosis of transplant rejection made?

There are various forms of rejection such as hyperacute, accelerated acute, acute, and chronic. Acute rejection is the most common, but less common with immunosuppressive agents. It is usually seen within days to a few months posttransplant. The diagnosis is made with a renal

biopsy. In patients with prolonged delayed graft function, surveillance biopsies can detect or exclude acute rejection episodes. The process is associated with systemic symptoms such as fever, chills, malaise, and arthralgias. However, with current immunosuppressive drugs, most acute rejection episodes are generally asymptomatic. Laboratory data note a rapid increase in creatinine of 10% to 25% over baseline with or without a decrease in urine output.

Nankivell BJ, Alexander SI. Rejection of the kidney allograft. *N Engl J Med.* 2010;363:1451-1462.

D.2. What are immunosuppressive agents and how do they affect anesthetic care?

Induction drugs are antirejection medicines used at the time of transplant. The patient is then placed on maintenance drugs for the long term.

There are generally four classes of maintenance drugs:

- Calcineurin inhibitors: tacrolimus, belatacept, cyclosporine
- Antiproliferative agents: mycophenolate mofetil, mycophenolate sodium, azathioprine
- TOR inhibitors: sirolimus, everolimus
- Steroids: prednisone

Some of the side effects of immunosuppressive agents may be encountered if a posttransplant patient presents for other surgeries and are pertinent to anesthetic care:

- Calcineurin inhibitors: nephrotoxicity, hypertension, hyperchloremic acidosis, hyperkalemia, hypomagnesemia, hypocalcemia, glucose intolerance, coarse tremor, dysesthesia, headache, seizure, prolonged QT interval, hypercoagulability, acute microvascular disease (similar to thrombotic thrombocytopenic purpura)
- Mycophenolate mofetil: nausea, vomiting, cytopenia (leukopenia, anemia, thrombocytopenia), leukocytosis
- TOR inhibitors: mucocutaneous ulceration, hypokalemia, hypomagnesemia, impaired wound healing, interstitial pneumonia, cytopenia

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- Azathioprine: cytopenia, hepatitis

Halleck F, Friedersdorff F, Fuller TF, et al. New perspectives of immunosuppression. *Transplant Proc.* 2013;45(3):1224-1231.

Laftavi MR, Sharma R, Feng L, et al. Induction therapy in renal transplant recipients: a review. *Immunol Invest.* 2014;43(8):790-806.

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Chapter 26
Robotic-Assisted Laparoscopic Surgery

Judith Weingram

A 72-year-old man with biopsy-proven carcinoma of the prostate had a prostatespecific antigen (PSA) of 22 ng per mL but negative pelvic computed tomography (CT) and bone scans. He weighed 120 kg. Despite hypertension, a 50 pack-year smoking history, and recent surgery for retinal detachments, he was vigorous and active. He chose to be treated surgically.

A. Medical Disease and Differential Diagnosis

1. What is the incidence of carcinoma of the prostate?
2. How is prostate cancer diagnosed?
3. How is prostate cancer treated?
4. Define laparoscopy.
5. Describe the development of robotic-assisted laparoscopy.
6. What are the advantages and disadvantages of laparoscopy?
7. What are the differences in pulmonary function after laparoscopic cholecystectomy compared with open cholecystectomy?
8. What are the contraindications to laparoscopic surgery? Is pregnancy a contraindication to laparoscopic surgery?
9. What other specialties commonly perform laparoscopic or other endoscopic surgery?
10. Why is carbon dioxide (CO_2) the gas of choice for laparoscopy? What are its disadvantages?
11. How much endogenous CO_2 is produced at basal level and at maximal exercise?
12. How much CO_2 is stored in the body? Where is it stored? Of what significance is this to laparoscopy?
13. Describe the diffusion and solubility properties of CO_2 and their significance in laparoscopy.
14. Is CO_2 soluble in water or plasma? Is it soluble in blood? Why?

B. Preoperative Evaluation and Preparation

1. What do you want to know about this patient's history and physical condition that may affect whether or not you clear him for laparoscopic surgery?
2. What factors increase this patient's risk of pulmonary complications?
3. What laboratory tests should be performed preoperatively?
4. What specific information should the patient be given about robotic surgery before obtaining informed consent?
5. What additional procedures should be done before surgery?

6. What are the three major forces that uniquely alter the patient's physiology during laparoscopy?

C. Intraoperative Management

1. What is the anesthetic technique of choice for robotic-assisted laparoscopy? Why?
2. Can a laryngeal mask airway (LMA) be used?
3. What anesthetic agents or adjuvant drugs are recommended for laparoscopy? Are any anesthetic agents

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contraindicated?

4. Should nitrous oxide (N_2O) be used during laparoscopy? What are the pros and cons? Does N_2O cause bowel distention during laparoscopy? Does N_2O cause nausea and vomiting after laparoscopy?
5. Can laparoscopy be performed under local anesthesia or regional anesthesia?
6. What monitors and devices would you apply to the patient? Why?
7. How is the patient to be positioned? What special precautions are required for robotic laparoscopy?
8. How will you ventilate the patient? What are the respiratory and circulatory effects of the Trendelenburg position during laparoscopy?
9. What techniques are available for initial laparoscopic access to the peritoneal cavity? What anesthetic problems can arise during insufflation?
10. What intravenous (IV) solution and how much fluid volume do you plan to infuse?
11. Under what circumstances should laparoscopy be converted to laparotomy?
12. What is the arterial to end-tidal CO_2 ($PETCO_2$) gradient ($PaCO_2$-$PETCO_2$) in the normal awake patient? What is the cause of the gradient? Does the gradient change during laparoscopy? Why?
13. Is an arterial line necessary? Why? Does end-tidal CO_2 tension accurately reflect arterial CO_2 tension? Under what circumstances may the $PETCO_2$ exceed the $PaCO_2$? Why?
14. What are the possible causes of hypercarbia?
15. What factors play a role in the unusually rapid and marked elevation of CO_2 that is sometimes seen in laparoscopy?
16. How rapidly does the $PaCO_2$ rise in the apneic patient (endogenous CO_2)? How rapidly does the $PaCO_2$ rise if 5% CO_2 gas is inhaled (exogenous)? How rapidly can the CO_2 rise during laparoscopy? What factors explain the differences?
17. What are the direct and indirect effects of hypercarbia on the cardiovascular system? How are these effects altered by increased intra-abdominal pressure and patient position during laparoscopy?
18. What are the direct and indirect effects of hypercarbia on the respiratory system? Are these effects altered by increased intra-abdominal pressure and patient position?
19. What are the direct and indirect effects of hypercarbia on the central nervous system? How are these effects altered by increased intra-abdominal pressure and patient position during laparoscopy?
20. What are the neuroendocrine changes that occur during laparoscopy?
21. What are the direct and indirect effects of laparoscopy on the renal system?
22. What is the effect of laparoscopy on the bowel and gastrointestinal system?
23. How would you recognize a CO_2 embolism during laparoscopy? How does this differ from an air embolism? Why should N_2O be discontinued during suspected embolization? Will N_2O increase the size of CO_2 emboli?
24. What is the mechanism of increase in shunting resulting from embolization?

25. How is a gas embolism (CO_2 or air) treated?
26. What are the causes of pneumothorax or pneumomediastinum during laparoscopy? How would you diagnose it? How would you treat it?
27. How would you decide when to extubate?

D. Postoperative Management

1. What are some of the unique complications of laparoscopy?
2. What postoperative orders will you write? When would you remove the Foley catheter and arterial line? Under what circumstances would you order a chest x-ray film?

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3. What is the incidence of postoperative nausea and vomiting?

A. Medical Disease and Differential Diagnosis

A.1. What is the incidence of carcinoma of the prostate?

Carcinoma of the prostate is the most frequently diagnosed cancer (except for skin cancer) in American men. In 1983, the incidence of carcinoma of the prostate was approximately 75,000 new cases along with 25,000 deaths of old cases. In 2014, the American Cancer Society estimates that the newly diagnosed incidence will be 233,000 (or 27% of all new cancers) and 29,480 deaths in existing cases (or 10% of all cancer deaths).

This “epidemic” increase in carcinoma of the prostate stems from widespread use of the PSA blood test to detect the disease earlier rather than from a true rise in incidence of the disease. Undetected microscopic prostate cancer cells are believed to be present in 30% to 40% of men older than the age of 50 years and in 75% of men older than the age of 75 years, but it is estimated that only approximately 8% of these men will develop clinically significant disease. It has been stated that more men die *with* prostate cancer than *from* it. Therefore, it is not yet known whether early detection of subclinical disease, much of which may have remained clinically insignificant, will improve survival.

Carcinoma of the prostate is rare in Asian men, whereas African-American men have about twice the incidence as white American men.

American Cancer Society. *Cancer Facts & Figures 2014.* Atlanta, GA: American Cancer Society; 2008. Jemal J, Siegel R, Xu J, et al. Cancer statistics, 2010. *CA Cancer J Clin.* 2010;60(5):277-300.

Potosky AL, Miller BA, Albertsen PC, et al. The role of increasing detection in the rising incidence of prostate cancer. *JAMA.* 1995;273:548-552.

A.2. How is prostate cancer diagnosed?

The most reliable methods for diagnosis include a digital rectal examination plus the serum PSA level. Palpation of a tumor or indurated area and finding an elevated PSA should be followed by prostatic needle biopsies, perhaps under transrectal ultrasound guidance.

Hayes JH, Barry MJ. Screening for prostate cancer with the prostate-specific antigen test: a review of current evidence. *JAMA.* 2014;311:1143-1149.

Qaseem A, Barry MJ, Denberg TD, et al. Screening for prostate cancer: a guidance statement from the Clinical Guidelines Committee of the American College of Physicians. *Ann Intern Med.* 2013;158:761-769.

A.3. How is prostate cancer treated?

Treatment choices vary not only with the stage of the disease but also with the patient's age and life expectancy, associated medical conditions, and lifestyle. In patients with localized disease, treatment choices include “watchful waiting,” brachytherapy (in which radioactive seeds are implanted in the prostate gland), radiation (including external beam, intensity modulated radiation therapy, stereotactic therapy, proton beam therapy, etc.), cryosurgery, vaccine therapy, and other nonsurgical treatments. Surgical options include traditional open radical prostatectomy performed through either a retropubic (lower abdominal) or perineal incision or laparoscopic radical prostatectomy, which can be hand-assisted or robot-assisted.

A patient with nonlocalized disease may choose to be treated with radiation, hormones, chemotherapy, other nonsurgical options, or even to have no treatment.

Coelho RF, Rocco B, Patel MB, et al. Retropubic, laparoscopic, and robot-assisted radical prostatectomy: a critical review of outcomes reported by high-volume centers. *J Endourol.* 2010;24:2003-2015.

D'Alonzo RC, Gan TJ, Moul JW, et al. A retrospective comparison of anesthetic management of robot-assisted

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laparoscopic prostatectomy versus radical retropubic prostatectomy. *J Clin Anesth.* 2009;21(5):322-328.

Lim SK, Kim KH, Shin TY, et al. Current status of robot-assisted laparoscopic radical prostatectomy: how does it compare with other surgical approaches? *Int J Urol.* 2013;20:271-284.

A.4. Define laparoscopy.

Laparoscopy (or peritoneoscopy) is a “minimally invasive” procedure allowing endoscopic access to the peritoneal cavity after insufflation of a gas (CO_2) to create space between the anterior abdominal wall and the viscera. The space is necessary for the safe manipulation of instruments and organs. Laparoscopic surgery can also be extraperitoneal. It can also be gasless with abdominal wall retraction, and more recently, it may be hand-assisted or robotically assisted.

Seifman BD, Wolf JS Jr. Technical advances in laparoscopy: hand assistance, retractors, and the pneumodissector. *J Endourol.* 2000;14:921-928.

A.5. Describe the development of robotic-assisted laparoscopy.

The era of open incisions in which surgeons could directly see, touch, and manipulate organs was superseded by minimally invasive surgery in which tiny cameras and laparoscopes could be inserted through small ports in the patient's body. However, conventional laparoscopy is limited by poor depth perception (visualization on a two-dimensional monitor) and the use of long, straight instruments that limit mobility and dexterity.

Robotic devices were initially designed by National Aeronautics and Space Administration (NASA) for the purpose of performing tasks outside the Space Shuttle while being controlled remotely from inside the spacecraft or from earth. This technology was adapted for surgery as the Da Vinci computer-assisted robotic system.

The surgeon sits at a remote control console near the patient and operating room table and views the operative field as a high-resolution magnified three-dimensional image transmitted from a video camera. By using hand-and-finger control devices, the surgeon can precisely manipulate the mechanical arms of the robot to achieve wrist-like motion. Foot pedals also allow the surgeon to more precisely control the robot, camera, and cautery.

Awad H, Walker CM, Shaikh M, et al. Anesthetic considerations for robotic prostatectomy: a review of the literature. *J Clin Anesth.* 2012;24:494-504.

Wilson T, Torrey R. Open versus robotic-assisted radical prostatectomy: which is better? *Curr Opin Urol.* 2011;21(3):200-205.

A.6. What are the advantages and disadvantages of laparoscopy?

The advantages include the cosmetic results of small, non-muscle-splitting incisions, decreased blood loss, less postoperative pain and ileus, shorter hospitalization and convalescence, and ultimately lower cost. Postoperative respiratory muscle function returns to normal more quickly than in open surgery, especially in laparoscopic cholecystectomy and other upper abdominal procedures. Wound complications such as infection and dehiscence are less frequent, and host defense mechanisms may be greater in laparoscopic than in open surgery.

The disadvantages include the long learning curve for the surgeon (most complications occur during the first 10 laparoscopies), the narrowed two-dimensional visual field on video in conventional laparoscopy, the need for general anesthesia, and the potentially longer operative duration. Ideally, surgeons should have more advanced laparoscopic skills, especially in knot tying, suturing, and working two instruments simultaneously. The use of simulators to enhance these skills has been advocated.

Robotic-assisted laparoscopy, by virtue of its high-resolution three-dimensional visualization and greater precision, offers a greater likelihood of nerve sparing in prostatectomy and, therefore, retention of continence and potency. The disadvantages of the robot include added

operative time, the high cost (in millions of dollars) of equipment purchase and maintenance, and the need for a permanently dedicated operating room location for this heavy and bulky equipment.

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Robot-assisted laparoscopic radical prostatectomy is now the most commonly performed robotic surgery in the United States.

Conacher ID, Soomro NA, Rix D. Anaesthesia for laparoscopic urological surgery. *Br J Anaesth.* 2004;93(6):859-864.

Soto E, Lo Y, Friedman K, et al. Total laparoscopic hysterectomy versus da Vinci robotic hysterectomy: is using the robot beneficial? *J Gynecol Oncol.* 2011;22:253-259.

A.7. What are the differences in pulmonary function after laparoscopic cholecystectomy compared with open cholecystectomy?

Pulmonary function is substantially impaired after a large upper abdominal or subcostal muscle-splitting incision, as in open cholecystectomy. Marked diaphragmatic dysfunction occurs postoperatively due to both reflex diaphragmatic changes and incisional pain. Vital capacity and functional residual capacity (FRC) may be reduced by 20% to 40% of preoperative values, and they may not return to normal until 2 to 3 days after surgery. The mini-incision of laparoscopic cholecystectomy results in far less pulmonary and diaphragmatic loss of function as well as less ileus.

Bablekos GD, Michaelides SA, Roussou T, et al. Changes in breathing control and mechanics after laparoscopic vs open cholecystectomy. *Arch Surg.* 2006;141(1):16-22.

Gunnarsson L, Lindberg P, Tokics L, et al. Lung function after open versus laparoscopic cholecystectomy. *Acta Anaesthesiol Scand.* 1995;39:302-306.

Hong SJ, Cho EJ, Lee JY, et al. The physiologic response to laparoscopic cholecystectomy: CO(2) pneumoperitoneum vs wall lift. *Can J Anaesth.* 2003;50(2):200-201.

A.8. What are the contraindications to laparoscopic surgery? Is pregnancy a contraindication to laparoscopic surgery?

Increasing experience with the laparoscopic technique has made most contraindications relative rather than absolute. However, it is probably best to avoid or to use extreme caution in patients with a coagulopathy, a diaphragmatic hernia, severe cardiovascular or pulmonary disease (including bullae), increased intracranial pressure or space-occupying masses, a retinal detachment, impending renal shutdown, a history of extensive surgery or adhesions, sickle cell disease (because sickle crisis may be precipitated by acidosis), peritonitis, a large intra-abdominal mass, a tumor of the abdominal wall, or hypovolemic shock. Patients with shunts (e.g., ventriculoperitoneal) are at risk for gas emboli, shunt obstruction, and intracranial hypertension, all of which may occur during laparoscopy and may require intracranial pressure monitoring and ventricular drainage if laparoscopic surgery is necessary. In summary, most of the contraindications concern patients who are unable to tolerate extremes of position, pneumoperitoneum, and/or hypercarbia.

Although pregnancy has been considered a contraindication to laparoscopic surgery in the past, an increasing number of such procedures are being performed in the parturient. Laparoscopic cholecystectomy is now more frequent than open cholecystectomy in the pregnant patient. The overall objective of laparoscopic and open surgery is to preserve fetal and maternal well-being and to prevent premature labor. In addition to the general problems of anesthesia for the parturient, the anesthesiologist also must consider the specific problems that result from the interplay between the anatomic and physiologic changes of pregnancy and the anatomic and physiologic triad of pneumoperitoneum, hypercarbia, and positional changes.

Factors to consider in the management of the pregnant patient include awareness of her increased blood volume, increased cardiac output, decreased systemic vascular resistance (SVR), hypercoagulability, the supine hypotensive syndrome, increased respiratory minute volume, decreased residual volume, decreased FRC, increased oxygen consumption, mild hypocapnia, increased risk of aspiration, and decreased anesthetic requirement. This combination of factors tends to promote hypercarbia and hypoxemia. However, extreme

hyperventilation may result in decreased uteroplacental perfusion. Arterial blood gas monitoring has been suggested to

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detect fetal acidosis because capnography may not reveal a large arterial to end-tidal difference in CO_2. In all cases, preoperative and postoperative fetal and uterine monitoring is essential.

Chohan L, Kilpatrick CC. Laparoscopy in pregnancy: a literature review. *Clin Obstet Gynecol.* 2009;52(4):557-569.

Ravaoherisoa J, Meyer P, Afriat R, et al. Laparoscopic surgery in a patient with ventriculoperitoneal shunt: monitoring of shunt function with transcranial Doppler. *Br J Anaesth.* 2004;92(3):434-437.

Steinbrook RA, Bhavani-Shankar K. Hemodynamics during laparoscopic surgery in pregnancy. *Anesth Analg.* 2001;93:1570-1571.

A.9. What other specialties commonly perform laparoscopic or other endoscopic surgery?

Laparoscopic procedures in urology have become standard, especially for prostatectomy, uncomplicated adrenalectomy, and nephrectomy, including live donor nephrectomy. Laparoscopic gynecologic surgery includes tubal surgery (sterilization, treatment of ectopic pregnancy, etc.), cystectomies, hysterectomies, various ablations (endometriosis), and so on. Laparoscopy is performed in pregnancy and also in pediatrics.

Laparoscopic general surgery includes cholecystectomy, hernia repair, antireflux procedures, splenectomy, appendectomy, bowel surgery including bariatric procedures, and various other upper and lower abdominal procedures.

Thoracoscopic, cardiovascular, and neurosurgical intracranial surgery, using modified laparoscopic instruments without the need for gas insufflation, are some of the more recent areas of endoscopic surgery. Lumbar discectomies and other types of spinal surgery also have been done laparoscopically through an anterior approach. Even autopsies have been attempted laparoscopically. The list continues to grow.

Brown SL, Biehl TR, Rawlins MC, et al. Laparoscopic live donor nephrectomy: a comparison with the conventional open approach. *J Urol.* 2001;165:766-769.

Pennant JH. Anesthesia for laparoscopy in the pediatric patient. *Anesthesiol Clin North America.* 2001;19(1):69-88.

Rodrigues ES, Lynch JJ, Suri RM, et al. Robotic mitral valve repair: a review of anesthetic management of the first 200 patients. *J Cardiothor Vasc Anesth.* 2014;28(1):64-68.

A.10. Why is carbon dioxide (CO_2) the gas of choice for laparoscopy? What are its disadvantages?

CO_2 is the insufflating gas of choice because it is nonflammable, does not support combustion, readily diffuses across membranes, is rapidly removed in the lungs, and is highly soluble because of rapid buffering in whole blood. The risk of CO_2 embolization is small. As much as 200 mL of CO_2 injected directly into a peripheral vein may not be lethal, whereas only 20 mL of air may prove to be so. In addition, CO_2 levels in blood and expired air can easily be measured, and its elimination can be facilitated by increasing ventilation. As long as oxygen requirements are met, a high concentration of blood CO_2 can be tolerated. Also, medical grade CO_2 is readily available and inexpensive.

It is for these reasons that the following gases are unsatisfactory for pneumoperitoneum: nitrous oxide (does not cause pain intra-abdominally but does not suppress combustion); oxygen (flammable); helium, air, and nitrogen (each has no hemodynamic or acid-base sequelae but can cause gas emboli); and argon (adverse effect on hepatic blood flow, emboli).

It should be emphasized, however, that CO_2 plays a dual role in the body, and it is not inert. Under normal circumstances, it is an intrinsic waste product of metabolism. During laparoscopic surgery, it acts as an extrinsic drug often present in quantities far larger than the body is physiologically capable of generating even with the most extreme exercise or hypermetabolic state.

The disadvantages mainly stem from the fact that CO_2 is not inert, and it has contradictory roles as an endogenous

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chemical and as an exogenous foreign substance. Changes in its concentration and tensions have enormous biochemical and physiologic consequences. Changes at the local tissue level are often at odds with the overall systemic effect. It causes direct peritoneal irritation and pain during laparoscopy under local anesthesia because it transiently forms carbonic acid when in contact with the moist peritoneum. In addition,

CO_2 is not very soluble in the absence of red blood cells, and therefore, it can remain in gaseous form intraperitoneally (subhepatic) after laparoscopy, causing referred shoulder pain. Hypercarbia and respiratory acidosis occur when the buffering capacity of blood is temporarily exceeded. In addition, CO_2 exerts widespread local and systemic effects that may manifest overall as hypertension, tachycardia, cerebral vasodilation, hypercarbia, and respiratory acidosis.

Menes T, Spivak H. Laparoscopy: searching for the proper insufflation gas. *Surg Endosc.* 2000;14(11):1050-1056.

Tsereteli Z, Terry ML, Bowers SP, et al. Prospective randomized clinical trial comparing nitrous oxide and carbon dioxide pneumoperitoneum for laparoscopic surgery. *J Am Coll Surg.* 2002;195(2):173-180.

Weingram J. Laparoscopic and laser surgery. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery.* New York: McGraw-Hill; 1996:157.

A.11. How much endogenous CO_2 is produced at basal level and at maximal exercise?

CO_2 and water are the major end products of aerobic metabolism in the mitochondria of the cells. Carbonic acid, the major acid produced in the body, is uniquely volatile, and therefore, it must be eliminated mainly by the lungs. (Other acids are eliminated by the kidney.)

At basal rate, an average adult manufactures approximately 200 mL of CO_2 per minute (while consuming 250 mL of O_2) or 12 L of CO_2 (35 g) per hour. At maximal metabolic rate, it is estimated that the body can produce, transport, and excrete 90 to 100 L per hour, an 800% increase over the basal rate.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010:159-173.

A.12. How much CO_2 is stored in the body? Where is it stored? Of what significance is this to laparoscopy?

The body contains approximately 120 L of stored CO_2, most of it in the form of carbonate ion in bone. (This is approximately 100 times the amount of stored oxygen.) CO_2 in the blood is in equilibrium with CO_2 in different tissues. The rate of uptake and distribution of CO_2 from the blood (where it exists as bicarbonate ion) depends on the perfusion and storage capacity of those different tissues. The well-perfused tissues, including brain, kidneys, and blood, come to rapid equilibrium. The medium-perfused compartment consists mainly of resting skeletal muscle. The slowly perfused compartment, mainly fat and bone (where it exists as the carbonate ion), has the largest CO_2 storage capacity. In contrast to rapidly changing oxygen levels, CO_2 levels reach equilibrium more slowly.

These storage sites serve to buffer and stabilize blood CO_2 levels because they provide a place for excess CO_2 to “park” until ventilation can catch up and restore equilibrium. The increase in CO_2 storage during laparoscopy is illustrated clinically by the decelerating rate of rise in $PETCO_2$ despite continuing insufflation. Blood or end-tidal CO_2 levels increase rapidly at first and plateau between 15 and 35 minutes despite continuing low flow insufflation. At constant ventilation, CO_2 levels increase but not as much as if no simultaneous storage processes were occurring. But if ventilation is increased to keep CO_2 constant, then the increase needed is only approximately 40% of the predicted volume of ventilation because of the drain off of CO_2 into the storage sites.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier;

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2010:159-173.

Seed RF, Shakespeare TF, Muldoon MJ. Carbon dioxide homeostasis during anaesthesia for laparoscopy. *Anaesthesia.* 1970;25:223-231.

A.13. Describe the diffusion and solubility properties of CO_2 and their significance in laparoscopy.

Diffusion describes the process by which gases travel from an area of higher partial pressure to one of lower partial pressure. For a gaseous environment, Graham's law states that the rate of diffusion of a gas is inversely proportional to the square root of its density (i.e., the smaller the molecule, the more easily it will diffuse).

TABLE 26.1 Influence of Physical Properties on the Diffusion of Gas through a Gas/Liquid Interface

GAS	MOLECULAR WEIGHT	DENSITY RELATIVE TO O_2	SOLUBILITY RELATIVE TO O_2	WATER DIFFUSION CAPACITY RELATIVE TO O_2
O_2	32	1.0	1.0	1.0
N_2	28	0.88	0.515	0.55
CO_2	44	1.37	24.0	20.5
N_2O	44	1.37	16.3	14.0
He	4	0.125	0.37	1.05

When that same gas molecule arrives at an aqueous membrane (e.g., a gas-liquid interface), the solubility of that gas in water now becomes the major factor in determining its diffusing capacity (as shown in Table 26.1). The water solubility of CO_2 is 24 times that of O_2, whereas the diffusion capacity of CO_2 is 20.5 times that of O_2. The capacity of a gas to diffuse across an aqueous membrane is directly proportional to its solubility in water and inversely proportional to its molecular weight. However, the actual movement of that gas across the aqueous membrane depends not only on its diffusing capacity but also more importantly on the pressure gradient across that membrane (Table 26.1).

The fate of CO_2 gas insufflated into the peritoneal cavity is the same that would occur in any other closed but distensible cavity. The pressure obtained within the cavity varies directly with the volume of gas insufflated and indirectly with the compliance of the closed cavity. Therefore, the ability of CO_2 to move from the closed peritoneal cavity to the lungs for excretion is dependent on its intrinsic diffusion and solubility properties, the rate of continuing CO_2 insufflation, the surface area of the cavity, and the partial pressure difference across membranes.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010:159-173.

McHoney M, Corizia L, Eaton S, et al. Carbon dioxide elimination during laparoscopy in children is age dependent. *J Pediatr Surg.* 2003;38(1):105-110.

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A.14. Is CO_2 soluble in water or plasma? Is it soluble in blood? Why?

CO_2 is relatively insoluble in plasma, interstitial fluid, and water. (Think of the rapid escape of gas from a freshly opened carbonated soft drink.) The solubility of CO_2 in water at 37°C (98.6°F) is only 0.03 mmol/L/mm Hg. This must be contrasted to the very high solubility of CO_2 in whole blood. This extremely important distinction exists because of a zinc-containing enzyme, carbonic anhydrase, that exists within the erythrocyte but not at all in plasma.

$$H_2O + CO_2 \xrightarrow{\text{carbonic anhydrase}} H_2CO_3 \rightarrow H^+ + HCO_3^-$$

In the equation shown, carbonic anhydrase catalyzes the left side of the equation (i.e., the hydration of CO_2 to H_2CO_3). Once formed, carbonic acid is unstable and immediately dissociates into H^+ and HCO_3^-. It is estimated that without carbonic anhydrase, it would take 200 seconds at 38°C (100.4°F) for the previous reaction to come to 10% equilibrium. Because blood travels through the pulmonary capillaries in less than 1 second, carbonic anhydrase speeds up the reaction by a factor of 7,500 times.

Carbonic anhydrase, therefore, allows the insufflated CO_2 gas to be dissolved and carried as bicarbonate in the blood. The process is reversed in the lungs, and the reconstituted CO_2 gas is removed by respiration.

Christian G, Greene NM. Blood carbonic anhydrase activity in anesthetized man. *Anesthesiology.* 1962;23:179-186.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010:159-173.

B. Preoperative Evaluation and Preparation

B.1. What do you want to know about this patient's history and physical condition that may affect whether or not you clear him for laparoscopic surgery?

All patient comorbidities must be evaluated to ensure optimal pharmacologic management preoperatively. Because of this patient's advanced age, it is best to form one's own observations of his mental and physical condition. Is he confused, short of breath, kyphoscoliotic, and so forth? A glimpse at where and how this patient's body weight is distributed means more than just knowing that he weighs 120 kg. Ask about smoking, wheezing, any change in exercise tolerance, cough, recent upper respiratory infection, or change in medications. Perform your usual preoperative evaluation and obtain any consultations that may be informative. Consult with the surgeon regarding the need for appropriate preoperative antibiotics. Find out when his retinal detachments were repaired and if intraocular gas was used.

Efron DT, Bender JS. Laparoscopic surgery in older adults. *J Am Geriatr Soc.* 2001;49:658-663.

B.2. What factors increase this patient's risk of pulmonary complications?

- *The laparoscopic procedure itself.* The basic laparoscopic Trendelenburg position and the increased intraperitoneal volumes and pressures in a paralyzed, mechanically ventilated patient cause respiratory dysfunction. Insufflation pressures should not exceed 12 to 15 mm Hg. Lower pressures are especially advantageous in American Society of Anesthesiologists (ASA) class III and IV patients with diminished cardiopulmonary reserve. In addition, an increased CO_2 load might call for respiratory minute volumes that are so large that further cardiopulmonary compromise occurs.
- *Age.* Pulmonary function declines with age, especially in a patient older than age 70 years.
- *Smoking/chronic obstructive pulmonary disease (COPD).* Smokers have increased tracheobronchial secretions with decreased ciliary transport function. They may already have significant pulmonary dysfunction, which may be manifested by diminished exercise tolerance. The forced vital capacity may be diminished in restrictive pulmonary disease, whereas the forced expired volume in 1 second is likely to be decreased in obstructive pulmonary disease.

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- *Obesity.* Obesity compounds the problems of increased intra-abdominal pressure in the Trendelenburg position. Excessive weight and pressure on the diaphragm and lung bases can lead to marked ventilation and perfusion abnormalities, difficulty in inserting trocars, upward displacement of the carina (leading to possible endobronchial intubation), barotrauma, and so forth.
- *Overhydration.* Patients often experience oliguria during laparoscopy. This may be interpreted as insufficient hydration, and a relative overhydration with intravenous fluids may ensue. Unless frank pulmonary edema occurs, this cause of mild or moderate respiratory distress in the postanesthesia care unit (PACU) may not be recognized without a chest x-ray film.

Kendall AP, Bhatt S, Oh TE. Pulmonary consequences of carbon dioxide insufflation for laparoscopic cholecystectomies. *Anaesthesia.* 1995;50:286-289.

B.3. What laboratory tests should be performed preoperatively?

Basic tests should include complete blood count, urinalysis, clotting functions, electrocardiogram (ECG), and blood typing and screening. In addition, baseline electrolytes, chemistries, and renal function tests (blood urea nitrogen, creatinine) should be obtained because of the possibility of oliguria during a long laparoscopy. Baseline pulmonary function tests, arterial blood gas measurement, and oxygen saturation values while breathing room air would be helpful in this patient. Markedly abnormal values might suggest the need for

bronchodilators, antibiotics, postural drainage, and delay in surgery until pulmonary function is optimal for this particular patient. Baseline chest films are necessary not only to rule out active disease but also for postoperative comparison of acute changes such as subcutaneous or mediastinal emphysema, pneumothorax, or interstitial or pulmonary edema. The presence of bullae on preoperative chest x-ray films may represent a contraindication to laparoscopic surgery because of the accompanying large tidal volumes and high intrathoracic pressures.

In patients with cardiac issues, echocardiogram, stress test, and cardiology clearance may be advisable.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia.* 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1085-1155.

B.4. What specific information should the patient be given about robotic surgery before obtaining informed consent?

In addition to the usual general complications of the planned surgery and anesthesia, the patient must also be told of the complications unique to robotic laparoscopy, and consent for possible laparotomy must be obtained. Emergency laparotomy may be required in the event of complications such as hemorrhage, organ perforation, or anatomic or technical difficulties. The patient should also be told about the possibility of having postoperative referred shoulder pain.

B.5. What additional procedures should be done before surgery?

Although the surgery is described as minimally invasive, the patient must be ready for maximally invasive surgery if necessary. Therefore, the patient must comply with preoperative orders regarding the following:

- Diet—it should consist of clear liquids the day before surgery; nothing orally after midnight.
- A complete bowel preparation is necessary.
- Preoperative antibiotics, as per surgeon

B.6. What are the three major forces that uniquely alter the patient's physiology during laparoscopy?

- *Pneumoperitoneum*, and problems related to the creation, maintenance, and consequences of the increase in intra-abdominal pressure and volume
- *Carbon dioxide*, including its chemical and physical properties and its local and systemic effects
- Extremes of patient *positioning* on the operating table, which in this case will be steep Trendelenburg

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It is vital that the anesthesiologist have a thorough understanding of the physiologic consequences of changes in these three forces. Separately or in combination, they have profound effects on the patient's hemodynamic, respiratory, and metabolic functions. The early gynecologic laparoscopies were usually brief, and they were performed on young, healthy women who tolerated these physiologic trespasses with nearly insignificant changes. These same three forces, however, may produce significant physiologic changes in long, complex laparoscopies in older, sicker patients who may be less able to compensate.

Henny CP, Hofland J. Laparoscopic surgery: pitfalls due to anesthesia, positioning, and pneumoperitoneum. *Surg Endosc.* 2005;19(9):1163-1171.

O'Malley C, Cunningham AJ. Physiologic changes during laparoscopy. *Anesthesiol Clin North America.* 2001;19(1):1-19.

Ost MC, Tan BJ, Lee BR. Urologic laparoscopy: basic physiologic considerations and immunological consequences. *J Urol.* 2005;174(4):1183-1188.

Sosa RE, Weingram J. Physiologic considerations in laparoscopic surgery. *J Endourol.* 1992;6:285-287.

C. Intraoperative Management

C.1. What is the anesthetic technique of choice for robotic-assisted laparoscopy? Why?

The technique of choice for robotic-assisted laparoscopy is general anesthesia with a cuffed endotracheal tube and controlled positive pressure ventilation because of the following reasons:

- Duration may be long.
- Patient may be anxious.
- The Trendelenburg position may cause respiratory compromise and dyspnea in the awake or in the spontaneously breathing patient with abdominal contents under pressure. The obese patient may be especially uncomfortable in this position.
- A nasogastric or orogastric tube, difficult to insert in a conscious patient, is necessary to decompress the stomach and minimize the risk of aspiration or perforation by trocars. CO_2, as well as N_2O, diffuses into the stomach.
- However, perhaps the most important reason relates to muscle relaxation. Muscle relaxation and paralysis are necessary because the increase in intra-abdominal pressure and splinting of the diaphragm make spontaneous breathing difficult. It provides a quieter surgical field and better surgical exposure. “Bucking” increases negative pressure in the chest, which increases the risk of pneumothorax or gas dissection. Coughing can further increase pressure in the abdomen and cause movement of, and perforation by, intra-abdominal instruments. Any movement of the patient while robotic instruments are docked may lead to devastating injuries. Moreover, muscle relaxation is necessary to control and augment ventilation to compensate for the hypercarbia and respiratory acidosis that results from absorption of CO_2.

Brull SJ. Anesthetic considerations for laparoscopic procedures. In: *ASA Refresher Courses in Anesthesiology.* Vol. 23. Park Ridge, IL: American Society of Anesthesiologists; 1995:15-28.

Whalley DG, Berrigan MJ. Anesthesia for radical prostatectomy, cystectomy, nephrectomy, pheochromocytoma, and laparoscopic procedures. *Anesthesiol Clin North America.* 2000;18(4):899-917.

C.2. Can a laryngeal mask airway (LMA) be used?

Although successful use of the LMA has been reported by several British groups for very brief laparoscopic procedures in healthy patients, its use is not recommended. The LMA does not protect against aspiration. It also limits the ability to

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apply positive pressure ventilation and interferes with the use of an orogastric tube.

Bapat PP, Verghese C. Laryngeal mask airway and the incidence of regurgitation during gynecological laparoscopies. *Anesth Analg.* 1997;85:139-143.

C.3. What anesthetic agents or adjuvant drugs are recommended for laparoscopy? Are any anesthetic agents contraindicated?

Almost any combination that provides amnesia, analgesia, and paralysis is suitable. Because closure of a laparoscopic procedure may be abrupt, because patients may be discharged soon after surgery, and because a large painful (stimulating) incision is absent, the most common combinations probably include various hypnotics, analgesics, muscle relaxants, and inhalational agents.

Use of an antiemetic is recommended to counteract the nausea resulting from peritoneal stimulation and bowel distention (secondary to diffusion of CO_2 into the bowel). Small doses of the antiemetic droperidol had been used effectively because it potentiated sedation, was long-acting, could be given early in the procedure, and, as an α-blocker, helped counteract the hypertensive effects of systemic CO_2. Other antiemetics include the serotonin ($5\text{-}HT_3$) receptor antagonists, ondansetron and dolasetron. These may be combined with dexamethasone.

Propofol also has an HT_3 antiemetic effect. However, a propofol-based maintenance anesthetic, when combined with neuromuscular block, may not adequately prevent patient awareness. A bispectral index (BIS) monitor may be helpful in that situation.

A vagolytic drug should be at hand because acute stretching of the peritoneum may cause reflex bradycardia. This is more likely to occur in young women than in older adults.

Halothane is the only anesthetic that should probably be avoided because it may cause arrhythmias in the presence of hypercarbia. Hypnotics and sedatives should be used cautiously in older adults because their duration may be prolonged.

Scuderi PE, D'Angelo R, Harris L, et al. Small-dose propofol by continuous infusion does not prevent postoperative vomiting in females undergoing outpatient laparoscopy. *Anesth Analg.* 1997;84:71-75.

Seed RF, Shakespeare TF, Muldoon MJ. Carbon dioxide homeostasis during anaesthesia for laparoscopy. *Anaesthesia.* 1970;25:223-231.

C.4. Should nitrous oxide (N_2O) be used during laparoscopy? What are the pros and cons? Does N_2O cause bowel distention during laparoscopy? Does N_2O cause nausea and vomiting after laparoscopy?

The use of N_2O has been considered controversial. The controversies surrounding the use of N_2O during laparoscopic surgery involve its effects on bowel distention during surgery and nausea and vomiting postoperatively.

In examining the issue of bowel distention with N_2O, note the following. The diffusion capacity of N_2O is approximately 14 times that of O_2 and 28 times that of nitrogen (see Table 26.1). Therefore, in a closed space that contains air, N_2O enters faster than N_2 can leave, thereby increasing the size of the closed space. It has been shown that the volume of an enclosed intestinal air pocket can be doubled by the inhalation of 70% N_2O for 2 hours and tripled in 4 hours. When N_2O is limited to 50%, pocket volume increases no more than 50%. A much more rapid increase in gas volume occurs in the pleural space, where volume was shown to double in 10 minutes, triple in 45 minutes, and quadruple in 2 hours. The faster rate of pleural gas expansion as compared to bowel gas expansion may in part be due to the greater blood flow to the pleura and possibly due to direct diffusion of N_2O from the alveoli adjacent to the pleura.

However, during laparoscopy, we are concerned about CO_2 pockets and not air pockets. N_2O, which has a diffusion capacity almost as great as CO_2, will diffuse from the bloodstream into the intraperitoneal pocket of 100% CO_2 at a rate determined by its solubility in water, its diffusing capacity through an aqueous membrane, and its pressure gradients (as

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discussed in section A.13). Similarly, CO_2 will leave the peritoneal cavity according to its pressure gradients and solubility and diffusion characteristics. Eventually, the amount of N_2O found in the peritoneal cavity can be significant, and theoretically, it can form an ignition hazard. (However, Hunter states that it is necessary for methane or hydrogen to occupy at least 5.5% of the gas volume for nitrous oxide to support combustion, a condition that does not naturally occur.)

In the situation of an air pocket in the bowel, it is well known that N_2O will diffuse in according to its gradients, thereby enlarging the pocket. However, few realize that even in the absence of N_2O, CO_2 also will diffuse into this pocket and expand it in a manner that is clinically indistinguishable from N_2O.

N_2O is often blamed for a distended bowel during laparoscopy; however, CO_2 is equally capable of diffusing into and distending the bowel. In a double-blinded study of bowel distention in patients undergoing laparoscopic cholecystectomy with either isoflurane 70%-N_2O-O_2 or isoflurane-air-O_2, the surgeon was able to identify the use of N_2O correctly only 44% of the time. In addition, postoperative nausea and vomiting was independent of the use of N_2O because the incidence was similar in both groups. Another study found no difference in the incidence of postoperative nausea and vomiting between groups receiving propofol-air-O_2 or propofol-N_2O-O_2 in gynecologic laparoscopy. In fact, the propofol-N_2O-O_2 group had the advantages of significantly more rapid emergence, using 30% less propofol, additional analgesia, and less risk of awareness.

Because of these issues, it is recommended that N_2O, if used, be limited to not more than 50% of the inspired mixture during laparoscopy. Alternatively, a mixture of 75% air and 25% oxygen (FIO_2 = 40%) may be a wiser choice.

Arellano RJ, Pole ML, Rafuse SE, et al. Omission of nitrous oxide from a propofol-based anesthetic does not affect the recovery of women undergoing outpatient gynecological surgery. *Anesthesiology.* 2000;93(2):332-339.

Diemunsch PA, Torp KD, Van Dorsselaer T, et al. Nitrous oxide fraction in the carbon dioxide pneumoperitoneum during laparoscopy under general inhaled anesthesia in pigs. *Anesth Analg.* 2000;90:951-953.

Diemunsch PA, Van Dorsselaer T, Torp KD, et al. Calibrated pneumoperitoneal venting to prevent N_2O accumulation in the CO_2 pneumoperitoneum during laparoscopy with inhaled anesthesia: an experimental studying pigs. *Anesth Analg.* 2002;94:1014-1018.

Eger EI II, Saidman LJ. Hazards of nitrous oxide anesthesia in bowel obstruction and pneumothorax. *Anesthesiology.* 1965;26:61-66.

Munson ES. Transfer of nitrous oxide into body air cavities. *Br J Anaesth.* 1974;46:202-209.

Sukhani R, Lurie J, Jabamoni R. Propofol for ambulatory gynecologic laparoscopy: does omission of nitrous oxide alter postoperative emetic sequelae and recovery? *Anesth Analg.* 1994;78:831-835.

Taylor E, Feinstein R, White PF, et al. Anesthesia for laparoscopic cholecystectomy. Is nitrous oxide contraindicated? *Anesthesiology.* 1992;76:541-543.

C.5. Can laparoscopy be performed under local anesthesia or regional anesthesia?

Yes. However, under local anesthesia, CO_2 may cause pain intraperitoneally, which is referred to the shoulder. It is for this reason that N_2O, which is nonirritating to the peritoneum, had been used as the insufflating gas for very brief diagnostic laparoscopy under local anesthesia without cautery. However, rapid peritoneal distention causes nausea that may be exacerbated without a nasogastric tube. Because of patient discomfort, the surgeon may obtain suboptimal visualization of the surgical field. Also, the possibility of having to open the abdomen, although unlikely, speaks against local anesthesia.

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Regional anesthesia can be used for laparoscopy. However, it too has serious drawbacks. It requires a high level of sensory block, possibly causing dyspnea in the Trendelenburg position. A nasogastric tube may not be tolerated. Hyperventilation in response to hypercarbia may cause too much movement in the surgical field, and spontaneous ventilation may be inadequate to compensate for hypercarbia in the Trendelenburg position.

Regional anesthesia may also be combined with general anesthesia. Because the systemic response to hypercarbia is mediated primarily through sympathetic stimulation, the sympathetic denervation resulting from high regional anesthesia will result in hypotension and decreased cardiac output rather than the hypertension and increased cardiac output usually seen with general anesthesia.

Use of IV analgesics or propofol during regional anesthesia may result in respiratory depression or obstruction, especially in steep Trendelenburg position. Hypoxia in the presence of hypercarbia may have serious cardiovascular consequences.

Collins LM, Vaghadia H. Regional anesthesia for laparoscopy. *Anesthesiol Clin North America.* 2001;19(1):43-55.

Vaghadia H, Solylo MA, Henderson CL, et al. Selective spinal anesthesia for outpatient laparoscopy. II: epinephrine and spinal cord function. *Can J Anaesth.* 2001;48:261-266.

C.6. What monitors and devices would you apply to the patient? Why?

The usual intraoperative monitors, including standard five-lead ECG with ST trending, systemic blood pressure (BP) using automated oscillometry, pulse oximetry, capnography, a nerve stimulator, and indicators of inspired oxygen fraction, minute ventilation, and peak airway pressures are necessary. An esophageal probe may be used for both temperature monitoring (optimal at the distal esophagus) and for breath, heart, and murmur sound monitoring (at heart level). Body temperature should be maintained with a forced warm air heating blanket, warmed intravenous fluids, or other means. (For robotic procedures, the warming blanket may be placed under the patient.) Rarely, central venous pressure (CVP), pulmonary artery pressure, pulmonary artery occlusion pressure (PAOP), and cardiac output may be measured in patients with severe cardiac or pulmonary abnormalities. A BIS monitor may be used. Other possibilities include Doppler, transesophageal echocardiography, and noninvasive assessment of cardiac output by thoracic bioimpedance or thoracic ultrasound. An arterial line is suggested during longer, more complex laparoscopic procedures in sicker (ASA classes III and IV) patients.

Intermittent sequential compression antiembolic stockings should be applied. Shoulder braces or adhesive taping are used for support in the Trendelenburg position. After induction, a nasogastric or orogastric tube and a Foley catheter are inserted for decompression of

stomach and bladder. Use of an orogastric tube is not optional. In addition to the danger of regurgitation from the increased abdominal pressure, reports have been made of stomach perforation by trocars. The orogastric tube should not be clamped after initial placement, and intermittent suctioning should continue because CO_2 gas continues to diffuse into the stomach and distend it.

In addition to mechanical monitoring, visual and tactile monitoring are necessary during laparoscopy. Skin color, skin turgor, and capillary refill should be monitored because they can change abruptly. The head, neck, and upper chest may assume a purplish color in the dependent position, especially during hypercarbia. The upper chest wall should be checked periodically for subcutaneous emphysema. The cornea and conjunctiva should be checked periodically for edema, especially in the Trendelenburg position, and also whenever oliguria occurs because the extent of the edema may influence your decision on when to extubate.

It is important to maintain accurate data on the volume of fluids infused, and the patient's hourly or half-hourly urine output, along with observations on its color and concentration. Despite adequate hydration, oliguria frequently occurs during pneumoperitoneum, especially at intra-abdominal pressures approaching or exceeding 15 mm Hg. The acute increase in intra-abdominal pressure is transmitted to the kidneys and is believed to cause shunting from the cortex to the medulla of the kidney, resulting in a decreased urine output. Diuresis usually occurs rapidly on release of intra-abdominal pressure.

Jacobs VR, Morrison JE Jr, Mettler L, et al. Measurement of CO_2 hypothermia during laparoscopy and pelviscopy: how cold it gets and how to prevent it? *J Am Assoc Gynecol Laparosc.* 1999;6:289-295.

Ogunnaike BO, Jones SB, Jones DB, et al. Anesthetic considerations for bariatric surgery. *Anesth Analg.*

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2002;95(6):1793-1805.

Tournadre JP, Chassard D, Berrada KR, et al. Effect of pneumoperitoneum and Trendelenburg position on gastro-esophageal reflux and lower oesophageal sphincter pressure. *Br J Anaesth.* 1996;76:130-132.

C.7. How is the patient to be positioned? What special precautions are required for robotic laparoscopy?

In pyeloplasties, the side to be worked on is usually elevated, enabling gravity to assist in separating the organs and allowing blood to pool away from the operative field. For other laparoscopies, the patient may be supine, in the Trendelenburg position (with possible lateral rotation) for urology, in dorsal lithotomy for gynecology, in the head-up position for upper gastrointestinal and biliary tract surgery, and in the lateral decubitus position for thoracoscopy, nephrectomy, and adrenalectomy. For standard conventional laparoscopy, you may or may not be able to keep one or both arms out on boards, depending upon the procedure and the surgeon's needs.

Robotically assisted laparoscopies require careful attention to detail before the robot is docked because no movement of any kind should be possible afterward. Thus, it is especially important to check that any intravenous or arterial lines as well as BP cuff, ECG leads, and pulse oximeter are functioning properly after the arms have been carefully padded and tucked at the patient's sides. This must be done before the patient is lowered into Trendelenburg position. Once the robot is locked into position, you will no longer have access to check the arms or look under the drapes. It is a good idea to cut off the clamps on the IV tubing that may press into the patient's skin while the arms are tightly tucked.

Next, after satisfactory general endotracheal anesthesia has been obtained, the surgeons must secure the patient's position on the table so that he does not slide when placed in extreme Trendelenburg position. One technique is to place towels or sponges across the patient's chest, followed by crisscrossing of wide adhesive tape reaching from one side of the table and patient's chest to the opposite shoulder and opposite side of the table. This X formation is designed to secure the patient to the table. While the surgeons are applying the tape, it is recommended that you put your hand under the chest sponge to ensure that the tape is not tight enough to restrict chest expansion. Other techniques such as padded shoulder braces may be used instead of tape, but the incidence of brachial plexus injury is higher with these.

With the knees flexed in padded leg holders, the patient is now carefully lowered into steep Trendelenburg position. Robotic laparoscopy frequently requires steeper Trendelenburg positioning than conventional laparoscopy, resulting in a greater number of positioning injuries. Care must also be taken to ensure that movements of the large bulky robotic arms do not come in contact with the patient.

Kalmar AF, Foubert L, Hendrickx JF, et al. Influence of steep Trendelenburg position and CO_2 pneumoperitoneum on cardiovascular, cerebrovascular, and respiratory homeostasis during robotic prostatectomy. *Br J Anaesth.* 2010;104(4):433-439.

Klauschie J, Wechter ME, Jacob K, et al. Use of anti-skid material and patient positioning to prevent patient shifting during robotic-assisted gynecologic procedures. *J Minim Invasive Gynecol.* 2010;17(4):504-507.

Phong SV, Koh LK. Anaesthesia for robotic-assisted radical prostatectomy: considerations for laparoscopy in the Trendelenburg position. *Anaesth Intensive Care.* 2007;35(2):281-285.

C.8. How will you ventilate the patient? What are the respiratory and circulatory effects of the Trendelenburg position during laparoscopy?

Respiratory

Vital capacity and FRC are reduced. The abdominal contents restrict movement of the diaphragm, especially in the obese and in older adults. Decreased compliance, increased ventilationperfusion abnormalities, and cephalad displacement of the mediastinum commonly occur. Upper airway edema and displacement of the endotracheal tube may occur.

Circulatory

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In healthy patients, the Trendelenburg position results in minimal circulatory changes. Venous return and cardiac output are increased, whereas CVP, pulmonary artery occlusion pressure (PAOP), systemic vascular resistance (SVR), and heart rate are essentially unchanged. In patients with cardiovascular disease, the Trendelenburg position may result in increased CVP, PAOP, and decreased cardiac output. The increase in venous return and myocardial oxygen demand that occurs in severe cardiovascular disease can precipitate acute heart failure.

These respiratory and circulatory changes caused by the Trendelenburg position are further amplified by the CO_2 insufflation. Ventilation may become difficult, especially in obese patients. Use of positive end-expiratory pressure (PEEP) is advised to prevent atelectasis. To prevent peak inspiratory pressures from becoming excessive, switching from volumecontrolled to pressure-controlled ventilation may be warranted. In addition, a prolonged inspiratory duration, such as an inspiratory-to-expiratory (I:E) ratio of 1:1 or 2:1 rather than the conventional 1:2, may provide better gas exchange.

Kim JY, Shin CS, Kim HS, et al. Positive end-expiratory pressure in pressure-controlled ventilation improves ventilatory and oxygenation parameters during laparoscopic cholecystectomy. *Surg Endosc.* 2010;24(5):1099-1103.

Kim WH, Hahm TS, Kim JA, et al. Prolonged inspiratory time produces better gas exchange in patients undergoing laparoscopic surgery: a randomised trial. *Acta Anaesthesiol Scand.* 2013;57:613-622.

Lestar M, Gunnarsson L, Lagerstrand L, et al. Hemodynamic perturbations during robot-assisted laparoscopic radical prostatectomy in 45° Trendelenburg position. *Anesth Analg.* 2011;113:1069-1075.

Oğurlu M, Küçük M, Bilgin F, et al. Pressure-controlled vs volume-controlled ventilation during laparoscopic gynecologic surgery. *J Minim Invasive Gynecol.* 2010;17(3):295-300.

Russo A, Di Stasio E, Scagliusi A, et al. Positive end-expiratory pressure during laparoscopy: cardiac and respiratory effects. *J Clin Anesth.* 2013;25:314-320.

Tyagi A, Kumar R, Sethi AK, et al. A comparison of pressure-controlled and volume-controlled ventilation for laparoscopic cholecystectomy. *Anaesthesia.* 2011;66:503-508.

C.9. What techniques are available for initial laparoscopic access to the peritoneal cavity? What anesthetic problems can arise during insufflation?

Pneumoperitoneum can be achieved by a “blind” or closed technique of percutaneous insertion of the 2-mm diameter hollow Veress needle, which after verification of correct positioning, is connected to the CO_2 insufflator. After Veress needle insertion and CO_2 insufflation, the first trocar is also inserted blindly.

Alternatively, if previous surgery or adhesions are to be avoided, an “open” approach is taken. A mini-incision is created, and the blunt-tipped Hasson cannula is inserted without prior pneumoperitoneum. The laparoscope is then inserted through the trocar to verify the intra-abdominal position before insufflation begins.

During insufflation, abdominal distention should be evenly distributed in all four quadrants. Respiratory variations of intraperitoneal pressure should be visible, and peak inspiratory pressures will gradually increase as the abdomen distends. It is at this time that the anesthesiologist should be alert to the possibility of vagally mediated reflexes. Bronchospasm, bradycardia, and even sinus arrest have been reported, especially in young women. Visceral and vascular perforations are also well-reported complications, especially with the blind technique. Cardiovascular collapse and gas emboli have been reported when CO_2 has been inadvertently insufflated directly into a blood vessel.

Merlin TL, Hiller JE, Maddern GJ, et al. Systematic review of the safety and effectiveness of methods used to establish pneumoperitoneum in laparoscopic surgery. *Br J Surg.* 2003;90(6):688-679.

Teoh B, Sen R, Abbott J. An evaluation of four tests used to ascertain Veress needle placement at closed

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laparoscopy. *J Minim Invasive Gynecol.* 2005;12(2):153-158.

Vilos GA, Vilos AG. Safe laparoscopic entry guided by Veress needle CO_2 insufflation pressure. *J Am Assoc Gynecol Laparosc.* 2003;10(3):415-420.

C.10. What intravenous (IV) solution and how much fluid volume do you plan to infuse?

Large-bore intravenous catheters should be placed because of the possibility of major hemorrhage. The amount of IV fluid infused is of vital importance, especially in older adults. Transient oliguria during laparoscopy is common. In calculating fluid requirements during laparoscopy, it is important to remember that much less “third spacing” occurs than in open surgery, no fluid loss is caused by evaporation, and the volume of retained (after suctioning) intraperitoneal saline used for irrigation by the surgeon should be added to the final total volume of infused IV fluids. In addition, the intra-abdominal humidification of the insufflated dry CO_2 gas results in only a negligible insensible water loss. Unlike open intraperitoneal cases, our starting fluid replacement is approximately 4 mL/kg/hr of Ringer's lactate solution; as needed, additional fluid is given based on the patient's preoperative hemodynamic status, intraoperative blood loss, and the volume of residual intraperitoneal irrigation fluid used by the surgeon.

After the pneumoperitoneum is released, diuresis occurs promptly and renal function quickly returns to normal (see section C.22).

For robotic laparoscopies, surgeons prefer that IV fluids are minimized until the anastomoses are completed. This keeps excessive fluids out of the surgical field and also helps prevent edema of the face, eyes, and larynx while in the steep Trendelenburg position. At our institution, after the anastomoses are complete, we infuse the majority of the IV hydration; the average duration for robotic prostatectomy is 3 to 3½ hours, the average blood loss is less than 250 mL, and the usual total fluid replacement is 3 to 3.5 L of lactated Ringer's solution.

Concha MR, Mertz VF, Cortínez LI, et al. The volume of lactated Ringer's solution required to maintain preload and cardiac index during open and laparoscopic surgery. *Anesth Analg.* 2009;108(2):616-622.

London ET, Ho HS, Neuhaus AM, et al. Effect of intravascular volume expansion on renal function during prolonged CO_2 pneumoperitoneum. *Ann Surg.* 2000;231:195-201.

Olsson J, Svensén CH, Hahn RG. The volume kinetics of acetated Ringer's solution during laparoscopic cholecystectomy. *Anesth Analg.* 2004;99(6):1854-1860.

C.11. Under what circumstances should laparoscopy be converted to laparotomy?

Laparotomy should be performed immediately in cases of major bleeding or organ damage. Other circumstances include persistent problems with inadequate exposure, a procedure beyond the surgeon's capability, a procedure taking too long, the inability to create or maintain pneumoperitoneum, patient deterioration, equipment failure, and discovery of other unsuspected disease.

Tabboush ZS. When hypotension during laparoscopic cholecystectomy indicates termination of the laparoscopy. *Anesth Analg.* 1994;79:195-196.

C.12. What is the arterial to end-tidal CO_2 ($PETCO_2$) gradient ($PaCO_2$-$PETCO_2$) in the normal awake patient? What is the cause of the gradient? Does the gradient change during laparoscopy? Why?

In the awake person at rest, the normal arterial to end-tidal PCO_2 difference is small, ranging from 2 to 6 mm Hg. The gradient and its variations are measures of the alveolar dead space. The gradient is the sum of the difference between the

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arterial and alveolar CO_2 plus the difference between the alveolar and end-tidal CO_2. It is commonly increased in emphysema. The difference is increased when underperfused alveoli are ventilated, as often occurs during hyperventilation in laparoscopy.

The total physiologic dead space consists of the anatomic dead space (passageways that do not participate in gas exchange, approximately 150 mL) and the alveolar dead space (i.e., underperfused alveoli). The alveolar dead space gas is expired at the same time as the alveolar ideal gas from well-perfused alveoli in equilibrium with pulmonary capillary blood. The dilution of the ideal alveolar gas by the alveolar dead space gas is represented by the end-tidal CO_2.

Some of the factors resulting in a relative increase in ventilation-to-perfusion ratio include mechanical ventilation, hyperventilation, rapid or shallow ventilation, and the Trendelenburg or lateral decubitus position.

Some of the factors resulting in a relative decrease in perfusion-to-ventilation ratio include hypotension, decreased cardiac output, myocardial depression from inhalational anesthetics, pulmonary emboli, high positive airway pressure, and ablation of the hypoxic pulmonary vasoconstriction reflex.

Christensen MA, Bloom J, Sutton KR. Comparing arterial and end-tidal carbon dioxide values in hyperventilated neurosurgical patients. *Am J Crit Care.* 1995;4:116-121.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010:327-354.

C.13. Is an arterial line necessary? Why? Does end-tidal CO_2 tension accurately reflect arterial CO_2 tension? Under what circumstances may the $PETCO_2$ exceed the $PaCO_2$? Why?

An arterial line is recommended whenever the laparoscopic procedure is unusually complex, long, or when the patient has significant cardiopulmonary disease. In such cases, ventilationperfusion abnormalities, intraoperative hypoxemia, marked hypercarbia, or high airway pressures may be expected. During these situations, and possibly in all laparoscopies, an unsteady state exists with respect to CO_2, and the assumption that $PETCO_2$ may accurately reflect a predictable relationship to $PaCO_2$ is not valid.

End-tidal CO_2 tension can either estimate $PaCO_2$, frequently underestimate $PaCO_2$, or infrequently overestimate $PaCO_2$. Furthermore, the values for these two measurements do not always change proportionally nor do they always change in the same direction. The relationship between $PETCO_2$ and $PaCO_2$ varies during the course of the procedure. At the beginning of insufflation, $PETCO_2$ can be used as a rough estimate of $PaCO_2$. However, when redistribution of the excess CO_2 from the well-perfused tissues to the less well-perfused tissues begins, $PETCO_2$ begins to underestimate the $PaCO_2$. Characteristically, the arterial to end-tidal CO_2 difference progressively increases as hyperventilation (and dead space) increases.

Especially during strenuous exercise when metabolic CO_2 production is increased and during laparoscopy when excess exogenous CO_2 must be excreted, the $PETCO_2$ may be found to exceed the $PaCO_2$. This condition has also been reported in a hyperventilating patient during cesarean section. This occurs because the $PaCO_2$ fluctuates during each deep breath and may not represent the highest value at that instant, whereas the $PETCO_2$ shows the maximal value (i.e., because of tidal ventilation and pulsatile blood flow in exercise, $PETCO_2$ may exceed mean alveolar and arterial CO_2).

Bhavani-Shankar K, Steinbrook RA, Brooks DC, et al. Arterial to end-tidal carbon dioxide difference during laparoscopic surgery in pregnancy. *Anesthesiology.* 2000;93(2):370-373.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010:327-354.

Scheid P, Meyer M, Piiper J. Arterial-expired PCO_2 differences in the dog during acute hypercapnia. *J Appl Physiol*

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Respir Environ Exerc Physiol. 1979;47:1074-1078.

Strang CM, Hachenberg T, Fredén F, et al. Development of atelectasis and arterial to end-tidal PCO_2 difference in a porcine model of pneumoperitoneum. *Br J Anaesth.* 2009;103(2);298-303.

Wulkan ML, Vasudevan SA. Is end-tidal CO_2 an accurate measure of arterial CO_2 during laparoscopic procedures in children and neonates with cyanotic congenital heart disease? *J Pediatr Surg.* 2001;36(8):1234-1236.

C.14. What are the possible causes of hypercarbia?

- Hypoventilation
- CO_2 in the inspired gas—rebreathing endogenous CO_2 will increase $PaCO_2$ by 3 to 6 mm Hg per minute.
- Increased endogenous CO_2 production or exogenous CO_2 supply—occurring in the hypermetabolic states of malignant hyperpyrexia, fever, and hyperthyroidism; and in laparoscopy, or following administration of bicarbonate or lactate (1 ampule of 50 mEq of bicarbonate liberates more than 1 L of CO_2)
- Increased dead space (rare) as in pulmonary embolism, ventilation of a lung cyst, or advanced COPD

Lumb AB. *Nunn's Applied Respiratory Physiology.* 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010:355-361.

Wolf JS Jr, Clayman RV, Monk TG, et al. Carbon dioxide absorption during laparoscopic pelvic operation. *J Am Coll Surg.* 1995;180:555-560.

C.15. What factors play a role in the unusually rapid and marked elevation of CO_2 that is sometimes seen in laparoscopy?

- Patients with significant cardiopulmonary disease
- Intra-abdominal pressure greater than 15 mm Hg
- Presence of subcutaneous emphysema
- Retroperitoneal rather than intraperitoneal approach
- Long duration of laparoscopy

Bozkurt P, Kaya G, Yeker Y, et al. Arterial carbon dioxide markedly increases during diagnostic laparoscopy in portal hypertensive children. *Anesth Analg.* 2002;95(5):1236-1240.

Liem MS, Kallewaard JW, de Smet AM, et al. Does hypercarbia develop faster during laparoscopic herniorrhaphy than during laparoscopic cholecystectomy? Assessment with continuous blood gas monitoring. *Anesth Analg.* 1995;81:1243-1249.

C.16. How rapidly does the $PaCO_2$ rise in the apneic patient (endogenous CO_2)? How rapidly does the $PaCO_2$ rise if 5% CO_2 gas is inhaled (exogenous)? How rapidly can the CO_2 rise during laparoscopy? What factors explain the differences?

In the apneic patient, $PaCO_2$ rises at the rate of 3 to 6 mm Hg per minute. Rebreathing, or inhalation of 5% CO_2 in oxygen, causes a much more rapid rise in $PaCO_2$ up to 8 to 10 mm Hg per minute. The difference in rate of rise between endogenous and exogenous CO_2 is explained by the presence of large body stores of CO_2. Approximately 120 L of CO_2

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exist in the body (100 times the amount for oxygen) distributed among well-perfused tissue (e.g., blood, brain), moderately perfused tissue (e.g., muscle), and poorly perfused tissue (e.g., fat, bone). These storage places adjust slowly to acute CO_2 changes. In the steady state, the amount of CO_2 produced metabolically in the body is equal to the amount expired through the lungs, and there is no change in the body stores of CO_2. During laparoscopy, an unsteady state exists, with the rate of rise of PCO_2 being greatest during the first 20 to 30 minutes. After that time, new equilibrium levels are reached between the different compartments, and the PCO_2 rate of rise is slower.

Frumin et al. studied the hypercarbic state during their classic study of apneic oxygenation. In paralyzed apneic intubated denitrogenated oxygenated patients receiving only thiopental for amnesia, Frumin et al. demonstrated at least a 3 mm Hg average rise in $PaCO_2$ per minute and an ultimate $PaCO_2$ as high as 250 mm Hg (pH 6.72) while maintaining 98% to

100% O_2 saturation after 53 minutes of apnea. They also found that the hypercarbia was accompanied by hypertension: Mean arterial pressure rose 26% and then fell 14% after the return of respirations and normocarbia. Other features accompanying apneic hypercarbic hypertension included normal sinus rhythm with an essentially unchanged rate, rising arterial epinephrine and norepinephrine concentrations, and rising arterial potassium levels (which rose still further after ventilation and normocarbia resumed) with unchanged sodium levels.

Frumin MJ, Epstein RM, Cohen G. Apneic oxygenation in man. *Anesthesiology.* 1959;20:789-798.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010:327-354.

C.17. What are the direct and indirect effects of hypercarbia on the cardiovascular system? How are these effects altered by increased intra-abdominal pressure and patient position during laparoscopy?

The effects of hypercarbia on the circulatory system are complex and often contradictory. At the cellular level, hypercarbia is a direct depressor of myocardial contractility and rate of contraction; it is also a direct stimulant of myocardial irritability and arrhythmicity. These effects may be enhanced by the reduced pH caused by hypercarbia.

The direct effect of hypercarbia on isolated or denervated blood vessels is a diminished responsiveness to catecholamines and vasodilation especially on the venous side, leading to peripheral pooling, decreased venous return, and decreased cardiac output. The exception to the dilatory effect of hypercarbia and acidosis on blood vessels exists in the pulmonary vessels, which vasoconstrict. It appears, however, that the effects on the pulmonary vessels are actually due to acidosis rather than hypercarbia because if the pH is kept constant while the PCO_2 rises, pulmonary vascular resistance (PVR) does not change.

In the patient, however, the direct or local effects of CO_2 can be overshadowed by a variety of systemic effects.

Simultaneous with these local or direct effects, hypercarbia causes profound systemic changes secondary to stimulation of the central nervous system and sympathoadrenal system. The net effect usually includes an increase in cardiac output, heart rate, force of myocardial contraction, BP, and CVP, vasoconstriction in the pulmonary (capacitance) vessels, and a decrease peripheral resistance. The rise in cardiac output of up to 50% exceeds the rise in BP because of the drop in peripheral resistance and increase in blood flow primarily in the cerebral and coronary circulations. This net stimulatory effect accompanies the elevation of $PaCO_2$ up to approximately 90 mm Hg. Above this level, further increases in CO_2 cause a marked drop in response.

In a normal anesthetized human breathing 7% to 15% inspired CO_2, these stimulatory changes were shown to correspond primarily to rising plasma concentrations of epinephrine and norepinephrine. When the sympathoadrenal response was prevented by subarachnoid block, ganglioplegics, or α-adrenergic blockers, the cardiovascular response to inhaled CO_2 was hypotension and decreased cardiac output. The stimulatory response also is diminished by general anesthesia.

Hypercarbia can cause arrhythmias during epinephrine infiltrations or in the presence of halothane but not other anesthetics. Other than in these two circumstances, hypercarbia is not arrhythmogenic unless hypoxia also is present.

The full range of possible effects of hypercarbia on the cardiovascular system are subject to many influences. Healthy (ASA class I) patients are less likely than ASA class III patients to undergo extreme changes. Similarly, a brief surgical duration, head-up positioning, low intra-abdominal pressures, and intraperitoneal (rather than extraperitoneal) surgery can

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limit the range of physiologic and metabolic responses to near normal.

In the patient with marginal cardiovascular function, however, peritoneal insufflation can result in a significant increase in cardiac workload. In this situation, transesophageal echocardiography can be a useful noninvasive method to assess left ventricular function.

Arrhythmias such as bradycardia, nodal rhythm, or even asystole can follow rapid peritoneal distention and vagal stimulation. In general, BP, pulse, cardiac output, and CVP will increase up to an intra-abdominal pressure of 15 mm Hg. At insufflation pressures of 20 to

30 mm Hg, a decrease in BP, cardiac output, and CVP will occur because of pressure on the inferior vena cava decreases venous return. Pneumoperitoneum also may induce changes in the cardiac electrical axis, which may affect interpretation of the ECG seen on the monitor during the operation.

Ekici Y, Bozbas H, Karakayali F, et al. Effect of different intra-abdominal pressure levels on QT dispersion in patients undergoing laparoscopic cholecystectomy. *Surg Endosc.* 2009;23:2543-2549.

Falabella A, Moore-Jeffries E, Sullivan MJ, et al. Cardiac function during steep Trendelenburg position and CO_2 pneumoperitoneum for robotic-assisted prostatectomy: a transesophageal Doppler probe study. *Int J Med Robot.* 2007;3(4):312-315.

Hofer CK, Zalunardo MP, Klaghofer R, et al. Changes in intrathoracic blood volume associated with pneumoperitoneum and positioning. *Acta Anaesthesiol Scand.* 2002;46:303-308.

Joshi GP, Hein HA, Mascarenhas WL, et al. Continuous transesophageal echo-Doppler assessment of hemodynamic function during laparoscopic cholecystectomy. *J Clin Anesth.* 2005;17(2):117-121.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010:327-354.

Rist M, Hemmerling TM, Rauh R, et al. Influence of pneumoperitoneum and patient positioning on preload and splanchnic blood volume in laparoscopic surgery of the lower abdomen. *J Clin Anesth.* 2001;13:244-249.

Russo A, Marana E, Viviani D, et al. Diastolic function: the influence of pneumoperitoneum and Trendelenburg positioning during laparoscopic hysterectomy. *Eur J Anaesthesiol.* 2009;26(11):923-927.

C.18. What are the direct and indirect effects of hypercarbia on the respiratory system? Are these effects altered by increased intra-abdominal pressure and patient position?

Hypercarbia and acidosis stimulate the respiratory center both directly and indirectly through chemoreceptors, hormones, and autonomic nerves. In the conscious patient breathing oxygen, the maximal stimulating effect occurs at 100 to 150 mm Hg, producing minute volumes of up to 75 L. Above these levels, CO_2 becomes a respiratory depressant. Current anesthetics blunt the stimulatory respiratory response to CO_2. Diethyl ether, however, the only volatile anesthetic known to stimulate respiration, reportedly allowed a patient to continue to breathe spontaneously with an inadvertent PCO_2 of 234 mm Hg.

In the awake patient, each mm Hg increase in $PaCO_2$ increases ventilation by 2 to 3 L per minute (if PaO_2 is constant). This response is diminished by anesthesia. Hypercarbia also produces bronchodilatation; acidosis rather than hypercarbia per se causes pulmonary vascular constriction.

General anesthesia with intubation and mechanical ventilation results in a decrease in FRC, which is caused by loss of muscle tone, diaphragmatic displacement, and loss of thoracic volume. Lung compliance drops, airway pressures increase, and V/Q abnormalities occur. However, most patients have no difficulty tolerating these changes. These changes are exaggerated in the Trendelenburg position, especially in older adults, the obese, and those with preexisting

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cardiopulmonary disease. Intrathoracic, peak inspiratory, and plateau pressures increase and then increase even further when pneumoperitoneum creates an increase in pressure and volume by pushing abdominal contents cephalad. Endobronchial intubation can occur as a result of cephalad movement of the carina, and it should be ruled out if hypoxemia occurs.

Andersson LE, Bååth M, Thórne A, et al. Effect of carbon dioxide pneumoperitoneum on development of atelectasis during anesthesia, examined by spiral computed tomography. *Anesthesiology.* 2005;102(2):293-299.

Kendall AP, Bhatt S, Oh TE. Pulmonary consequences of carbon dioxide insufflation for laparoscopic cholecystectomies. *Anaesthesia.* 1995;50:286-289.

Lobato EB, Paige GB, Brown MM, et al. Pneumoperitoneum as a risk factor for endobronchial intubation during laparoscopic gynecologic surgery. *Anesth Analg.* 1998;86:301-303.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010:327-354.

Rauh R, Hemmerling TM, Rist M, et al. Influence of pneumoperitoneum and patient positioning on respiratory system compliance. *J Clin Anesth.* 2001;13:361-365.

Sprung J, Whalley DG, Falcone T, et al. The effects of tidal volume and respiratory rate on oxygenation and respiratory mechanics during laparoscopy in morbidly obese patients. *Anesth Analg.* 2003;97:268-274.

Whalen FX, Gajic O, Thompson GB, et al. The effects of the alveolar recruitment maneuver and positive endexpiratory pressure on arterial oxygenation during laparoscopic bariatric surgery. *Anesth Analg.* 2006;102:298-305.

C.19. What are the direct and indirect effects of hypercarbia on the central nervous system? How are these effects altered by increased intra-abdominal pressure and patient position during laparoscopy?

The brain is particularly sensitive to changes in $PaCO_2$. Slight elevations of CO_2 cause direct cortical depression and increase the threshold for seizures. Higher levels of CO_2 (25% to 30%) stimulate subcortical hypothalamic centers, resulting in increased cortical excitability and seizures. This hyperexcitability level is enhanced by adrenal cortical and medullary hormones released secondary to hypercarbia-induced stimulation of the hypothalamus. Further elevations of CO_2 cause an anesthetic-like state of cortical and subcortical depression.

CO_2 was first used as an anesthetic by Hickman in 1824 and reintroduced by Leake and Waters in 1928. CO_2 caused an N_2O-like narcosis at approximately 90 to 120 mm Hg. However, hypercarbia also causes increased excitability of neurons so that seizures occurred shortly afterward. In dogs, however, general anesthesia is achieved at a higher level of $PaCO_2$, approximately 245 mm Hg, probably due to intracellular derangements caused by low pH.

CO_2, not H^+, crosses the blood-brain barrier and the brain cell membrane and affects the cells' metabolism. Therefore, a change in $PaCO_2$ also causes a rapid change in cerebrospinal fluid (CSF) pH. CO_2 is the most important factor in regulating cerebral blood flow (CBF). The relation between CBF and $PaCO_2$ is essentially linear from 20 to 100 mm Hg, with maximal vasodilatation occurring at approximately 120 mm Hg. Normal CBF is approximately 12% to 15% of cardiac output, or 50 mL/100 g/min. For each 1 mm Hg increase in $PaCO_2$ between 20 and 80 mm Hg, CBF increases by 2% to 4%. Hypercarbia decreases cerebral vascular resistance, causing CBF to increase.

Hypercarbia causes an increase in intracranial pressure, probably secondary to vasodilation. When the patient is placed in the Trendelenburg position, venous congestion of the head and neck occurs. Additional increases in intra-abdominal and intrathoracic pressures contribute to further increase intracranial and CSF pressures.

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Therefore, an acute rise in intra-abdominal pressure (pneumoperitoneum) causes an immediate rise in intracranial pressure. This occurs through intermediary steps that include compression of the inferior vena cava (resulting in decreased drainage in the lumbar plexus), increased CVP, increased mean arterial pressure, increased intrathoracic pressure, increased venous stasis, increased pressure in the sagittal sinus, and decreased resorption of CSF. Hypercarbia contributes to the increased intracranial pressure, but hyperventilation will not decrease the elevated intracranial pressure until the elevated intra-abdominal pressure is released.

Intraocular pressure is also increased during Trendelenburg position with pneumoperitoneum but apparently is well tolerated by most patients.

Awad H, Santilli S, Ohr M, et al. The effects of steep Trendelenburg positioning on intraocular pressure during robotic radical prostatectomy. *Anesth Analg.* 2009;109:473-478.

Hoshikawa Y, Tsutsumi N, Ohkoshi K, et al. The effect of steep Trendelenburg positioning on intraocular pressure and visual function during robotic-assisted radical prostatectomy. *Br J Ophthalmol.* 2014;98:305-308.

Irgau I, Koyfman Y, Tikellis JI. Elective intraoperative intracranial pressure monitoring during laparoscopic cholecystectomy. *Arch Surg.* 1995;130:1011-1013.

Kalmar AF, Dewaele F, Foubert L, et al. Cerebral haemodynamic physiology during steep Trendelenburg position and CO(2) pneumoperitoneum. *Br J Anaesth.* 2012;108:478-484.

Kim MS, Bai SJ, Lee JR, et al. Increase in intracranial pressure during carbon dioxide pneumoperitoneum with steep Trendelenburg positioning proven by ultrasonographic measurement of optic nerve sheath diameter. *J Endourol.* 2014;28:801-806.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010:327-354.

Park EY, Koo BN, Min KT, et al. The effect of pneumoperitoneum in the steep Trendelenburg position on cerebral oxygenation. *Acta Anaesthesiol Scand.* 2009;53(7):895-899.

Schramm P, Treiber AH, Berres M, et al. Time course of cerebrovascular autoregulation during extreme Trendelenburg position for robotic-assisted prostatic surgery. *Anaesthesia.* 2014;69:58-63.

C.20. What are the neuroendocrine changes that occur during laparoscopy?

Excessive intra-abdominal pressure and hypercarbia may activate the sympathoadrenal axis, resulting in increased plasma levels of epinephrine and norepinephrine. Renin, cortisol, aldosterone, antidiuretic hormone, and atrial natriuretic peptide levels are also increased. In awake patients in the Trendelenburg position, increased secretion of atrial natriuretic peptide occurs, probably in response to increased venous return and atrial stretching. During pneumoperitoneum, however, secretion of atrial natriuretic peptide diminishes, suggesting interference with venous return.

Mann C, Boccara G, Pouzeratte Y, et al. The relationship among carbon dioxide pneumoperitoneum, vasopressin release, and hemodynamic changes. *Anesth Analg.* 1999;89:278-283.

Marana E, Colicci S, Meo F, et al. Neuroendocrine stress response in gynecological laparoscopy: TIVA with propofol versus sevoflurane anesthesia. *J Clin Anesth.* 2010;22(4):250-255.

Mikami O, Fujise K, Matsumoto S, et al. High intra-abdominal pressure increases plasma catecholamine concentrations during pneumoperitoneum for laparoscopic procedures. *Arch Surg.* 1998;133:39-43.

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C.21. What are the direct and indirect effects of laparoscopy on the renal system?

Oliguria has been observed frequently during laparoscopy despite adequate hydration. Although prerenal causes such as hypovolemia, positive pressure ventilation, and PEEP can contribute to oliguria, it is believed that neurohumoral changes (e.g., antidiuretic hormone secretion) secondary to hypercarbia and increased intra-abdominal pressure secondary to insufflation may be responsible for the oliguria that occurs during laparoscopy. Sympathetic stimulation causes a release of catecholamines, resulting in decreased renal cortical blood flow with shunting of blood to the adrenal medulla, constriction of glomerular afferent arterioles, and decreased glomerular filtration rate. It has been shown recently that when intraperitoneal insufflation reaches a pressure of 15 mm Hg, renal cortical blood flow decreases approximately 60% and a reversible 50% drop in urine volume occurs. In contrast, no decrease in urine output occurred when the abdominal wall was lifted with a force of 15 mm Hg during “gasless laparoscopy.” It has also been shown that pneumoretroperitoneum, which causes a more gradual increase in intra-abdominal pressure, also caused a more gradual decrease in renal perfusion. Finally, it has been shown that unilateral retroperitoneal insufflation causes decreased renal cortical perfusion of only the ipsilateral kidney if the intra-abdominal pressure is not elevated.

Ben-David B, Croitoru M, Gaitini L. Acute renal failure following laparoscopic cholecystectomy: a case report. *J Clin Anesth.* 1999;11:486-489.

Cho JE, Shim JK, Chang JH, et al. Effect of nicardipine on renal function after robotic-assisted laparoscopic radical prostatectomy. *Urology.* 2009;73:1056-1060.

Demyttenaere S, Feldman LS, Fried GM. Effect of pneumoperitoneum on renal perfusion and function: a systematic review. *Surg Endosc.* 2007;21:152-160.

Dunn MD, McDougall EM. Renal physiology. Laparoscopic considerations. *Urol Clin North Am.* 2000;27:609-614.

Hazebroek EJ, de Vos tot Nederveen Cappel R, Gommers D, et al. Antidiuretic hormone release during laparoscopic donor nephrectomy. *Arch Surg.* 2002;137:600-605.

Nguyen NT, Perez RV, Fleming N, et al. Effect of prolonged pneumoperitoneum on intraoperative urine output during laparoscopic gastric bypass. *J Am Coll Surg.* 2002;195:476-483.

Wiesenthal JD, Fazio LM, Perks AE, et al. Effect of pneumoperitoneum on renal tissue oxygenation and blood flow in a rat model. *Urology.* 2011;77:1508-1515.

C.22. What is the effect of laparoscopy on the bowel and gastrointestinal system?

Although CO_2 directly causes vasodilatation of the splanchnic capillary beds, the increased intra-abdominal pressure of laparoscopy decreases perfusion, increases systemic vascular resistance, impairs gastric submucosal perfusion and metabolism, and may cause bowel hypoxia at high pressures. On release of the intra-abdominal pressure, residual CO_2 again causes vascular dilation, allowing additional CO_2 to enter the bloodstream. Myoelectric activity and recovery from ileus is faster after laparoscopic than after open surgery. The combined effect of the increase in abdominal pressure, stretching of the

peritoneum by insufflation, and diffusion of CO_2 into bowel is probably responsible for any postoperative nausea.

Böhm B, Milsom JW, Fazio VW. Postoperative intestinal motility following conventional and laparoscopic intestinal surgery. *Arch Surg.* 1995;130:415-419.

Meierhenrich R, Gauss A, Vandenesch P, et al. The effects of intraabdominally insufflated carbon dioxide on hepatic

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blood flow during laparoscopic surgery assessed by transesophageal echocardiography. *Anesth Analg.* 2005;100:340-347.

Schwarte LA, Scheeren TW, Lorenz C, et al. Moderate increase in intraabdominal pressure attenuates gastric mucosal oxygen saturation in patients undergoing laparoscopy. *Anesthesiology.* 2004;100:1081-1087.

Takagi S. Hepatic and portal vein blood flow during carbon dioxide pneumoperitoneum for laparoscopic hepatectomy. *Surg Endosc.* 1998;12:427-431.

Trencheva K, Dhar P, Sonoda T, et al. Physiologic effects of simultaneous carbon dioxide insufflation by laparoscopy and colonoscopy: prospective evaluation. *Surg Endosc.* 2011;25:3279-3285.

C.23. How would you recognize a CO_2 embolism during laparoscopy? How does this differ from an air embolism? Why should N_2O be discontinued during suspected embolization? Will N_2O increase the size of CO_2 emboli?

The incidence of venous gas embolism is less in robotic-assisted laparoscopic radical prostatectomies than in radical retropubic prostatectomies. It is more likely to occur during the transection of the deep dorsal venous plexus than during the initial insufflation.

Gas embolism can occur whenever the internal pressure of an open vessel is less than the external pressure. Gas embolism may cause increased ventilatory dead space, increased PVR, increased pulmonary artery pressure, and decreased cardiac output. Early signs include a rapid drop in end-tidal CO_2 and PaO_2 and an increased $PaCO_2$. During laparoscopy, insufflation of a large amount of CO_2 directly into a blood vessel can occur initially after blind Veress needle insertion, especially at high pressures. Hypotension, hypoxia, cyanosis, and/or cardiac arrest can occur. If the gas volume is large enough, a “mill-wheel” murmur may be heard through a precordial or esophageal stethoscope. If ventilation is kept constant, a sudden decrease in end-tidal CO_2 may be noted. The most sensitive means to detect gas emboli are the precordial and transesophageal Doppler and transesophageal echocardiography. Aspiration of foamy blood from a central venous catheter is diagnostic.

CO_2 embolism, however, must be distinguished from air embolism, which is a far more ominous event, as shown in Table 26.2. CO_2, being extremely soluble in the presence of red blood cells, is much less life-threatening than an identically sized intravascular bolus of air. It has been reported that the lethal volume of intravascular CO_2 gas in cats is 30 times greater than the lethal volume of intravascular air.

Air emboli can be entrained into open veins above the level of the heart (e.g., head and neck surgery, neurosurgery, cesarean section). Other gases that are present, N_2O, for example, will diffuse into that air space according to their diffusion capacities and pressure gradients. Therefore, N_2O will diffuse in, oxygen will be consumed and/or diffuse out, and the size or pressure of the bubble will increase in proportion to the concentration and duration of N_2O being administered until equilibrium is reached. It has been demonstrated that inhalation of 70% N_2O increased the volume of intestinal gas pockets in dogs by twofold in 2 hours and up to threefold in 4 hours. They calculated that at equilibrium bowel volume could increase up

to a maximum of 400%. When N_2O is limited to 50%, however, the size of the gas pocket will not be more than doubled at equilibrium. They also demonstrated that inhalation of 68% to 78% N_2O would cause 300 mL of air in the pleural space to double in volume in 10 minutes and to triple in 45 minutes. A gas bubble composed of 100% CO_2, however, will not enlarge in a patient inhaling 50% or even 75% N_2O because more CO_2 will diffuse out, be absorbed, or be buffered (also more quickly) than N_2O will move in. CO_2 gas has caused fatal embolisms, and N_2O should be discontinued if embolism is suspected. A study using transesophageal echocardiography in 16 patients undergoing laparoscopic cholecystectomy reported that 11 of the 16 patients (5 during peritoneal insufflation and 6 during gallbladder dissection) had a gas embolism, but all were subclinical with no signs of cardiorespiratory instability. In addition, conditions for creating a CO_2

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embolism differ from the conditions required for an air embolism. Other than direct insufflation of CO_2 into a vein, as during Veress needle insufflation, the capillaries and veins within the abdomen are collapsed by the positive pressure within the abdomen, thereby minimizing the chance for CO_2 to enter open vessels.

TABLE 26.2 Differences between Air and Carbon Dioxide Emboli

EMBOLISM	AIR	CO_2
Composition	79% N_2, 21% O_2	100% CO_2
Origin	Vein open to air	No contact with air
Pressure source	Hydrostatic	Insufflator
Solubility	Negligible	Large
Effect of N_2O	Enlarged	Not enlarged

Fong J, Gadalla F, Pierri MK, et al. Are Doppler-detected venous emboli during cesarean section air emboli? *Anesth Analg.* 1990;71:254-257.

Hong JY, Kim WO, Kil HK. Detection of subclinical CO_2 embolism by transesophageal echocardiography during laparoscopic radical prostatectomy. *Urology.* 2010;75(3):581-584.

Ishiyama T, Hanagata K, Kashimoto S, et al. Pulmonary carbon dioxide embolism during laparoscopic cholecystectomy. *Can J Anaesth.* 2001;48:319-320.

Jayaraman S, Khakhar A, Yang H, et al. The association between central venous pressure, pneumoperitoneum, and venous carbon dioxide embolism in laparoscopic hepatectomy. *Surg Endosc.* 2009;23(10):2369-2373.

Kim CS, Kim JY, Kwon JY, et al. Venous air embolism during total laparoscopic hysterectomy: comparison to total abdominal hysterectomy. *Anesthesiology.* 2009;111(1):50-54.

C.24. What is the mechanism of increase in shunting resulting from embolization?

Emboli in the pulmonary capillaries cause an increase in PVR (i.e., vasoconstriction), which leads to increased pulmonary artery, right ventricle, and right atrium pressures and an opening of pulmonary precapillary arteriovenous anastomoses, resulting in shunt and hypoxemia.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010:119-144.

C.25. How is a gas embolism (CO_2 or air) treated?

- N_2O should be discontinued, and the FIO_2 should be increased to 1.0.
- Identify and occlude the air entrainment site. Insufflation (in the case of CO_2) should be halted, and the

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pneumoperitoneum should be released immediately.

- An increase in the rate and volume of controlled ventilation with PEEP has been suggested as a method of minimizing air entrainment. However, this may decrease the cardiac output and excessively increase the airway pressure and PVR and can lead to paradoxical air embolization.
- If possible, the patient should be placed in steep left lateral decubitus Trendelenburg position to prevent obstruction of the pulmonary outflow tract and right ventricular failure. However, during robotic surgery, movement of the patient is prevented until the robot is undocked.
- A CVP catheter can be useful for diagnosis and for therapeutic aspiration of air. Radial artery cannulation can be useful to track improvement or deterioration.
- Therapy is essentially supportive and may include fluids, vasopressors, and pulmonary arterial catheterization. A large bolus of gas may form a gas lock in the right atrium, decreasing the cardiac output. Smaller bubbles can lodge in the lungs, causing pulmonary hypertension, right ventricular failure, and pulmonary edema. Venous gas emboli may also enter the arterial circulation through an atrial septal defect or patent foramen ovale, a condition that may exist in 20% of patients.

Hong JY, Kim JY, Choi YD, et al. Incidence of venous gas embolism during robotic-assisted laparoscopic radical prostatectomy is lower than during radical retropubic prostatectomy. *Br J Anaesth.* 2010;105:777-781.

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology.* Philadelphia, PA: Lippincott Williams &Wilkins; 2008:198-200.

C.26. What are the causes of pneumothorax or pneumomediastinum during laparoscopy? How would you diagnose it? How would you treat it?

A pneumothorax can result from the migration of the laparoscopic gas under pressure or from direct pulmonary barotrauma. CO_2 gas insufflated retroperitoneally gains rapid direct access to a vast space and may result in widespread subcutaneous emphysema and a pneumomediastinum.

During laparoscopy, CO_2 under pressure can pass from the abdominal cavity into the pleural and pericardial spaces through anatomic or congenital paths (e.g., the hiatus around the esophagus) or through acquired defects in the diaphragm. (Embryologically, before the formation of the diaphragm, the peritoneal and pleural cavities are derived from one sac.)

A pneumothorax can be diagnosed by a sudden decrease in pulmonary compliance, an increase in airway pressure, an increase in $PETCO_2$ and $PaCO_2$, an unchanged or decreased PaO_2, an unchanged or decreased BP, abnormal motion of the involved side hemidiaphragm, and the absence of breath sounds without wheezing on the affected side. The shape of the capnogram usually is unchanged. Fiberoptic bronchoscopy will rule out endobronchial intubation, and an intraoperative chest fluoroscopy or x-ray film will confirm the diagnosis.

A pneumothorax caused by laparoscopic gas is easily treated, or it can resolve spontaneously. One study reports an incidence of pneumothorax in 7 of 46 patients undergoing laparoscopic fundoplication for repair of hiatus hernia. In these cases, intraoperative treatment consisted of PEEP and increased minute ventilation to reinflate the lung and increased pressure to decrease the gradient from abdomen to pleural cavity and possibly to seal the tear.

Alternatively, a pneumothorax may be undetected until the patient wakes up and exhibits respiratory distress and restlessness, which can be misinterpreted as pain or inadequate reversal of the muscle relaxant. Treatment consists of 100% oxygen by mask. CO_2 will quickly diffuse out, as can be easily seen by serial blood gases and x-ray films; invasive treatment is unnecessary.

Subcutaneous emphysema is usually identified by finding crepitus on physical examination; it can also be seen on a radiograph. A pneumomediastinum is diagnosed with a portable chest radiograph. The treatment usually only consists of oxygen and supportive measures. However, tension pneumomediastinum and a compartment syndrome due to severe subcutaneous emphysema will require surgical intervention.

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Because of the increased volumes and pressures in the lung during laparoscopy, pneumothorax, pneumomediastinum, and subcutaneous emphysema can also result from barotrauma. This cause of pneumothorax is far more serious and may require tube thoracostomy. Attempts at hyperventilating to decrease the $PETCO_2$ can result in overdistention and rupture of alveoli, with subsequent dissection of the anesthetic gases into the perivascular sheaths, mediastinum, pleura, and fascial planes of the head and neck. Large tidal volumes and rapid ventilator rates can be especially dangerous in patients with COPD or bullae because insufficient emptying time may increase air trapping.

Bartelmaos T, Blanc R, De Claviere G, et al. Delayed pneumomediastinum and pneumothorax complicating laparoscopic extraperitoneal inguinal hernia repair. *J Clin Anesth.* 2005;17:209-212.

Joris JL, Chiche JD, Lamy ML. Pneumothorax during laparoscopic fundoplication: diagnosis and treatment with positive end-expiratory pressure. *Anesth Analg.* 1995;81:993-1000.

C.27. How would you decide when to extubate?

In addition to the usual criteria for extubation, prolonged laparoscopy in the Trendelenburg position requires that the following problems are resolved before the patient is extubated. If significant subcutaneous emphysema has occurred (diagnosed by crepitus and persistent hypercarbia), continue mechanical ventilation with oxygen. A significant amount of CO_2 may be held in the vast retroperitoneal space.

Delay extubation if the patient has edema, venous congestion, and duskiness of the head and neck. Check the tongue for edema and the eyes for periorbital, conjunctival, or lid edema. The cuff of the endotracheal tube should be deflated to make sure that a gas leak exists. If it does not, the patient should remain intubated. Keep the patient in head-up position until the conjunctivae no longer seem raised or watery. Potential laryngeal edema will also be diminished by the head-up position.

Causes of edema include dependent stasis from the Trendelenburg position, resistance from elevated abdominal and thoracic pressures, and temporary fluid overload after intraoperative oliguria or anuria. In some cases, it is best to leave the patient intubated with a Foley catheter in place until diuresis has begun.

D. Postoperative Management

D.1. What are some of the unique complications of laparoscopy?

Injuries from Instruments

Improper placement of Veress needle or trocars can cause abdominal wall bleeding, blood vessel or visceral puncture, subcutaneous emphysema, peritonitis, wound infections, hernia at the trocar site, and hemorrhage. Thermal injuries may occur from cautery or laser use. Staples and clips can cause nerve entrapment.

Complications of Pneumoperitoneum

Increased intra-abdominal pressure can result in bowel ischemia, omental or bowel herniation, gastric regurgitation, excessive compression of vena cava, decreased venous return, venous stasis in legs, hypotension, increased intrathoracic pressure, mediastinal and subcutaneous emphysema, pneumothorax, barotrauma, CO_2 gas embolism, atelectasis, bradyarrhythmias from vagal stimulation of trocar insertion and peritoneal distention, dysfunction of ventriculoperitoneal shunts, referred shoulder pain from CO_2 gas retained under the diaphragm, and nausea and vomiting.

Systemic Effects of CO_2 Absorption

Among the systemic effects of CO_2 absorptions are hypercarbia, acidosis, increased sympathoadrenal stimulation, hypertension, tachycardia, increased intracranial pressure, embolization, and sickle cell crisis. Arrhythmias can occur from hypercarbia, hypoxia, and catecholamines and in combination with halothane.

Trendelenburg Position

Venous congestion of head and neck; increased venous pressure; increased intracranial pressure; retinal hemorrhage; retinal detachment; increased intraocular pressure and glaucoma attack; corneal and conjunctival edema; endobronchial

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intubation and hypoxemia; ventilation-perfusion mismatch and hypoxia; edema of airway including larynx; airway obstruction and closure; brachial plexus injury from shoulder braces, femoral nerve, peroneal, and other neuropathies; and an assortment of respiratory complications have been reported with use of the Trendelenburg position.

Late Complications

Among the late complications are bowel obstruction from injury, cautery burn, intestine or omentum herniation through the trocar site, adhesions, deep vein thrombosis, and nerve injury resulting from improper padding. Fever may indicate infection from bowel necrosis. Cutaneous metastasis can occur at the port site.

Awad H, Santilli S, Ohr M, et al. The effects of steep Trendelenburg positioning on intraocular pressure during robotic radical prostatectomy. *Anesth Analg.* 2009;109(2):473-478.

Fahlenkamp D, Rassweiler J, Fornara P, et al. Complications of laparoscopic procedures in urology: experience with 2,407 procedures at 4 German centers. *J Urol.* 1999;162:765-771.

Fuller J, Ashar BS, Carey-Corrado J. Trocar-associated injuries and fatalities: an analysis of 1399 reports to the FDA. *J Minim Invasive Gynecol.* 2005;12:302-307.

Joshi GP. Complications of laparoscopy. *Anesthesiol Clin North America.* 2001;19:89-105.

Koç G, Tazeh NN, Joudi FN, et al. Lower extremity neuropathies after robot-assisted laparoscopic prostatectomy on a split-leg table. *J Endourol.* 2012;26:1026-1029.

Miele VJ, Bendok B, Bloomfield SM. Ventriculoperitoneal shunt dysfunction in adults secondary to conditions causing a transient increase in intraabdominal pressure: report of three cases. *Neurosurgery.* 2004;55:434.

Mills JT, Burris MB, Warburton DJ, et al. Positioning injuries associated with robotic assisted urological surgery. *J Urol.* 2013;190:580-584.

Nishikawa K, Nagashima C, Shimodate Y, et al. Migration of the endotracheal tube during laparoscopyassisted abdominal surgery in young and elderly patients. *Can J Anaesth.* 2004;51:1053-1054.

Sharma A, Berkeley A. Intraoperative drug-eluting stent thrombosis in a patient undergoing robotic prostatectomy. *J Clin Anesth.* 2009;21(7):517-520.

D.2. What postoperative orders will you write? When would you remove the Foley catheter and arterial line? Under what circumstances would you order a chest x-ray film?

Immediate chest x-ray film is ordered if respiratory distress, subcutaneous emphysema, and actual or suspected pneumothorax occurred; the case was prolonged and retroperitoneal; the patient was oliguric despite adequate hydration; or the intra-abdominal pressure was greater than 15 mm Hg.

Do not remove the arterial line until the patient is stable and blood gas values are normal. Check urine volumes. Expect an immediate diuresis. Do not remove the Foley catheter until the patient is stable, with fluid intake and volume output stable. Order IV fluids. Check voiding after the catheter is removed. Appropriate medications for nausea and pain control must be written. Ketorolac may be given if the surgeon agrees and there is no contraindication. Prophylactic antimuscarinic belladonna and opium (B&O) suppositories may be given to reduce the pain from bladder spasms. Patient-controlled analgesia usually is not necessary. For ambulatory patients, an adult escort must be available to take them home. Most patients, however, stay overnight.

Scavonetto F, Lamborn DR, McCaffrey JM, et al. Prophylactic belladonna suppositories on anesthetic recovery after robotic assisted laparoscopic prostatectomy. *Can J Urol.* 2013;20:6799-6804.

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D.3. What is the incidence of postoperative nausea and vomiting?

The incidence of nausea and vomiting after laparoscopy has been reported to be as high as 42%. It is the most important factor in causing an overnight admission after ambulatory surgery. IV antiemetics such as ondansetron, often with dexamethasone, may be given, preferably during surgery. The cause of nausea and vomiting is believed to be rapid peritoneal distention. Neurogenic pathways are activated by traction reflexes and by splanchnic pressure and manipulation.

McKeen DM, Arellano R, O'Connell C. Supplemental oxygen does not prevent postoperative nausea and vomiting after gynecological laparoscopy. *Can J Anaesth.* 2009;56(9):651-657.

Wilson EB, Bass CS, Abrameit W, et al. Metoclopramide versus ondansetron in prophylaxis of nausea and vomiting for laparoscopic cholecystectomy. *Am J Surg.* 2001;181:138-141.

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Chapter 27
Placenta Previa/Placenta Accreta

Jill Fong

A 41-year-old woman, gravida 5 para 4, is electively scheduled for her fourth cesarean section at 36 weeks of gestation. She has placenta previa that was diagnosed by sonography after a single episode of painless vaginal bleeding at 28 weeks of gestation which resolved spontaneously. Her vital signs are as follows: blood pressure, 110/56 mm Hg; heart rate, 85 beats per minute; respiratory rate, 22 breaths per minute; and oxygen saturation (SpO2) 98% on room air. Her hematocrit is 35%.

A. Medical Disease and Differential Diagnosis

1. What are the leading causes of maternal mortality, and what role does anesthesia play in this mortality?
2. What is the differential diagnosis for an antepartum hemorrhage?
3. How would you diagnose the etiology of antepartum bleeding after midpregnancy?
4. What is the incidence of placenta previa, and what are the associated conditions?
5. What are the different types of placenta previa?
6. What is the usual obstetric management for placenta previa?
7. What is vasa previa? How is it diagnosed and managed?
8. What are the risk factors for the development of a placental abruption?
9. How is placental abruption diagnosed and managed?
10. What complications are associated with placental abruption?
11. Who is at risk for uterine rupture, and how is uterine rupture diagnosed?
12. What is the treatment for uterine rupture?
13. Is this patient at risk for postpartum bleeding?
14. What are the different types of placenta accreta syndromes?
15. How is placenta accreta diagnosed?
16. How is placenta accreta managed obstetrically?
17. What tests and/or interventions can improve neonatal outcome of a preterm birth?

B. Preoperative Evaluation and Preparation

1. How does pregnancy change respiratory function, and what impact does this have on anesthetic care?
2. What are the maternal cardiovascular changes of pregnancy?
3. What are the maternal gastrointestinal changes of pregnancy?

4. What hematologic changes occur during pregnancy?
5. What laboratory data do you need before taking this patient to the operating room?
6. What preoperative medications would you administer to this patient?

C. Intraoperative Management

1. What monitors would you use for this patient?

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2. What anesthetic could be used in this patient?
3. What are the absolute and relative contraindications for neuraxial anesthesia?
4. What is the usual amount of blood loss expected with delivery?
5. What are the physical findings associated with blood loss?
6. How is postpartum hemorrhage defined, and what are the etiologies of this bleeding?
7. After delivery of the fetus, the placenta is removed with some difficulty in one small area and generalized oozing from the placental implantation site is noted. What is the most likely cause of this patient's bleeding?
8. After delivery of the placenta in a cesarean section, what maneuvers and drugs can enhance myometrial contractility and therefore decrease blood loss?
9. If this patient had ongoing bleeding intraoperatively, what guidelines help determine when red blood cell (RBC) transfusions should be given?
10. If this patient had a massive blood loss, what blood replacement therapy would be indicated?
11. What is the role of type O Rh-negative (universal donor) uncrossmatched blood in emergency transfusions, and how does this change your future management?
12. What complications can occur from the transfusion of blood products?
13. What is the role of autologous transfusion in obstetric patients?
14. Significant intraoperative blood loss required the transfusion of 8 units of typespecific, crossmatched packed RBCs (pRBCs). This patient had generalized oozing in the surgical field and hematuria. What is your differential diagnosis?
15. What is disseminated intravascular coagulation (DIC)?
16. What is the role of recombinant activated factor VII (rFVIIa) in obstetric patients?
17. What laboratory tests should be ordered during the resuscitation of this patient?
18. Define amniotic fluid embolism (AFE) syndrome and discuss treatment.

D. Postoperative Management

1. If the patient received epidural anesthesia and subsequently developed disseminated intravascular coagulation (DIC), when should the epidural catheter be removed?
2. You have successfully treated the patient's massive hemorrhage. Her laboratory values have returned to normal. Her central venous pressure (CVP) is within normal limits and urine output is appropriate. The patient, however, is still hypotensive despite appropriate intravascular volume replacement and support with vasopressors. What is your concern in this case?

A. Medical Disease and Differential Diagnosis

A.1. What are the leading causes of maternal mortality, and what role does anesthesia play in this mortality?

The exact measures of maternal death are defined differently by the different agencies collecting the statistics. The World Health Organization (WHO) defines the maternal mortality ratio (MMR) as the number of direct and indirect maternal deaths per 100,000 live births; it does not include late maternal deaths occurring more than 42 days but less than 1 year after pregnancy termination. In the United States, the pregnancy-related mortality ratio tallies the pregnancyrelated deaths per 100,000 live births; it includes maternal deaths while pregnant and within

1 year of the termination of pregnancy that occur from any cause related to or aggravated by the pregnancy regardless of the duration or site of that pregnancy but excludes accidental or incidental causes. The maternal mortality rate used by the United Kingdom Confidential Enquiry includes direct and indirect maternal deaths per 100,000 maternities, defined as pregnancies resulting in a live or stillbirth ≥20 gestational weeks; late maternal deaths are not included.

Developed versus developing countries have a markedly different incidence of maternal death; 99% of maternal deaths occur in developing countries. According to the WHO in 2010, there were approximately 210 maternal deaths per 100,000 live births globally with a range of uncertainty of 170 to 300 deaths per 100,000 live births. This is a decrease

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from the 1990 WHO estimates of a worldwide MMR of 400. The 2010 MMR's were 16 (range of uncertainty 14 to 18) and 240 (range of uncertainty 190 to 330) for developed and developing regions, respectively. Hemorrhage, hypertensive disorders of pregnancy, and sepsis cause more than half of the maternal deaths globally and about one-third of the deaths in the developed world. Obstetric hemorrhaging is the single most common cause of maternal mortality worldwide and accounts for about 25% of all postpartum deaths. Anemia, obstructed labor, HIV/AIDS, and unsafe abortions also play a role. Early marriage (a girl <18 years old) is a major health risk for girls; for girls, ages 15 to 19 years, pregnancy is the leading cause of death worldwide. Women in their 20s are five times less likely to die in childbirth than girls younger than 15 years old. In developed countries, hypertensive disorders of pregnancy, embolic disorders, and hemorrhage account for slightly less than 50% of maternal deaths. Fourteen percent are attributed to indirect deaths due most commonly to cardiovascular disease, and the risk of maternal death is increased by cesarean section delivery, advanced maternal age, non-white race, maternal obesity, and multifetal gestation.

In the United States, based on data from the Pregnancy Mortality Surveillance System of the Centers for Disease Control and Prevention, the aggregate 1998 to 2005 pregnancy-related mortality ratio (PRMR) of 14.5 maternal deaths per 100,000 live births was higher than those reported for any period in the previous 20 years. Hemorrhage accounted for 12% of these pregnancy-related maternal deaths, whereas hypertensive disorders of pregnancy, sepsis, thrombotic pulmonary embolism, cardiomyopathy, other cardiovascular disorders, and noncardiovascular medical disorders each accounted for 10% to 13% of the deaths. Some data suggests that the MMR in the United States may be increasing; the reason for this increase is unclear. It may be that more actual deaths are occurring, that reporting has improved, or that there is an artificial increase due code changes with the new International Statistical Classification of Diseases, 10th Revision (ICD-10) that was begun in 1999. Clark et al. evaluated maternal deaths from 2007 to 2012 after introducing disease-specific protocols. Their MMR was 6.4 of 100,000 live births in greater than 1.2 million deliveries, and the disease-specific protocols aided in the reduction of maternal deaths from hypertensive disease and postoperative pulmonary embolism but not hemorrhage.

In the United Kingdom, the Confidential Enquiry into Maternal Deaths found that from 2006 to 2008, the overall maternal mortality rate was 11.29 per 100,000 maternities with a significant decline in direct deaths rates from 6.24 in 2003-2005 to 4.67. The reduction was due mainly to a decrease in deaths due to thromboembolism and to a lesser extent from hemorrhage. Mortality from indirect causes, most commonly cardiac disease, remained unchanged. Substandard care was found in 70% of the direct deaths and 55% of the indirect deaths.

In developed regions, the estimated anesthesia-related MMR ranges between 1 and 3 deaths per 1,000,000 live births. If a maternal death can be attributed to an anesthetic complication and if an ideal anesthetic would have likely avoided this death, the death is considered anesthetic-related. Based on data from the United States, historically, cesarean sections under general anesthesia were more hazardous than those under neuraxial anesthesia, but case fatality rates for general anesthesia have decreased considerably, whereas those for neuraxial anesthesia have risen slightly leading to no significant difference between the two in the 1997 to 2002 time period. Looking at 257,000 parturients receiving neuraxial or general anesthesia between 2004 and 2009, the Serious Complication Repository Project of the Society for Obstetric Anesthesiology and Perinatology found that approximately 1 of 3,000 patients had serious anesthesia-related complications with high neuraxial block,

respiratory arrest in the labor suite, and unrecognized spinal catheters being the most common of these complications.

Berg CJ, Callaghan WM, Syverson C, et al. Pregnancy-related mortality in the United States, 1998 to 2005. *Obstet Gynecol*. 2010;116:1302-1309.

Cantwell R, Clutton-Brock T, Cooper G, et al. Saving Mothers' Lives: reviewing maternal deaths to make motherhood safer; 2006-2008. The Eighth Report of Confidential Enquiries into Maternal Deaths in the United Kingdom. *BJOG*. 2011;118(suppl 1):1-203.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:932-944.

Clark SL, Belfort MA, Dildy GA, et al. Maternal death in the 21st century: causes, prevention, and relationship to cesarean delivery. *Am J Obstet Gynecol*. 2008;199:36.e1-36.e5.

Clark SL, Christmas JT, Frye DR, et al. Maternal mortality in the United States; predictability and the impact of

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protocols on fatal postcesarean pulmonary embolism and hypertension-related intracranial hemorrhage. *Am J Obstet Gynecol*. 2014;211(1):32.e1-32.e9.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:5-7.

D'Angelo R, Smiley RM, Riley ET, et al. Serious complications related to obstetric anesthesia: the serious complication respiratory project of the Society for Obstetric Anesthesiology and Perinatology. *Anesthesiology*. 2014;120(6):1505-1512.

Hawkins JL, Chang J, Palmer SK, et al. Anesthesia-related maternal mortality in the United States: 1979-2002. *Obstet Gynecol*. 2011;117:69-74.

World Health Organization. *Trends in Maternal Mortality 1990 to 2010: WHO, UNICEF, UNFPA, and The World Bank estimates*. Geneva, Switzerland: World Health Organization; 2012.

A.2. What is the differential diagnosis for an antepartum hemorrhage?

Up to one-fourth of pregnant women may have antepartum vaginal bleeding, but only a small fraction experience antepartum hemorrhage. Most of this bleeding occurs in the first trimester, and bleeding in the first 20 weeks is presumed to be a threatened abortion or an ectopic pregnancy. Even if pregnancy loss does not occur, the risk for adverse outcomes later in pregnancy is increased. The rest of the discussion will be confined to pregnancies with a viable living fetus. Antepartum bleeding generally poses a greater threat to the fetus than the mother. The most common causes of antepartum hemorrhage are placenta previa and placental abruption. From the Canadian Perinatal Network, Sabourin et al. looked at 806 women with antepartum hemorrhage between 22 and 28 weeks of gestation. The most common causes were placental abruption (31.7%), placenta previa (21.2%), and cervical bleeding (6.6%), whereas no cause for hemorrhage was found in a third of the cases. Placenta previa is the abnormal implantation of the placenta over or adjacent to the cervical os and in front of the fetal presenting part. *Placental abruption*, or abruptio placentae, refers to the premature separation of a normally implanted placenta from the uterus' decidua basalis before delivery of the fetus.

Rare causes of antepartum bleeding include velamentous insertion of the umbilical cord with the involved placental vessels overlying the cervix, which is known as vasa previa, uterine rupture, cervicitis, and local genital tract lesions.

In the remaining cases, it is not always possible to identify the source of antepartum bleeding. Usually, this type of bleeding begins with minimal symptoms, if any, and stops; no anatomic cause is identified at delivery, and it is likely attributable to marginal placenta separation. However, these pregnancies have a higher risk of poor neonatal outcome and preterm delivery.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:354, 782-783.

McCormack RA, Doherty DA, Magann EF, et al. Antepartum bleeding of unknown origin in the second half of pregnancy and pregnancy outcomes. *BJOG*. 2008;115(1):1451-1457.

Sabourin JN, Lee T, Magee LA, et al. Indications for, timing of, and modes of delivery in a national cohort of women admitted with antepartum hemorrhage at 22+0 to 28+6 weeks' gestation. *J Obstet Gynaecol Can*. 2012;34(11):1043-1052.

A.3. How would you diagnose the etiology of antepartum bleeding after midpregnancy?

With antepartum uterine bleeding after midpregnancy, placenta previa and placenta abruption should always be considered in the differential diagnosis. Digital examination of the

cervix *should be avoided* until the diagnosis of placenta previa has been excluded because digital examination of a placenta previa can cause immediate, severe hemorrhaging. Classically, it has been taught clinically that painless uterine

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bleeding is indicative of placenta previa, while painful uterine bleeding signifies placental abruption. The differential diagnosis, however, is not actually that straightforward; for instance, labor or placental separation accompanying a previa may cause pain, whereas pain from an abruption may mimic normal labor. Transabdominal sonography is a simple and safe method of locating the placenta in a suspected placenta previa. Transvaginal sonography has been shown to be superior to transabdominal sonography and is currently the imaging modality of choice. Recently, transperineal sonography has been shown to have a 98% positive-predictive value and 100% negative-predictive value of placenta previa. On the other hand, sonography infrequently aids in the diagnosis of an acute placental abruption because fresh clot and placenta appear sonographically similar. Negative findings on sonographic examination do not rule out a placental abruption. Magnetic resonance imaging (MRI) has been used by numerous investigators to visualize placental abnormalities, including placenta previa and placental abruption, but is unlikely to replace sonography any time soon due to availability and cost limitations.

Based on the accuracy and safety of transvaginal sonography in detecting placental position, the “double setup” is rarely, if ever, used. The double setup was a vaginal examination done in an operating room with the patient and medical personnel completely prepared to do an emergency cesarean section if hemorrhaging should occur.

Glantz C, Purnell L. Clinical utility of sonography in the diagnosis and treatment of placental abruption. *J Ultrasound Med*. 2002;21(8):837-840.

Masselli G, Brunelli R, Di Tola M, et al. MR imaging in the evaluation of placental abruption: correlation with sonographic findings. *Radiology*. 2011;259(1):222-230.

Rani PR, Haritha PH, Gowri R. Comparative study of transperineal and transabdominal sonography in the diagnosis of placenta previa. *J Obstet Gynaecol Res*. 2007;33(3):134-137.

A.4. What is the incidence of placenta previa, and what are the associated conditions?

The incidence of placenta previa in the United States is about 1 in 300 to 400 deliveries. The risk of having placenta previa increases with advancing maternal age, multiparity, multifetal gestations, previous cesarean delivery, prior uterine surgery, cigarette smoking, cocaine use, infertility treatments, and unexplained increases in maternal serum α-fetoprotein levels. In approximately 90% of the patients with sonographic evidence of placenta previa at 20 weeks, the placenta moved away from the cervix and out of the lower uterine segment by term.

Placenta previa is associated with an increased risk of antepartum bleeding, intrapartum and postpartum hemorrhage, abnormalities of placental adherence, peripartum hysterectomy, blood transfusions, preterm birth with perinatal morbidity and mortality, congenital malformations, and septicemia. In the presence of a prior cesarean section, the patient with placenta previa is at greater risk for having a placenta accreta; this risk increased as the number of cesarean sections increased. Silver et al. found that in women with placenta previa, the risk of placenta accreta was 3%, 11%, 40%, 61%, and 67% for the first, second, third, fourth, and fifth or greater repeat cesarean deliveries, respectively.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:799-804.

Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstset Gynecol*. 2006;107:927-941.

Rosenberg T, Pariente G, Sergienko R, et al. Critical analysis of risk factors and outcome of placenta previa. *Arch Gynecol Obstet*. 2011;284(1):47-54.

Silver RM, Landon MB, Rouse DJ, et al. Maternal morbidity associated with multiple repeat cesarean deliveries. *Obstet Gynecol*. 2006;107(6):1226-1232.

A.5. What are the different types of placenta previa?

Classifications and terminology for placenta previa based on the degree to which the internal cervical os is covered have

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been confusing; they have been simplified to two terms. Currently, placenta previa is a term used to describe a placenta that partially or totally covers the internal cervical os, whereas the term low-lying placenta refers to a placenta implanted in the

lower uterine segment but remains at least 2 cm away from the os; this was previously called a marginal placenta previa. Normally, the placenta implants in the upper uterine segment. Clearly, the classification in some cases of placenta previa depends on the degree of cervical dilation at the time of cervical assessment. In vasa previa, the fetal vessels course through the membranes and cover the internal cervical os.

Bronsteen R, Whitten A, Balasubramanian M, et al. Vasa previa: clinical presentations, outcomes, and implications for management. *Obstet Gynecol*. 2013;122(2 pt 1):352-357.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:800.

Dashe JS. Toward consistent terminology of placental location. *Semin Perinatol*. 2013;37(5):375-379.

A.6. What is the usual obstetric management for placenta previa?

Obstetric management of placenta previa patients depends upon three things: fetal age and therefore maturity, presence or absence of labor, and severity of bleeding. The goal of management is to maximize fetal growth and minimize the possibility of antepartum hemorrhage. With many previas, the first episode of bleeding usually begins without warning or pain, stops spontaneously, and rarely causes maternal or fetal compromise, but bleeding often recurs. A mature fetus with or without labor should be delivered; if bleeding occur at or beyond 36 weeks, immediate delivery is indicated. If hemorrhaging is severe or there is concern about the fetal condition, delivery should take place regardless of gestational age. Otherwise, conservative management may safely prolong the pregnancy by an average of 4 weeks after the initial bleed. Between 24 and 34 weeks of gestation, betamethasone, a corticosteroid, often is given to the patient with placenta previa to accelerate fetal lung maturity.

With a preterm fetus and no persistent active uterine bleeding, management consists of close observation for bleeding and activity restriction in an inpatient setting or, in certain selected patients, an outpatient setting. For stable patients with no bleeding in the previous 48 hours who have ready access to hospital care, maternal and fetal outcome did not differ between outpatient and inpatient management. Maternal vital signs and hemoglobin (Hgb) are checked at regular intervals depending on when the bleeding, if it exists, subsides. The American Association of Blood Banks recommends that a blood type and screen be done every 3 days in actively bleeding pregnant women because of the risk for developing new alloantibodies. Fetal well-being also is assessed regularly. The use of tocolytic therapy in placenta previa patients with preterm labor and bleeding is controversial; it has been used to prolong gestation if both the mother and fetus are stable.

Elective delivery for women with placenta previa should take place at 36 to 37 weeks, and if a placenta accreta is suspected, it has been recommended by Spong et al. that delivery take place after 34 weeks. As gestational age increases, there is an increased risk of significant bleeding that would necessitate delivery: 4.7% at 35 weeks, 15% at 36 weeks, 30% at 37 weeks, and 59% at 38 weeks. If an indication for delivery is present, the use of amniocentesis to assess fetal lung maturity would not aid in guiding management.

Patients with placenta previa almost always are delivered by cesarean section, and some contend that all women whose placentas lie within 2 cm of the cervical os should be delivered by cesarean section. When the placenta is greater than 1 cm away from the cervical os, however, Vergani et al. and Bronsteen et al. suggest that vaginal delivery may be safe. Normally, with placenta removal, the myometrium of the uterus contracts and reestablishes vascular integrity by constricting the open vessels in the placental bed. In patients with placenta previa, bleeding after placenta removal can be brisk because the lower uterine segment contracts poorly and therefore does not constrict the avulsed vessels. There is a known association between placenta previa and placenta accreta that may further exacerbate uterine bleeding and require additional surgical and/or radiologic interventions to staunch the bleeding.

As needed, adequate intravenous access and laboratory studies, including a complete blood count, coagulation profile, and a type and screen/crossmatch should be obtained as circumstances dictate. Rh (anti-D) immune globulin is routinely administered to Rh-negative women at 28 weeks of gestation when the fetal blood type is unknown or known to be Rhpositive and again after delivery if the neonate is Rh-positive. With an acute bleeding episode

in an Rh-negative parturient, a qualitative rosette test or the quantitative Kleihauer-Betke test or flow cytometry should be

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done to determine if a fetal-maternal transfusion has occurred and if additional immune globulin is required.

Bronsteen R, Valice R, Lee W, et al. Effect of low-lying placenta on delivery outcome. *Ultrasound Obstet Gynecol*. 2009;33:204-208.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:883.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:311-313, 802-804.

Rao KP, Belogolovkin V, Yankowitz J, et al. Abnormal placentation: evidence-based diagnosis and management of placenta previa, placenta accreta, and vasa previa. *Obstet Gynecol Surv*. 2012;67:503-519.

Spong CY, Mercer BM, D'alton M, et al. Timing of indicated late-preterm and early-term birth. *Obstet Gynecol*. 2011;118(2 pt 1):323-333.

Vergani P, Ornaghi S, Pozzi I, et al. Placenta previa: distance to internal os and mode of delivery. *Am J Obstet Gynecol*. 2009;201(3):266.e1-266.e5.

A.7. What is vasa previa? How is it diagnosed and managed?

Vasa previa refers to intramembranous fetal vessels, unprotected by placenta or umbilical cord, coursing through the membranes over the cervical os and under the fetal presenting part. The incidence is approximately 1 in 2,500 deliveries and associated risk factors include a second trimester low-lying placenta/placenta previa, a placenta with accessory lobes, velamentous umbilical cord insertions, multiple pregnancies, and pregnancies from in vitro fertilization. An undiagnosed vasa previa is associated with a high fetal mortality (about 60%). Because fetal blood volume is small, any bleeding puts the fetus in jeopardy. When membranes rupture, either spontaneously or artificially, the fetal vessels running through these membranes often rupture. Vaginal bleeding with fetal distress or death when the membranes rupture is seen in an undiagnosed vasa previa and necessitate an emergency cesarean section based on fetal distress. If vaginal blood is present, the presence of fetal (RBCs) can be determined using a Kleihauer-Betke test or flow cytometry, although there is rarely time for this. Fortunately, the majority of cases of vasa previa can be diagnosed prenatally by routinely evaluating placental cord insertion by ultrasound examination and transvaginal sonographic color Doppler if the insertion site cannot be delineated clearly. Good outcomes in patients with vasa previa require a prenatal diagnosis and delivery by cesarean section before the membranes rupture. Robinson and Grobman suggest that women with vasa previa be delivered by 34 to 35 weeks of gestation to achieve the best balance between the risks of perinatal morbidity and mortality; at any given gestational age, amniocentesis for fetal lung maturity verification did not improve outcomes.

Bronsteen R, Whitten A, Balasubramanian M, et al. Vasa previa: clinical presentations, outcomes, and implications for management. *Obstet Gynecol*. 2013;122(2 pt 1):352-357.

Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstet Gynecol*. 2006;107:927-941.

Robinson BK, Grobman WA. Effectiveness of timing strategies for delivery of individuals with vasa previa. *Obstet Gynecol*. 2011;117(3):542-549.

A.8. What are the risk factors for the development of a placental abruption?

The frequency of placental abruption is about 1 in 200 deliveries. The premature separation of the normally implanted placenta can be total or partial and can lead to external or concealed bleeding. Concealed hemorrhage is associated with greater maternal and fetal risks. The most common conditions associated with placental abruption are gestational hypertension, preeclampsia, and chronic hypertension. The incidence of placental abruption is increased with increased

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maternal age, African-American or Caucasian race, prematurely ruptured membranes, cigarette smoking, cocaine use, leiomyomas, history of previous abruption, external trauma, and possibly lupus anticoagulant and high parity. The bleeding almost always is maternal because the placental separation is within the maternal decidua.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:793-798.

A.9. How is placental abruption diagnosed and managed?

The signs and symptoms of placental abruption vary considerably. Ultrasonography often does not confirm the diagnosis as the placenta and fresh clots have similar appearances. In severe placental abruptions, the diagnosis often is obvious with fetal distress and demise common. With a live fetus and vaginal bleeding, milder abruptions may be difficult to diagnose. If knowing would change the patient's management, MRI is a highly sensitive test for detecting placental abruption and should be considered.

Treatment depends on fetal gestational age and fetal and maternal condition. If the diagnosis is uncertain and the fetus is uncompromised, inpatient expectant management with close observation can be practiced. However, further placental separation can occur at any time and lead to serious fetal compromise or death. The use of tocolytics to prolong pregnancy is controversial. Rapid delivery of the compromised, but alive, fetus is by cesarean delivery. Kayani et al. looked at 33 pregnancies with a clinically overt placental abruption and fetal bradycardia. Of the 22 of the neurologically intact neonates, 15 were delivered within a 20-minute decision to delivery time, whereas 8 of the 11 neonates who died or had cerebral palsy on 1 year follow-up had a >20-minute interval.

If placental separation has led to fetal death, a vaginal delivery usually is preferred; there are two exceptions: a massive hemorrhage that cannot be managed with vigorous blood replacement and obstetric complications that prevent vaginal delivery will necessitate an operative delivery.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:796-799.

Kayani SI, Walkinshaw SA, Preston C. Pregnancy outcome in severe placental abruption. *BJOG*. 2003;110(7):679-683.

Masselli G, Brunelli R, Di Tola M, et al. MR imaging in the evaluation of placental abruption: correlation with sonographic findings. *Radiology*. 2011;259(1):222-230.

A.10. What complications are associated with placental abruption?

Maternal complications with severe abruption can include postpartum hemorrhage, hemorrhagic shock, a consumptive coagulopathy, acute renal injury, and Sheehan syndrome (pituitary failure). Placental abruption can lead to fetal compromise or fetal demise.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:796-799.

A.11. Who is at risk for uterine rupture, and how is uterine rupture diagnosed?

Primary uterine rupture is defined as a rupture occurring in a previously intact unscarred uterus, whereas a secondary rupture is associated with a preexisting myometrial incision, injury, or anomaly. In developed countries, Getahun et al. report the uterine rupture incidence to be 1 in 4,800, whereas in developing countries, the incidence is higher. Uterine rupture is typically classified as either complete, with all of the uterine wall layers separated, or incomplete (uterine dehiscence), with the uterine muscle separated but the visceral peritoneum intact. Uterine dehiscence is more common; it is less likely to cause adverse maternal and fetal derangements or necessitate cesarean delivery. The morbidity and mortality rates are higher when the rupture is complete. Prior cesarean delivery is the greatest risk factor associated with

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uterine rupture. Fortunately, uterine ruptures are rare. Other risk factors associated with uterine rupture include previous uterine surgery involving the myometrium, a tumultuous labor, difficult forceps delivery, uterine trauma, breech extraction, external and internal version, labor stimulation with oxytocin or prostaglandins, inappropriate uterotonic medication use, uterine anomalies, placenta increta/percreta, connective tissue defects such as Marfan or Ehlers-Danlos syndrome, and uterine overdistention by fetal macrosomia, hydramnios, or multifetal pregnancy.

Uterine rupture can be difficult to diagnose because of the varied symptoms and physical findings that can occur. The most consistent sign of uterine rupture is a nonreassuring fetal heart rate pattern. In some patients, the symptoms of uterine rupture will be indistinguishable from those of placental abruption. Other signs that may be present include hypotension, vaginal bleeding, abdominal pain, change in the uterine contour, changes in the uterine

contraction pattern, and cessation of labor. There may be little pain, and because most of these ruptures occur during labor, any pain may be masked by the analgesics given to treat the discomfort of labor.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:617-619, 887-888.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:790-793.

Getahun BS, Yeshi MM, Roberts DJ. Case records of the Massachusetts General Hospital: Case 34-2012: a 27-year-old woman in Ethiopia with severe pain, bleeding, and shock during labor. *N Engl J Med*. 2012;367(19):1839-1845.

Porreco RP, Clark SL, Belfort MA, et al. The changing specter of uterine rupture. *Am J Obstet Gynecol*. 2009;200(3):269.e1-269.e4.

A.12. What is the treatment for uterine rupture?

With a complete uterine rupture, fetal distress and maternal bleeding occur; an emergent cesarean delivery is imperative to deliver the fetus and stabilize the mother. After delivery of the fetus, the uterus can be repaired, the uterine arteries can be ligated, or a hysterectomy can be performed, depending on the size of the rupture and the patient's condition. Fetal distress and/or death are common while maternal death in the developed world is not.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:792-793.

A.13. Is this patient at risk for postpartum bleeding?

Yes, this patient has a higher chance of postpartum bleeding because of her known placenta previa and the increased risk of having an associated placenta accreta syndrome. There is a strong association between placenta previa, prior uterine surgery, and placenta accreta syndromes. Clark et al. found that placenta previa patients had a 5%, 24%, and 67% risk of having an associated placenta accreta with no, one, and four or more prior cesarean sections, respectively. Similarly, in patients with placenta previa, Silver et al. found a 3%, 11%, 40%, 61%, and 67% incidence of placenta accreta with zero, one, two, three, and four or more prior cesarean sections, respectively.

Clark SL, Koonings PP, Phelan JP. Placenta previa/accreta and prior cesarean section. *Obstet Gynecol*. 1985;66(1):89-92.

Silver RM, Landon MB, Rouse DJ, et al. Maternal morbidity associated with multiple repeat cesarean deliveries. *Obstet Gynecol*. 2006;107(6):1226-1232.

A.14. What are the different types of placenta accreta syndromes?

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Placenta accreta syndromes refer to a placenta that adheres abnormally to the myometrium of the uterus due to a partial or total absence of the decidual basalis and an incomplete development of the fibrinoid layer. The normal placenta has three general layers: the decidua, which is maternal in origin and adherent to the uterus; the chorion, including the chorionic villi; and the amnion. Both the chorion and amnion are of fetal origin. Normally, in the first few minutes after delivery of the neonate, the placenta separates from its implantation site at a physiologic cleavage line through the spongy layer of the decidua basalis. In placenta accreta syndromes, evidence suggests that not only is the decidua basalis scanty or absent but also that the cytotrophoblasts may exert some control of over decidua invasion via angiogenesis and growth expression allowing chorionic villi to attach and invade uterine myometrium. Placenta accreta occurs when the placental chorionic villi are attached directly to the uterine myometrium without a decidual layer. With placenta increta, the villi invade into the myometrium, and with placenta percreta, the villi penetrate through the myometrium and serosa of the uterus and, sometimes, into adjacent organs. Based on histologic evidence in patients with placenta accreta syndromes, placenta accreta occurs most frequently, increta occurs much less frequently, and percreta occurs the least. The abnormal adherence may involve the entire placenta (total placenta accreta), several placental lobules (partial accreta), or part or all of a single lobule (focal placenta accreta). The term placenta accreta often is used as a general term to describe all of these conditions.

The incidence of placenta accreta syndromes is increasing due mainly to rising cesarean section rates. The incidence was approximately 1 in 2,510 deliveries in the 1980s versus 1 in 533 deliveries for the period from 1982 to 2002. Decidual formation is commonly defective over a previous cesarean section scar, in the lower uterine segment, and/or after uterine curettage. Increasing cesarean section rate and placenta previa are by far the two most important risk factors. Maternal age greater than 35 years, increasing parity, endometrial defects (Asherman syndrome), submucous leiomyomata, and otherwise unexplained elevations in maternal serum α-fetoprotein concentration and B-human chorionic gonadotropin (B-hCG) are other risk factors associated with placenta accreta.

Committee on Obstetric Practice. Committee opinion no. 529: placenta accreta. *Obstet Gynecol*. 2012;120(1):207-211. Reaffirmed 2014.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:804-808.

Silver RM, Landon MB, Rouse DJ, et al. Maternal morbidity associated with multiple repeat cesarean deliveries. *Obstet Gynecol*. 2006;107(6):1226-1232.

Wu S, Kocherginsky M, Hibbard JU. Abnormal placentation: twenty-year analysis. *Am J Obstet Gynecol*. 2005;192:1458-1461.

A.15. How is placenta accreta diagnosed?

In patients with conditions such as placenta previa and previous uterine surgery that are highly associated with placenta accreta, it is important to have a high index of suspicion and to look carefully for signs of accreta beginning at 20 to 24 weeks of gestation. Prenatal diagnosis of placenta accreta allows for effective planning that helps minimize maternal morbidity. Transabdominal and transvaginal ultrasonography are useful modalities for evaluating placental position and implantation; the loss of the hypoechoic boundary between the placenta and bladder, placental continuity with the bladder wall, and intraplacental sonolucent spaces, venous lakes, or placental lacunae adjacent to the involved uterine wall are strongly suggestive of placenta accreta. The sensitivity and specificity of grayscale ultrasonography in detecting placenta accreta are approximately 77% to 87% and 96% to 98%, respectively. Color flow Doppler and MRI do not significantly improve the diagnostic sensitivity of grayscale ultrasonography alone. However, they can be used as adjunctive diagnostic tools. When the diagnosis is uncertain or the suspected placenta accreta is posteriorly placed, MRI may be helpful. Although antepartum diagnosis of placenta accreta would be ideal, currently, there is no single diagnostic modality that determines the diagnosis of placenta accreta with absolute accuracy. Unfortunately, the diagnosis of placenta accreta is occasionally made postpartum during the third stage of labor when separation of the placenta does not occur. The first clinical manifestation of placenta accreta is usually profuse, potentially life-threatening bleeding that occurs at the time of attempted manual placental separation. During vaginal delivery, uterine inversion can occur. Placenta accreta has become one of the most common reasons for peripartum hysterectomy.

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Chalubinski KM, Pils S, Klein K, et al. Prenatal sonography can predict degree of placental invasion. *Ultrasound Obstet Gynecol*. 2013;42(5):518-524.

Committee on Obstetric Practice. Committee opinion no. 529: placenta accreta. *Obstet Gynecol*. 2012;120(1):207-211. Reaffirmed 2014.

A.16. How is placenta accreta managed obstetrically?

Optimal management of placenta accreta has yet to be defined. Care should be individualized for each patient, and a multidisciplinary approach to delivery planning should be taken. Prenatal diagnosis and management appear to improve outcome. The problems associated with placenta accreta depend upon the site of implantation, depth of myometrial penetration, and the number of placental lobules involved. Only a focal placenta accreta may not require aggressive surgical intervention. Otherwise, surgical management can be difficult and requires a multidisciplinary approach in order to minimize maternal complications. If placenta accreta is known to exist antenatally, it is generally accepted that it is ideally treated with an elective cesarean section and hysterectomy; the placenta should be left in place during surgery. The optimal timing for the delivery of the patient with placenta accreta remains controversial

and should be individualized. In a retrospective series, Warshak et al. found that patients with a predelivery diagnosis of accreta, who had a planned en bloc hysterectomy without the removal of the placenta at 34 to 35 weeks of gestation after betamethasone administration, had decreased maternal hemorrhagic morbidity and no significant increase in neonatal morbidity. Optimal maternal and neonatal outcome in a stable patient seems to occur with a planned delivery at 34 weeks of gestation without amniocentesis. For women with suspected placenta accreta, some suggest preoperative placement of balloon catheters into the internal iliac arteries. After delivery of the fetus, the catheters may be inflated intermittently during hysterectomy, which may potentially decrease blood loss and provide optimum exposure of the operative field. They also may be used for intraoperative or postoperative embolization of persistent bleeders. The placement of these catheters is not risk-free; thrombosis and thromboemboli have been reported. The American College of Obstetricians and Gynecologists (ACOG) found that data on the efficacy of this intervention are unclear. Some investigators suggest that the placement of preoperative ureteral stents reduced morbidity in cesarean hysterectomies; others use stents intraoperatively as needed.

Because a hysterectomy renders the patient infertile, there has been some interest in attempting to leave the uterus intact in those patients with a strong desire to maintain their fertility. Timmermans et al. reviewed publications using “conservative” management. They found that in some reports, the placenta was partially removed, while in others, it was left intact; some reported the use of methotrexate and/or uterine artery embolization. Overall, 15% of this whole patient population required hysterectomy for hemorrhaging and 3% for infection; approximately 13% of the patients had subsequent pregnancies. They concluded that only in highly select cases when blood loss is minimal and maintenance of fertility is desired can “conservative” management be considered. ACOG states that “there is no convincing data for the use of methotrexate for postpartum management of placenta accreta.” This method of management is rarely indicated, but if the placenta is left in situ, these women should have serial ultrasounds or MRIs because serum B-hCG test are not helpful.

Committee on Obstetric Practice. Committee opinion no. 529: placenta accreta. *Obstet Gynecol*. 2012;120(1):207-211. Reaffirmed 2014.

Eller AG, Porter TF, Soisson P, et al. Optimal management strategies for placenta accreta. *BJOG*. 2009;116:648-654.

Fitzpatrick KE, Sellers S, Spark P, et al. The management and outcomes of placenta accreta, increta, and percreta in the UK: a population-based descriptive study. *BJOG*. 2014;121(1):62-70.

Timmermans S, van Hof AC, Duvekot JJ. Conservative management of abnormally invasive placentation. *Obstet Gynecol Surv.* 2007;62(8):529-539.

Warshak CR, Ramos GA, Eskander R, et al. Effect of predelivery diagnosis in 99 consecutive cases of placenta accreta. *Obstet Gynecol*. 2010;115:65-69.

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Wright JD, Silver RM, Bonanno C, et al. Practice patterns and knowledge of obstetricians and gynecologists regarding placenta accreta. *J Matern Fetal Neonatal Med*. 2013;26(16):1602-1609.

A.17. What tests and/or interventions can improve neonatal outcome of a preterm birth?

Since significant neonatal morbidity has been reported with elective delivery before 39 weeks of gestation, elective planned repeat cesarean deliveries are to be done after 39 weeks of gestation. The pivotal complication of preterm delivery is respiratory distress syndrome (RDS). Accurate gestational dating by timed serial ultrasound measurements, fetal heart sounds by Doppler ultrasound, or positive serum or urine B-hCG tests should be done. Documented fetal lung maturity by amniotic fluid analysis may be helpful in identifying fetuses at risk for developing RDS, but results indicating lung maturity may not reliably predict adverse outcomes and do not justify a delivery without other indications.

If an indication for delivery is present, the use of amniocentesis to assess fetal lung maturity does not aid in guiding management. In our case of preterm vaginal bleeding from a sonographically documented placenta previa, the patient should be electively delivered before 39 weeks because the risk of bleeding increases as gestation progresses. If there is maternal hemorrhaging, fetal maturity would not impact the decision to perform an immediate cesarean delivery.

Neonatal survival increases as birth weight and/or gestational age increases. The use of maternal antenatal steroids and neonatal exogenous surfactant have helped decrease neonatal

morbidity and mortality. Between 24 and 34 weeks of gestation, a single-dose therapy of corticosteroid, such as betamethasone (two doses of 12 mg intramuscularly, 24 hours apart) or dexamethasone (four doses of 6 mg intramuscularly, 12 hours apart), should be given to accelerate fetal lung maturity in a parturient who is at risk for imminent preterm delivery such as a patient with placenta previa or preterm rupture of membranes. Between 32 and 34 weeks of gestation, there is no consensus on the use of steroids, but before 24 weeks, it is not recommended.

The use of magnesium sulfate for fetal neuroprotection in threatened preterm delivery varies. Of those physicians using magnesium sulfate, some give a 6-g loading bolus followed by a 2 g per hour infusion to patients at risk for a preterm delivery from 24 0/7 to 27 6/7 weeks of gestation, whereas others use 31 6/7, not 27 6/7, weeks as the cut-off time.

The use of amniocentesis for fetal lung maturity (FLM) tests is declining in the United States and may become obsolete except perhaps in patients with poorly dated gestations who desired elective repeat cesarean delivery fall into this category. The use of maternal antenatal corticosteroids to induce lung maturity has a variable effect on these tests, and they should not be done in these patients. There are two types of tests used to determine pulmonary maturity. One type measures the concentration of particular components of pulmonary surfactant; the other evaluates the surfactant function of these. None of the tests performs significantly better than another, and it is recommended that only one test be done. *Fluorescence polarization*, the recently modified *TDx-FLM II*, is no longer available; this automated assay measured the surfactant-to-albumin ratio in uncentrifuged amniotic fluid and yielded results in approximately 30 minutes. For many years, the labor-intensive *lecithin-sphingomyelin (L/S) ratio* was the gold-standard test. By approximately 32 weeks of gestation, lecithin and sphingomyelin concentrations in amnionic fluid are similar, but after that, the concentration of lecithin compared to sphingomyelin begins to rise. By about 35 weeks of gestation, the L/S ratio is approximately 2.0, and a ratio of 2.0 or greater predicts that 98% of the neonates will not have RDS. *Lamellar body counts* increase with maturity; a count greater than 50,000 per μL is highly predictive of fetal lung maturity. *Phosphatidylglycerol*, which appears after 35 weeks of gestation and increases rapidly between 37 and 40 weeks, can be measured and is an indicator of lung maturity. The *foam stability* or *shake test* depends on the functionality of surfactant in amniotic fluid; when amniotic fluid is mixed appropriately with ethanol, the formation of stable foam at the air-liquid interface indicates lung maturity. Other tests exist, and the choice of test should be based on availability, presence or absence of contaminants, and physician preference.

American College of Obstetricians and Gynecologists. ACOG committee opinion no. 561: nonmedically indicated early-term deliveries. *Obstet Gynecol*. 2013;121(4):911-915.

American College of Obstetricians and Gynecologists. Practice bulletins no.139: premature rupture of membranes. *Obstet Gynecol*. 2013;122(4):918-930.

Chiossi G, Lai Y, Landon MB, et al. Timing of delivery and adverse outcomes in term singleton repeat cesarean

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deliveries. *Obstet Gynecol*. 2013;121(3):561-569.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:615, 653, 655, 854-855.

Varner S, Sherman C, Lewis D, et al. Amniocentesis for fetal lung maturity: will it become obsolete? *Rev Obstet Gynecol*. 2013;6(3-4):126-134.

B. Preoperative Evaluation and Preparation

B.1. How does pregnancy change respiratory function, and what impact does this have on anesthetic care?

A number of maternal respiratory changes are seen:

- Capillary engorgement of the mucosa is found throughout the respiratory tract, causing swelling of the nasal and oral pharynx, larynx, and trachea; this begins in the first trimester and increases progressively throughout pregnancy.
- By term, there are increases in minute ventilation (45%), tidal volume (45%), and oxygen consumption (30% to 40%); respiratory rate does not change. These changes do not return to their prepregnancy state for at least 6 to 8 weeks after delivery.

- Arterial $PaCO_2$ decreases to about 30 mm Hg by 12 weeks of gestation and remains there until it slowly increases after delivery over about 6 to 8 weeks postpartum.
- Arterial pH increases to about 7.44, and there is a partial metabolic compensation for the respiratory alkalosis (HCO_3^- 20 mEq per L).
- Functional residual capacity (FRC) begins to decrease by the fifth month and by term is 20% below prepregnancy values. After delivery, FRC increases and by 1 to 2 weeks postpartum returns to its prepregnant level. Additionally, the supine position will further decrease the FRC to approximately 70% of prepregnant volume.

Capillary engorgement of the airway mucosa necessitates the use of a smaller, 6.0, 6.5, or 7.0 mm, cuffed endotracheal tube in pregnant women. This vascular engorgement results in airway edema and increased airway friability, which may potentially make tracheal intubation more difficult. Because epistaxis is more likely to occur, nasal intubation is relatively contraindicated. Pilkington et al. showed that the number of pregnant women with a Mallampati class IV airway increased 34% between 12 and 38 weeks of gestation. Boutonnet et al. found that the incidence of Mallampati classes III and IV increased during labor when compared to the prelabor period; these changes are not fully reversed by 48 hours after delivery. No predictive factors for the increase in airway class were found; these changes occurred irrespective of any increase in body weight, the duration of first and second stages of labor, or volume of intravenous fluid. Regardless of the cause, difficult and failed intubations are more common in the pregnant than in the nonpregnant population.

The combination of a decreased FRC and increased oxygen consumption make the pregnant patient more susceptible to the rapid onset of hypoxemia in the apneic state. Therefore, before the induction of general anesthesia, the parturient should be “preoxygenated” with 100% oxygen for 3 to 5 minutes while taking normal tidal breaths or, if time is limited, for four vital capacity breaths. This effectively washes nitrogen out of FRC and provides maximal maternal oxygen reserves to allow longer apneic time during tracheal intubation. The reduced FRC combined with the increased minute ventilation increase the rapidity of changes in the depth of anesthesia while employing an inhaled anesthetic technique. In addition, the minimum alveolar concentration (MAC) of inhaled anesthetic agents has been found to be decreased by about 40% in pregnancy. In a small prospective electroencephalographic study, Ueyama et al. found that pregnancy not enhance the hypnotic effect of sevoflurane, and they suggest that the decreased MAC during pregnancy is not indicative of an enhanced volatile anesthetic effect on the brain but reflects the anesthetic effect on the spinal cord.

Bobrowski RA. Pulmonary physiology in pregnancy. *Clin Obstet Gynecol*. 2010;53(2):285-300.

Boutonnet M, Faitot V, Katz A, et al. Mallampati class changes during pregnancy, labour, and after delivery: can these be predicted? *Br J Anaesth*. 2010;104(1):67-70.

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Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:19-22, 31.

Pilkington S, Carli F, Dakin MJ, et al. Increase in Mallampati score during pregnancy. *Br J Anaesth*. 1995;74:638-642.

Ueyama H, Hagihira S, Takashina M, et al. Pregnancy does not enhance volatile anesthetic sensitivity on the brain: an electroencephalographic analysis study. *Anesthesiology*. 2010;113(3):577-584.

B.2. What are the maternal cardiovascular changes of pregnancy?

Most cardiovascular changes of pregnancy begin early in the first trimester and peak by 30 to 34 weeks of gestation. At term, the cardiovascular changes include the following:

- Cardiac output increases 40% to 50%. During the first trimester of pregnancy, the cardiac output increases to 40% or 50% above normal and plateaus at approximately 28 weeks of gestation. It remains fairly stable until the stresses imposed by labor increase it further. During labor, cardiac output increases approximately 15% with uterine contractions during the latent phase, 30% in the active phase, and 45% in the expulsive phase when compared to prelabor values. The greatest increase in cardiac output occurs immediately

  postpartum when it increases an average of 80% above prelabor values. Cardiac output and heart rate decline to prelabor values within 1 hour of delivery. Postpartum, over the next 2 to 4 weeks, cardiac hemodynamic parameters return toward pregravid levels. It can take a year, however, for the residual effects of cardiovascular remodeling to subside.
- Stroke volume increases approximately 30%.
- Heart rate increases to about 15%.
- Systolic blood pressure is minimally affected by pregnancy.
- Diastolic blood pressure decreases up to 20% by midpregnancy but returns to its prepregnant level at term.
- Systemic vascular resistance decreases 20%.
- CVP remains unchanged.
- *Aortocaval compression* refers to the gravid uterus compressing the inferior vena cava and/or the abdominal aorta. The extent of the compression depends on the patient's position and weeks of gestation. In the supine position, compression of the inferior vena cava occurs as early as 13 to 16 weeks of gestation. At term in the supine position, the inferior vena cava is occluded almost completely with venous return from the lower extremities occurring through the dilated paravertebral, intraosseous, vertebral, and epidural collateral circulation. At term, compression of the aorta also occurs to some degree when sitting. Despite this impaired blood flow and concomitant decrease in cardiac output, the majority of supine women are not hypotensive or symptomatic because of the compensatory rise in systemic vascular resistance. However, up to 15% of supine women at term develop supine hypotension syndrome with hypotension, bradycardia, and symptoms of dizziness, light-headedness, nausea, and even syncope. Aortocaval compression decreases uteroplacental perfusion. For these reasons, all patients after 20 weeks of gestation should be positioned with left lateral uterine displacement.

Armstrong S, Fernando R, Columb M, et al. Cardiac index in term pregnant women in the sitting, lateral, and supine positions: an observational, crossover study. *Anesth Analg*. 2011;113(2):318-322.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:15-19.

B.3. What are the maternal gastrointestinal changes of pregnancy?

Parturients are considered to be at an increased risk for aspiration of gastric contents. Pregnancy itself does not alter gastric emptying of liquid or solid materials, but during labor, gastric motility does decrease. Gastric acid secretion

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appears to be unchanged. Because of the upward displacement of the stomach by the gravid uterus, tone in lower esophageal high-pressure zone, however, is decreased. This zone normally prevents the reflux of gastric contents. In the first trimester, the tone in this zone may be unchanged, but in the second and third trimesters, lower esophageal high-pressure zone tone falls gradually to about 50% of its preconceptual level. By 36 weeks of gestation, it reaches its lowest point and does not return to prepregnancy levels until 1 to 4 weeks postpartum. As a result, 30% to 50% of women experience heartburn during pregnancy. The increased aspiration risk is thought to be due to the parturient's decrease lower esophageal high-pressure zone tone and the increased risk of having difficulty with intubation.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:25-26.

Ramu B, Mohan P, Rajasekaran MS, et al. Prevalence and risk factors for gastroesophageal reflux in pregnancy. *Indian J Gastroenterol*. 2011;30:144-147.

B.4. What hematologic changes occur during pregnancy?

The hematologic changes seen by term are as follows:

- Intravascular fluid volume increases 45%.
- Plasma volume increases 55%.
- RBC volume increases 30%.

The disproportionate increase in plasma volume compared to RBC volume results in the relative, or physiologic, anemia of pregnancy. By midgestation, hematocrit has typically fallen approximately 15% below prepregnant levels; the Hgb and hematocrit are approximately 11.2 g per dL and 34%, respectively. In late gestation, RBC volume increases, and at term, maternal Hgb and hematocrit are approximately 11.6 g per dL and 35.5%, respectively. This decreased viscosity may aid in maintaining the patency of the uteroplacental vascular bed.

In addition, the following coagulation factors are increased at term: factors I (fibrinogen), VII, VIII, IX, X, and XII. Plasminogen, fibrin degradation products, and fibrinopeptide A are also increased. Factors II and V are unchanged. Factors XI and XIII are decreased as is antithrombin III. Overall, pregnancy is associated with an accelerated, but compensated, rate of intravascular coagulation. Both, the prothrombin time (PT) and activated partial thromboplastin time (aPTT) are shortened 20%, and thromboelastography suggests a hypercoagulable state. The platelet count is typically unchanged at term. However, 0.9% of otherwise normal women will have a platelet count less than 100,000 per μL; gestational thrombocytopenia refers to maternal platelet counts of less than 150,000 μL in otherwise normal women.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:22-25.

B.5. What laboratory data do you need before taking this patient to the operating room?

The laboratory values needed in this healthy parturient having an elective scheduled cesarean section are minimal. A complete blood count with platelets and a type and crossmatch should probably be sent because this patient is at an increased risk for bleeding due to not only to her placenta previa but also to the increased likelihood of an associated placenta accreta since it is her third cesarean delivery. There is no consensus on the type or amount of blood products that should be available. However, many obstetricians and anesthesiologists suggest that at least four units of pRBCs be immediately available with other blood products readily available. Unless the patient has a coagulation disorder or is actively bleeding, a PT, an aPTT, and a fibrinogen level are not needed because the values should be within normal limits.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:884-885.

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B.6. What preoperative medications would you administer to this patient?

Patients at increased risk for aspiration should receive a nonparticulate oral antacid such as sodium citrate 30 minutes prior to the induction of anesthesia. Intravenous H_2-receptor antagonists, such as ranitidine, and/or metoclopramide may also be given preoperatively for aspiration prophylaxis. This patient is having an elective cesarean delivery and should have a fasting period for solids consistent with the hospital's policy for nonobstetric patients undergoing elective surgery.

This patient should receive antimicrobial prophylaxis within the 60-minute period before skin incision for the cesarean delivery. A single dose of a first-generation cephalosporin, such as cefazolin, is the first-line antibiotic of choice unless a patient is allergic to this medication. If an allergy exists, then a single dose of clindamycin and an aminoglycoside is a reasonable alternative.

American College of Obstetricians and Gynecologists. ACOG practice bulletin no. 120: use of prophylactic antibiotics in labor and delivery. *Obstet Gynecol*. 2011;117(6):1472-1483.

American Society of Anesthesiologists Task Force on Obstetric Anesthesia. Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia. *Anesthesiology*. 2007;106(4):843-863.

Sun J, Ding M, Liu J, et al. Prophylactic administration of cefazolin prior to skin incision versus antibiotics at cord clamping in preventing postcesarean infectious morbidity: a systematic review and meta-analysis of randomized controlled trials. *Gynecol Obstet Invest*. 2013;75:175-178.

C. Intraoperative Management

C.1. What monitors would you use for this patient?

Standard monitors should be used and include the following: electrocardiogram (ECG), blood pressure cuff, pulse oximeter, end-tidal carbon dioxide monitor, and Foley catheter. In addition, two large-bore intravenous lines, a forced air body warming blanket, intravenous fluid warmers, and intermittent pneumatic compression stockings should be used. If hemorrhaging occurs and urine output falls below 0.5 mL/kg/hr, despite adequate volume replacement, central venous line placement should be considered. A radial arterial line should also be considered if multiple blood samples will be needed and/or hemodynamic instability occurs. Equipment for the rapid infusion of intravenous fluids and blood products should be readily available.

Bates SM, Greer IA, Middledorp S, et al. VTE, thrombophilia, antithrombotic therapy, and pregnancy. *Chest*. 2012;141(2 suppl):e691S-e736S.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:883-884, 926.

C.2. What anesthetic could be used in this patient?

In the patient with placenta previa, a regional or general anesthetic technique could be used. Many anesthesiologists would choose to perform a continuous neuraxial anesthetic in this patient. The choice of anesthetic depends on the cesarean section indication and urgency and the maternal volume status. All patients with placenta previa are at risk for increased intraoperative blood loss due to the poor contractility of the lower uterine segment, the increased risk of an associated placenta accreta, and the possibility of an anterior placenta being cut during uterine incision. Hong et al. prospectively compared epidural to general anesthesia in women undergoing cesarean section for placenta previa. They found that postoperative hematocrits were lower in the patients receiving general anesthesia; there were no group differences with respect to operative times, estimated blood loss, urine output, or Apgar scores. Chestnut et al. found that none of the patients receiving continuous epidural anesthesia for elective or emergency peripartum hysterectomy required an intraoperative induction of general anesthesia in a multi-institutional study. Although these studies looked at epidural anesthesia, options for neuraxial include continuous spinal, combined spinal epidural, and continuous epidural anesthesia.

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Single-injection spinal anesthesia can be used, but the unpredictable length of the surgery may make this a poor choice. All patients having neuraxial anesthesia should be informed that if the need arises, general anesthesia may be induced.

If the patient had a known placenta accreta, neuraxial anesthesia could still be used depending upon the urgency of the cesarean section and the maternal volume status. If continuous epidural anesthesia was chosen and internal iliac balloons were to be placed preoperatively to assist with intraoperative hemostasis, the epidural anesthetic could be utilized during their placement. If hemorrhaging occurs intraoperatively and the patient becomes hemodynamically unstable, conversion to general anesthesia may be necessary. This possibility should be discussed with the patient and obstetric team before surgery. On the other hand, if the patient has a suspected placenta percreta, a general anesthetic is the usual choice for the operative cesarean section and hysterectomy because of the extensive surgery that may be required.

If postpartum hemorrhaging occurs, a coordinated team approach aimed at early recognition and treatment is essential. Good communication between *all* the involved specialties is imperative. In Lewis and Drife's report, poor communication between specialties was believed to have been a contributor to maternal death.

Chestnut DH, Dewan DM, Redick LF, et al. Anesthetic management of obstetric hysterectomy: a multiinstitutional study. *Anesthesiology*. 1989;70:607-610.

Hong JY, Jee YS, Yoon HJ, et al. Comparison of general and epidural anesthesia in elective cesarean section for placenta previa totalis: maternal hemodynamics, blood loss and neonatal outcome. *Int J Obstet Anesth*. 2003;12:12-16.

Lewis G, Drife J. *Why mothers die 2000-2002:The sixth report of the confidential enquiries into maternal deaths in the United Kingdom.* London: RCOG Press; 2004:27.

C.3. What are the absolute and relative contraindications for neuraxial anesthesia?

Absolute contraindications

- Patient inability to cooperate or patient refusal
- Uncorrected maternal hypovolemia or hypovolemic shock
- Infection at the site of needle insertion
- Frank coagulopathies
- Recent pharmacologic anticoagulation
- Mass lesions causing increased intracranial pressure
- Providers' lack of experience in techniques
- Lack of appropriate monitoring and/or resuscitative equipment

Relative contraindications have included maternal systemic infection, neurologic disease, severe stenotic heart lesions, and some isolated blood coagulation test abnormalities. Most cases of properly treated systemic infection or neurologic disease, however, do not currently contraindicate the use of neuraxial anesthesia. Each patient should be treated individually with careful consideration of the benefits and risks of neuraxial anesthesia.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:459.

C.4. What is the usual amount of blood loss expected with delivery?

The usual amount of delivery-related blood loss depends upon the type of delivery. The average blood loss is 500 mL for a vaginal delivery, 1,000 mL for a cesarean delivery, and 1,500 mL for a cesarean hysterectomy. Estimated blood loss values often are underestimated clinically.

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Stafford I, Dildy GA, Clark SL, et al. Visually estimated and calculated blood loss in vaginal and cesarean delivery. *Am J Obstet Gynecol*. 2008;199(5):519.e1-519.e7.

C.5. What are the physical findings associated with blood loss?

The physical findings in relation to percentage of blood loss defined by the American College of Surgeons Committee on Trauma are listed in Table 27.1.

The applicability of these clinical findings to the obstetric population is unclear because the data comes from a nonobstetric population. Depending on the nonpregnant blood volume and the corresponding magnitude of pregnancy-induced hypervolemia, a dangerous feature of postpartum bleeding is the failure of the pulse and blood pressure to undergo more than moderate alterations until large amounts of blood (>1,500 mL) have been lost. There is substantial variability between the relationship of clinical signs and blood loss, which makes clinical interventions based on physical findings difficult.

TABLE 27.1 Advanced Trauma Life Support Classification of Shock

	CLASS 1	CLASS 2	CLASS 3	CLASS 4
Blood loss (%)[a]	<15	15-30	30-40	>40
Heart rate (beats/min)	<100	>100	>120	>140
Systolic blood pressure (mm Hg)	Normal	Normal	Decreased	Decreased
Pulse pressure	Normal or increased	Decreased	Decreased	Decreased
Respiratory rate (breaths/min)	14-20	20-30	30-40	>35
Mental state	Slightly anxious	Mildly anxious	Anxious, confused	Confused, lethargic

[a] Percent total blood volume.

From American College of Surgeons Trauma Committee. *Advanced Trauma Life Support for Doctors*. 8th ed. Chicago, IL: American College of Surgeons; 2008.

TABLE 27.2 Trigger Thresholds for Modified Early Obstetric Warning System Parameters

	RED TRIGGER	YELLOW TRIGGER
Temperature (°C)	<35 or >38	35-36

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Systolic BP (mm Hg)	<90 or >160	150-160 or 90-100
Diastolic BP (mm Hg)	>100	90-100
Heart rate (beats/min)	<40 or >120	100-120 or 40-50
Respiratory rate (breaths/min)	<10 or >30	21-30
Oxygen saturation (%)	<95	—
Pain score[a]	—	2-3
Neurologic response	Unresponsive, pain	Voice

BP, blood pressure.

[a] Pain score: 0 = No pain at all; 1 = No pain at rest, light pain with movement; 2 = Intermittent pain at rest, moderate pain with movement; 3 = Moderate pain at rest, severe pain with movement.

From Singh S, McGlennan A, England A, et al. A validation study of the CEMACH recommended modified early obstetric warning system (MEOWS). *Anaesthesia*. 2012;67:12-18.

Although not specific for the hemorrhaging parturient, the 2003 to 2005 Confidential Enquiry into Maternal and Child Health report recommended the use of the Modified Early Obstetric Warning System (MEOWS) to help in the early identification and treatment of acutely ill parturients (Table 27.2). It had a positive predictive value of 39% and a negative predictive value of 98% for predicting maternal morbidity. A single red trigger or the combination of two yellow triggers prompted an urgent medical assessment.

American College of Surgeons Trauma Committee. *Advanced Trauma Life Support for Doctors*. 8th ed. Chicago, IL: American College of Surgeons; 2008.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:781-782.

Pacagnella RC, Souza JP, Durocher J, et al. A systematic review of the relationship between blood loss and clinical signs. *PLos One*. 2013;8(3):e57594.

Singh S, McGlennan A, England A, et al. A validation study of the CEMACH recommended modified early obstetric warning system (MEOWS). *Anaesthesia*. 2012;67:12-18.

C.6. How is postpartum hemorrhage defined, and what are the etiologies of this bleeding?

In the literature, the definition of postpartum hemorrhage has been variable and has included subjective assessments of blood loss greater than the standard norms (>500 mL for vaginal deliveries and >1,000 mL in cesarean sections), a 6% to 10% decline in hematocrit, and/or the need for a blood transfusion. There is no absolute numeric definition of postpartum hemorrhage. The etiologies of postpartum hemorrhage generally can be categorized as those occurring early within 24 hours of delivery and those occurring late, 24 hours after delivery. Because the obstetrician typically is faced with early postpartum hemorrhage, the remainder of this discussion will focus on its causes. The two broad etiologies of early postpartum hemorrhage are based on bleeding from the placental implantation site and genital tract trauma. Within the

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category of placental site bleeding, bleeding is usually due to either myometrial hypotonia, such as that seen with uterine atony and placenta previa, or retained placental tissue as can be seen with invasive placentation such as placenta accreta and uterine inversion. Genital tract traumas that lead to postpartum bleeding include genital tract lacerations and uterine rupture. Coagulation defects intensify the bleeding that occurs with any of the earlier abnormalities.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:784-793.

C.7. After delivery of the fetus, the placenta is removed with some difficulty in one small area and generalized oozing from the placental implantation site is noted. What is the most likely cause of this patient's bleeding?

The most likely causes of bleeding in this patient are myometrial hypotonia due to the poor contraction of the lower uterine segment and a focal placenta accreta. Near term, at least 600 mL per minute of blood flows through the intervillous space carried by about 120 spiral arteries and their accompanying veins. Due to endotrophoblastic remodeling to create a lowpressure system, these arteries have no muscular layer. With placental separation, these vessels are avulsed; hemostasis at the placental implantation site is first achieved by contraction of the myometrium that compresses these relatively large vessels and reestablishes vascular integrity. Subsequently, clotting occurs and the vessel lumens are obliterated. Ineffective myometrial contractions, such as occur with retained placenta or massive blood clots, can impair hemostasis at the implantation site. In this patient, the lower uterine segment, which contains less myometrial tissue, contracts poorly, and hemorrhaging can result despite normal coagulation. Bleeding that occurs after placenta delivery is usually a steady, not a sudden massive, hemorrhage. The constant seepage, however, can lead to an enormous blood loss. Severe postpartum hemorrhage, therefore, can result from uterine atony despite normal coagulation. Conversely, even if coagulation is impaired, vigorous myometrial contraction within and adjacent to the denuded placental implantation site makes severe hemorrhage from this implantation site unlikely. During rapid bleeding, the hematocrit may not accurately reflect the amount of blood lost due to the lack of equilibration with other fluid compartments.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:93-94, 780-781.

C.8. After delivery of the placenta in a cesarean section, what maneuvers and drugs can enhance myometrial contractility and therefore decrease blood loss?

Uterotonics seem to be the most important method to decrease postpartum bleeding. Uterotonic medications, such as oxytocin, also cause myometrial contractions. Synthetic oxytocin (Pitocin, Syntocinon) is the drug of choice and is given once the fetus is born and the placenta is delivered. Oxytocin increases the frequency and duration of uterine contractions; these contractions are most likely mediated through an increase in intracellular calcium levels. The number of oxytocin receptors in the uterus increases from about 20 weeks of gestation to 34 weeks of gestation, and receptor sensitivity increases during labor. Although oxytocin is routinely given, there is no standard prophylactic dose for either vaginal delivery or cesarean section. Intravenous therapy is the preferred route of administration, but intramuscular and intrauterine dosing is possible. Intravenous oxytocin has a rapid onset of about 1 minute and a fast mean elimination half-life of 3 to 5 minutes. Initial intravenous treatment usually starts with 20 units of oxytocin in 1,000 mL of crystalloid solution infused at a rate of 0.3 IU per minute (the ED_{90}). Munn et al. found that higher doses (80 units in 500 mL over 30 minutes) were safe, efficacious, and reduced the need for additional uterotonic therapy by 20% when compared with standard dosing of 10 units in 500 mL over 30 minutes. Roach et al. agree that higher rates prophylactic oxytocin seem to be more effective at preventing various measures of postpartum hemorrhage especially after cesarean delivery. The posterior pituitary produces the polypeptide hormones, oxytocin and antidiuretic hormone. Because they differ from one another by only two amino acids, oxytocin exhibits a small antidiuretic effect that is clinically insignificant unless very large doses are given; in this situation, water intoxication might occur. A bolus of oxytocin can decrease peripheral vascular resistance due to a direct relaxing effect on vascular smooth muscle leading to hypotension that on occasion requires treatment with appropriate vasopressors (ephedrine or phenylephrine). Patients may also exhibit tachycardia and arrhythmias. In some countries other than the United States, carbetocin (Duratocin), a long-acting oxytocin analogue, and a combination agent of oxytocin and ergonovine (Syntometrine) are available.

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Manual uterine massage is often done and is thought to stimulate the myometrium to contract. The evidence for this common practice, however, is not strong. McCurdy et al.

found that spontaneous delivery of the placenta during cesarean delivery reduced blood loss by 30% when compared to manual removal.

When oxytocin fails to produce adequate uterine tone and uterine atony is present, other uterotonic medications should be used. Uterine atony is the most common cause of postpartum hemorrhage and accounts for up to 80% of the cases. The second-line agent chosen depends on its side effect profile and contraindications. Ergot alkaloids, methylergonovine (Methergine) and ergonovine (ergometrine), are effective uterotonic agents; they are usually given intramuscularly and produce tetanic contractions of the uterus that may be mediated through α-adrenergic receptors. Their usefulness is limited because the induced hypertension, due to vasoconstriction, can be prominent. These agents should be avoided in patients with preexisting hypertensive disease. Other cardiovascular affects include coronary artery spasm leading to myocardial infarction, arrhythmias, or cerebrovascular accidents. Pulmonary complications have been reported including pulmonary artery vasoconstriction and pulmonary hypertension. Associated side effects include headache, dizziness, nausea, and vomiting.

Prostaglandins are uterotonic agents. The prostaglandins cause an increase in myometrial intracellular calcium levels leading to an increase in myosin light-chain kinase activity and uterine contraction. Intramuscular and intrauterine administration of 15-methyl prostaglandin $F_{2\alpha}$ (carboprost tromethamine [Hemabate]) can be used to control of uterine atony. Due to its bronchoconstrictive properties, its use is strongly contraindicated in asthma patients. Rectally administered prostaglandin E_2 (Prostin E_2) is a naturally occurring uterotonic agent that has not been tested in clinical trials for postpartum bleeding, and its unfavorable side effects include fever/chills, nausea/vomiting, diarrhea, and headaches. In Europe, there is an intravenous prostaglandin E_2 available (Sulprostone). Finally, Mousa and Alfirevic recently reported that rectally administered misoprostol (Cytotec), a synthetic prostaglandin E_1 analogue, provided no added benefit when compared to standard therapy with oxytocin and ergometrine (ergonovine) in primary postpartum hemorrhage patients.

If pharmacologic methods fail to control atony-related hemorrhage, alternative measures, including uterine tamponade, selective arterial embolization, and surgical intervention must be undertaken.

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Svanström MC, Biber B, Hanes M, et al. Signs of myocardial ischaemia after injection of oxytocin: a randomized double-blind comparison of oxytocin and methylergometrine during Caesarean section. *Br J Anaesth*. 2008;100:683-689.

C.9. If this patient had ongoing bleeding intraoperatively, what guidelines help determine when red blood cell (RBC) transfusions should be given?

Treatment of serious bleeding demands prompt and adequate refilling of the intravascular compartment. Normovolemia should be maintained, and usually non-dextrose-containing crystalloid solutions are used for the initial volume resuscitation. These solutions rapidly equilibrate into the extravascular space, and therefore, the volume of crystalloid given should be three times as much as the estimated blood loss. Colloid solutions can also be used to maintain normovolemia but confer no greater benefit than crystalloid solutions. Depending on

colloid solution (e.g., 5% albumin), the volume that should be administered is the same as that of the estimate blood loss; this may be helpful in facilitating a more rapid repletion of a preexisting volume deficit.

Defining a universal hematocrit (Hct) or Hgb value below or above which transfusion is either mandatory or contraindicated is difficult. RBCs carry oxygen to the tissues, and the goal of RBC transfusions is to maintain adequate tissue oxygenation. The 2006 American Society of Anesthesiologists Practice Guidelines state that patients with an Hgb concentration ≥10 g per dL usually do not require RBC transfusion, and if a patient's Hgb concentration is less than 6 g per dL, RBCs should usually be administered. RBC transfusions should be considered in all patients with clinical evidence of inadequate oxygen carrying capacity. In most bleeding obstetric patients, maintaining an Hgb level above 7 g per dL is suggested unless evidence of impaired pulmonary or cardiac function indicates a need for a higher Hgb level.

American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. *Anesthesiology*. 2006;105:198-208.

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Fong J, Gurewitsch ED, Kang HJ, et al. An analysis of transfusion practice and the role of intraoperative blood salvage during cesarean delivery. *Anesth Analg*. 2007;104:666-672.

C.10. If this patient had a massive blood loss, what blood replacement therapy would be indicated?

When blood replacement therapy is indicated, compatible whole blood is ideal for maintaining intravascular volume in the treatment of hypovolemia from catastrophic acute hemorrhage. One unit of whole blood raises the Hct by 3 to 4 volume percent and replaces many coagulation factors, especially fibrinogen. Importantly, using whole blood versus packed red blood cells and components decreases the exposure of women with severe hemorrhage to blood donors. When whole blood transfusions were compared with packed red blood cells transfusions or blood product combinations, Alexander et al. reported that the incidence of renal failure, adult RDS, pulmonary edema, hypofibrinogenemia, admission to an intensive care unit, and maternal death decreased significantly in women delivered at Parkland Hospital. However, availability of whole blood is limited; few units of whole blood are kept in the modern blood bank as over 90% of donor blood is fractionated into blood components. For women who do not have massive blood loss, pRBC transfusions are suitable, and component therapy provides better treatment because only the specific component needed is given.

Blood component therapy provides the patient with only the components that they require. The products available are pRBCs, fresh frozen plasma (FFP), cryoprecipitate, and platelets. A unit of pRBC is prepared from 1 unit of whole blood; its plasma is removed and replaced with additives such as citrate, phosphate, dextrose, and adenine. Its volume is about 250 to 325 mL with an Hct of 55 to 80 volume percent depending upon the method used for preparation and storage. A unit of pRBCs increases the patient's Hct approximately 3 volume percent and Hgb by about 1 g per dL. Crystalloid infusion and pRBC transfusion are the mainstays of therapy in the bleeding obstetric patient.

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FFP contains all the necessary coagulation factors, and a unit has a volume of approximately 250 mL. Charbit et al. found that a simple fibrinogen measure could anticipate the severity of bleeding; a fibrinogen level less than 200 mg per dL was associated with a high risk of severe bleeding as defined by either a ≥4 g per dL decrease in Hgb, ≥4 RBC unit transfusion, invasive hemostatic intervention, or death. When replacement of coagulation factors is needed for hemostasis as occurs after massive transfusion, FFP transfusion is indicated. In a parturient with surgical bleeding, a fibrinogen level of less than 100 mg per dL, a prolonged PT, and/or a prolonged aPTT are indications for FFP administration in initial doses of 10 to 15 mL per kg. The 2010 revised European trauma guidelines recommend a higher trigger level, 150 to 200 mg per dL, for the transfusion of a fibrinogen-rich solution. FFP administration is not indicated for hypovolemia. During active hemorrhaging, attempts should be made to maintain the fibrinogen level higher than 150 to 200 mg per dL. Cryoprecipitate is prepared from FFP and 15 mL contains 200 mg fibrinogen, factor VIII:C,

factor VIII:von Willebrand, factor XIII, and fibronectin. Ten pooled bags (10 to 15 mL per bag) of cryoprecipitate will increase the fibrinogen level by 65 to 70 mg per dL. In the bleeding obstetric patient, general clotting factor replacement with cryoprecipitate provides no advantage over FFP and should not be used unless volume is problematic or there is a specific factor deficiency. Virus-inactivated fibrinogen concentrate can also be used to increase the fibrinogen level; each gram increases the fibrinogen level approximately 40 mg per dL.

With obstetric hemorrhage, the platelet count should be maintained above 50,000 per μL with the infusion of platelet concentrates. One unit of platelets increases the platelet count from 5,000 to 10,000 per μL in an adult woman. A single-donor platelet apheresis unit provides the equivalent amount of platelets as six random-donor platelet units and should be used if available. Platelets are difficult to store and have a short shelf life (5 days). Typically, the blood bank provides platelets from ABO- and Rh-compatible donors. Platelet unit donor plasma must be compatible with, not identical to, recipient erythrocytes, but only units from D-negative donors should go to D-negative recipients.

The relationship of massive transfusion, defined as 10 or more units of blood, to the resultant coagulopathy has been studied by both civilian trauma groups and military combat hospitals. Although replacement therapy with plasma, platelets, and red blood cells generally should not be based on any set formula, the results from these studies suggest that patients with severe trauma, massive blood replacement, and coagulopathy have improved survival when the ratio of transfused pRBCs (units) to FFP (units) to platelet (units) approaches 1:1:1. Most of these studies found that patients receiving between 5 and 10 units of pRBCs rarely needed component replacement. Pasquier et al. retrospectively found that postpartum hemorrhage patients transfused a higher ratio of FFP:pRBC (1:1.2 vs. 1:1.6) had more successful bleeding control with the uterotonic therapy, sulprostone alone, and less need for advanced interventional procedures. Because there are only a limited number of studies in patients requiring massive transfusion, the value of this approach is still controversial and remains to be prospectively proven.

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Sambasivan CN, Kunio NR, Nair PV, et al. High ratios of plasma and platelets to packed red blood cells do not affect mortality in nonmassively transfused patients. *J Trauma*. 2011;71(2 suppl 3):S329-S336.

C.11. What is the role of type O Rh-negative (universal donor) uncrossmatched blood in emergency transfusions, and how does this change your future management?

When typed and screened/crossed blood is unavailable and the hemodynamically unstable, hemorrhaging obstetric patient requires an RBC transfusion in addition to crystalloid and/or colloid solutions, uncrossmatched type O Rh-negative blood can be given. People with type O blood are considered universal donors because they lack A and B antigens, and therefore, their erythrocytes are not hemolyzed by a recipient's anti-A or anti-B antibodies if present. Some type O donors, however, produce high titers of hemolytic anti-A and anti-B antibodies. pRBCs, therefore, are preferable to whole blood because packed erythrocytes have a smaller volume of plasma and therefore a minimal amount of anti-A and anti-B antibodies if present. If whole blood is to be used, the blood bank should supply type O blood that is free of anti-A and anti-B antibodies. Some confusion exists as to when it is safe to switch back to the patient's native blood type. After a patient has received two units of type O Rh-negative

uncrossmatched whole blood, the patient should not be switched to their type-specific (A, B, AB) blood; additional transfusions should be continued with type O blood. The patient must not receive a transfusion of her correct blood type until the blood bank determines that switching back to the patient's native blood type is safe. Patients who have received uncrossmatched type O Rh-negative pRBCs can receive many more units without concern for antibody reactions. Individual centers have different policies governing the maximum number of uncrossmatched type O Rh-negative blood units that can be given before switching back to the patient's specific blood type. Most centers do recommend switching to the patient's native blood type as soon as safely possible in order to conserve the emergency supply of type O Rh-negative blood. Recommendations should be received from your local blood bank representative.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1830-1867.

C.12. What complications can occur from the transfusion of blood products?

Blood transfusion safety has improved over the past several decades. Deaths from transfusions are rare. When they occur, they are primarily due to transfusion-related acute lung injury (16% to 22%), administrative errors leading to ABO-incompatible blood transfusion (12% to 15%), and infection due to bacterial platelet contamination (11% to 18%). Other transfusion-related adverse reactions include transfusion-associated circulatory overload, delayed hemolytic transfusion reactions, febrile and allergic nonhemolytic transfusion reactions, transfusion-associated graft-versus-host disease, transfusion-related immunomodulation, and posttransfusion purpura.

The accidental transfusion of ABO-incompatible blood can result in acute intravascular hemolysis. This is typically characterized by the symptoms of fever, chills, nausea, flushing, chest and flank pain, tachycardia, hypotension, DIC, hemoglobinuria, acute renal failure, and potentially death. Immediate supportive care includes the discontinuation of the transfusion, treatment of the hypotension and hyperkalemia, administration of a diuretic, and urine alkalinization. The unused blood product should be sent back to the blood bank along with a new patient specimen for a second crossmatch. Assays for urine and plasma Hgb concentration and a direct antiglobulin antibody screen confirm the diagnosis.

Transfusion-related acute lung injury (TRALI) is a noncardiogenic pulmonary edema that occurs within 6 hours after transfusion; this life-threatening complication is characterized by severe dyspnea and hypoxia. A delayed form of TRALI has been reported to occur 6 to 72 hours after transfusion. All blood products can cause TRALI, but plasma-containing products account for 50% to 63% of the fatalities. Its pathogenesis is incompletely understood, but the lung injury appears to involve the activation of recipient white blood cells by human leukocyte antigen antibodies and/or human neutrophil antigen antibodies in the donor plasma. Because the risk of multiparous female donors having these offending antibodies is increased, male-only plasma donation policies have decreased the TRALI rate. Currently, the American Red Cross plasma distribution from male donors exceed 99% for blood groups A, B, and O but is only 60% for group AB. The risk of TRALI after plasma transfusion has been markedly reduced for groups A, B, and O (1.8 per million distributed products) but not for AB (26.3 per million distributed products) due to the continuing use of AB plasma from female donors to meet

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Because they are stored at room temperature, platelets present the greatest risk of bacterial contamination; the introduction of culture-negative platelets has decreased the risk of receiving an infected platelet transfusion to 1 in 75,000 units.

The use of serologic screening and nucleic acid amplification testing (NAT) on donor blood products have decreased the risk of viral infection transmission. The risk of contracting HIV or hepatitis C is approximately 1 in 2 million units transfused. The risk of *hepatitis B* transmission is estimated to be less than 1 per 200,000 to 500,000 units transfused. The risk of transfusion-transmitted cytomegalovirus can lead to serious morbidity in the immunocompromised patient and/or the fetus or neonate; therefore, pregnant women should receive blood that is seronegative and leukocyte-depleted to decrease the

risk of cytomegalovirus infection. There have been reports of West Nile virus infection, variant Creutzfeldt-Jakob disease, human T-lymphocyte virus type 1, and parvovirus acquired via transfusion.

The biochemical changes that occur with the storage of blood can lead to problems in the recipient especially when large amounts are rapidly infused. Hypocalcemia, hyperkalemia, and hypothermia can occur and should be promptly corrected.

Brunicardi FC, Andersen DK, Billiar TR, et al. *Schwartz's Principles of Surgery* . 10th ed. New York: McGraw-Hill; 2015:100-102.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:900-901.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:817-818.

Eder AF, Dy BA, Perez JM, et al. The residual risk of transfusion-related acute lung injury at the American Red Cross (2008-2011): limitations of a predominantly male-donor plasma mitigation strategy. *Transfusion*. 2013;53(7):1442-1449.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1830-1867.

C.13. What is the role of autologous transfusion in obstetric patients?

Autologous blood transfusion may avoid the risks of alloimmunization, hemolytic reactions, and viral infections; may potentially decrease the demands on the allogenic blood supply; and may provide a psychological benefit to the patient. There are three methods of autologous transfusion: preoperative (antepartum) donation, normovolemic hemodilution, and intraoperative blood salvage. Each technique may have potential benefits in the properly selected patient population, but applicability is limited and safety anecdotal. Due to the inability to correctly anticipate which patients will require transfusions and the limited amount of transfusable blood obtained, preoperative donation and normovolemic hemodilution are ineffective strategies for avoiding allogenic transfusions in the obstetric patient.

Intraoperative blood salvage has been used in obstetric patients. During cesarean section after placenta delivery, blood is suctioned from the surgical site, collected, and processed through a cell salvage machine that yields a washed, pRBC product for transfusion. There are no prospective randomized studies evaluating the safety of intraoperative blood salvage in obstetrics, but the review of over 400 case reports by Allam et al. did not reveal any complications leading to poor maternal outcome that were directly attributable to the use of this technique. The safety of blood salvage during cesarean section has been questioned because of the theoretical risk of developing an AFE; unfortunately, the pathophysiology of AFE is unknown. In the United States, the American Society of Anesthesiologists recommends that “in cases of intractable hemorrhage when banked blood is not available or the patient refuses banked blood, intraoperative cell salvage should be considered if available.” In United Kingdom, intraoperative blood salvage during cesarean section is widely accepted. Leukocyte depletion filters may improve the margin of safety of the salvaged pRBC product. Because washed pRBCs may contain fetal RBCs, isoimmunization of the mother is possible; anti-D immune globulin should be given when appropriate.

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Jehovah's Witness patients have an increased risk of maternal death due to maternal hemorrhage because their religious beliefs prevent them from receiving blood transfusions. The use of intraoperative blood salvage during surgery sometimes is accepted because continuity of the salvaged blood with the patient's circulatory system can be maintained. The exact possibilities for acceptable treatment options should be discussed with each individual patient early in pregnancy.

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American Society of Anesthesiologists Task Force on Obstetric Anesthesia. Practice guidelines for obstetric anesthesia. *Anesthesiology*. 2007;104:869-875.

Massiah N, Athimulams S, Loo C, et al. Obstetric care of the Jehovah's Witnesses: a 14-year observational study. *Arch Gynecol Obstet*. 2007;276(4):339-343.

Van Wolfswinkel ME, Zwart JJ, Schutte JM, et al. Maternal mortality and serious morbidity in Jehovah's Witnesses in the Netherlands. *BJOG*. 2009;116(8):1103-1108.

C.14. Significant intraoperative blood loss required the transfusion of 8 units of typespecific, crossmatched packed RBCs (pRBCs). This patient had generalized oozing in the surgical field and hematuria. What is your differential diagnosis?

The obstetric patient can rapidly develop a coagulopathy. It may be a dilutional coagulopathy or DIC. A dilutional coagulopathy can occur when massive blood loss is replaced with crystalloid solutions and pRBCs leading to a relative depletion of platelets and soluble clotting factors. Thrombocytopenia, hypofibrinogenemia, and factor depletion occur. Pregnancy-related causes of DIC include hemorrhagic shock, AFE, placental abruption, intrauterine fetal demise, and sepsis due to uterine infection. Additionally, hemolytic transfusion reactions with acute intravascular hemolysis can cause DIC. Acidosis and hypothermia both interfere with the normal functioning of the coagulation system and worsen any coagulopathy.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:903.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:816.

Santoso JT, Saunders BA, Grosshart K. Massive blood loss and transfusion in obstetrics and gynecology. *Obstet Gynecol Surv*. 2005;60:827-837.

C.15. What is disseminated intravascular coagulation (DIC)?

DIC, a consumptive coagulopathy, is a pathologic activation of the coagulation system that occurs in response to a variety of diseases. The process of coagulation is dysregulated and widespread intravascular clotting and resultant bleeding due to the inappropriate consumption of factors and platelets occurs. Thrombi are deposited in the microcirculation and can diminish blood flow to the organs and lead to multisystem organ failure. Simultaneously, increased fibrinolysis occurs with the formation of fibrin degradation products (also called fibrin split products). Once DIC begins, the pathophysiology is the same regardless of the inciting cause. Resolution of DIC requires treatment of the underlying cause. Supportive treatment is aimed at replacing the consumed blood products-“feeding the fire.” Laboratory values are indicative of this consumption of clotting products and the increased fibrinolysis that this excess clotting activates and can help guide management. Thrombocytopenia, decreased levels of fibrinogen and coagulation factors, increased levels of fibrin degradation products, increased PT, and increased aPTT are seen.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:809-810.

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Thachil J, Toh CH. Disseminated intravascular coagulation in obstetric disorders and its acute haematological management. *Blood Rev*. 2009;23(4):167-176.

C.16. What is the role of recombinant activated factor VII (rFVIIa) in obstetric patients?

rFVIIa (NovoSeven), a synthetic vitamin K-dependent glycoprotein, has been used to facilitate hemostasis in patients bleeding from other coagulopathies, surgery, trauma, and severe obstetric hemorrhage. Use of rFVIIa in obstetrics has been reported in case series and international registries; no randomized controlled trials have been published. At pharmacologic doses, rFVIIa directly activates factor X on the surface of activated platelets at the site of injury independent of tissue factor and factors VIII and IX causing a "thrombin burst" with the conversion of prothrombin into large amounts of thrombin and the local formation of a stable fibrin clot that may control bleeding. Currently, it has not been ruled out that a small amount of tissue factor-dependent activity also might contribute to its hemostatic effect. There are case reports of rFVIIa being used in obstetric cases after massive hemorrhage with symptoms suggesting DIC. Franchini et al. reviewed the literature and found that a median dose of 81.5 μg per kg of rFVIIa has been effective in stopping or decreasing bleeding in 85% of obstetric cases where it has been utilized. Based on personal experience and literature review, they have outlined a treatment scheme for the off-label use of rFVIIa in the treatment of postpartum hemorrhage. They suggest that rFVIIa be considered only after the failure of medical treatment, blood component therapy, and conservative surgical/invasive treatment. Before administering rFVIIa, acidosis, thrombocytopenia, hypofibrinogenemia, hypocalcemia, and hypothermia should be corrected. Then, 90 μg per kg should be given intravenously

over 3 to 5 minutes. If no response has occurred 20 minutes later, a second dose of 90 μg per kg should be given. If there is no response after two doses, hysterectomy should be considered. Because to date all of the information about rFVIIIa in obstetrics is anecdotal, the use of rFVIIa should be determined on an individual case basis. There are unanswered concerns about the increased likelihood of thrombotic events, and the role of rFVIIa remains undefined. The American Society of Anesthesiologists guidelines, however, recommend that rFVIIa administration be considered when "traditional well tested options for treating microvascular bleeding (i.e. coagulopathy) have been exhausted."

American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. *Anesthesiology*. 2006;105:198-208.

Franchini M, Franchi M, Bergamini V, et al. The use of recombinant activated FVII in postpartum hemorrhage. *Clin Obstet Gynecol*. 2010;53(1):219-227.

Phillips LE, McLintock C, Pollack W, et al. Recombinant activated factor VII in obstetric hemorrhage: experiences from the Australian and New Zealand Haemostasis Registry. *Anesth Analg*. 2009;109(6):1908-1915.

C.17. What laboratory tests should be ordered during the resuscitation of this patient?

Blood specimens for an Hct, Hbg level, platelet count, coagulation tests (aPTT, PT, and fibrinogen levels), and an arterial blood gas should be sent as soon as possible to determine an early baseline. During the resuscitation, the above blood tests should be sent periodically to help guide treatment including blood component therapy. If the volume of blood lost requires treatment with a massive transfusion, then electrolyte levels, including a potassium and calcium, also will need to be followed. Patients can develop hyperkalemia due to the elevated potassium levels in transfused blood and the cellular shifts caused by acidosis. Patients can develop hypocalcemia from citrate toxicity; citrate is the anticoagulant found in transfused pRBCs. Arterial blood gases and lactate levels also should be monitored to evaluate the acidosis that may develop due to poor tissue perfusion and the development of shock. If DIC is a concern, the level of fibrin degradation product also should be checked.

There are reports of thromboelastography (TEG) use in the obstetrical population to assess the coagulation status of normal and high-risk patients, to manage postpartum coagulopathy, to assess a thrombocytopenic patient before neuraxial anesthesia, and to quantify the effect of unfractionated heparin in postcesarean section patients. In trauma patients with

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substantial bleeding, Holcomb et al. found TEG clinically superior to conventional coagulation tests in identifying the need for platelet and plasma transfusions than platelet count and fibrinogen, respectively. Based on limited evidence from reviewing observational studies, Da Luz et al. found that TEG and rotational thromboelastometry (ROTEM) may diagnose early trauma coagulopathy and predict blood product transfusion, but TEG/ROTEM resuscitation was not associated with a lower mortality in most studies. In the setting of ongoing obstetric hemorrhage, Karlsson et al. found that although TEG provided faster feedback indicating hemostasis impairment, laboratory analyses found greater differences in coagulation variables which correlated better with estimated blood loss and provide more specific information on the factors contributing to this impairment (also see Chapter 12, section A.22; Chapter 16, section C.14; and Chapter 57, section C.25).

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Karlsson O, Jeppsson A, Hellgren M. Major obstetric haemorrhage: monitoring with thromboelastography, laboratory analyses or both? *Int J Obstet Anesth*. 2014;23(1):10-17.

C.18. Define amniotic fluid embolism (AFE) syndrome and discuss treatment.

AFE is a complex disorder that is poorly understood. Classically, it is characterized by the abrupt onset of a maternal collapse associated with hypotension, dyspnea, hypoxemia, cyanosis, loss of consciousness, seizures, cardiopulmonary arrest, and hemorrhaging associated with disseminated intravascular coagulation. There are, however, great individual variations in symptomatology from none to catastrophic systemic complications. The overall maternal mortality is reported to be between 11% and 90%. The reported incidence and outcome vary greatly in part because it is a diagnosis of exclusion and because of reporting bias with the syndrome being underdiagnosed in all but the most severe cases. The changing mortality rates may reflect improved intensive care and the recognition of the fact that “milder” cases do occur. The estimated AFE incidence ranges from 1.9 to 7.7 cases per 100,000 births in high-resource countries. Advanced maternal age, labor induction or augmentation, rapid labor, meconium-stained amniotic fluid, uterine or pelvic vein tears, eclampsia, cesarean/forceps or vacuum delivery, placenta abruption or previa, postterm delivery, and hydramnios were risk factors. In survivors, the neurologic outcome is often poor. Clark et al. found a disappointingly high incidence (92%) of neurologic dysfunction among the surviving women that had a cardiac arrest as an initial symptom. The neonatal survival rate is around 70%, but the incidence of impaired neurologic function is high, over 50%.

The cause of AFE syndrome is unknown. The diagnosis of AFE is a clinical one of exclusion; no diagnostic tests exist. The detection of squamous cells, trophoblasts, and other debris of fetal origin is neither sensitive nor specific for AFE. Multiple possible mechanisms have been proposed, but none adequately explains this complex syndrome. Clark et al. suggested that the syndrome of acute peripartum hypoxia, hemodynamic collapse, and coagulopathy would be more aptly described as anaphylactoid syndrome of pregnancy than AFE. The suggestion that AFE may be related in some way to anaphylaxis has led to a number of reports describing tryptase and histamine levels in cases of AFE; however, some reported cases had elevated tryptase and/or histamine levels while others did not. Therefore, anaphylactoid syndrome

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seems to be an unsupported classification. A nine-case series suggests that complement activation, due to the low levels of complement found rather than mast cell degranulation (anaphylaxis), plays a role in AFE. Other proposed mechanisms include reactions to amniotic fluid tissue factor or an amniotic fluid thromboplastin-like effect.

Treatment is prompt supportive resuscitation. There is no data that any type of intervention improves maternal prognosis with AFE although case reports using hemofiltration, exchange transfusion, cardiopulmonary bypass, or extracorporeal membrane oxygenation exist.

Benson MD. Current concepts of immunology and diagnosis in amniotic fluid embolism. *Clin Dev Immunol*. 2012;2012:946576.

Clark SL, Hankins GD, Dudley DA, et al. Amniotic fluid embolism: analysis of the national registry. *Am J Obstet Gynecol*. 1995;172:1158-1167.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:812-814.

Knight M, Berg C, Brocklehurst P, et al. Amniotic fluid embolism incidence, risk factors and outcomes: a review and recommendations. *BMC Pregnancy Childbirth*. 2012;12:7.

Knight M, Tuffnell D, Brocklehurst P, et al. Incidence and risk factors for amniotic fluid embolism. *Obstet Gynecol*. 2010;115:910-917.

Kramer MS, Rouleau J, Liu S, et al. Amniotic fluid embolism: incidence, risk factors, and impact on perinatal outcomes. *BJOG*. 2012;119(7):874-879.

D. Postoperative Management

D.1. If the patient received epidural anesthesia and subsequently developed disseminated intravascular coagulation (DIC), when should the epidural catheter be removed?

There is little information available concerning this topic. Sprung et al. made recommendations about the removal of an epidural catheter after DIC. First, they suggest that the patient's neurologic status be evaluated frequently and that the coagulopathy be treated; if there is no indication of intraspinal bleeding, they recommend removing the catheter as

early as possible. If, however, bleeding is occurring around the catheter insertion site, the catheter may be left in place to tamponade this bleeding. Any neurologic deficits should be evaluated immediately; prompt surgical decompression may be needed. However, if a patient's neurologic status cannot be evaluated (e.g., postoperative intubation and sedation), an argument can be made for the removal of an indwelling catheter as soon as possible after the replacement of coagulation factors has created a state of normal coagulation even if it is temporary. The recommendations for the best hemostatic conditions for epidural catheter removal should reflect those used for placement of a neuraxial block.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:1048.

Horlocker TT, Wedel D, Rowlingson JC, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). *Reg Anesth Pain Med*. 2010;35(1):64-101.

Sprung J, Cheng EY, Patel S. When to remove an epidural catheter in a parturient with disseminated intravascular coagulation? *Reg Anesth*. 1992;17(6):351-354.

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D.2. You have successfully treated the patient's massive hemorrhage. Her laboratory values have returned to normal. Her central venous pressure (CVP) is within normal limits and urine output is appropriate. The patient, however, is still hypotensive despite appropriate intravascular volume replacement and support with vasopressors. What is your concern in this case?

She may have developed Sheehan syndrome. Sheehan syndrome refers to the development of a postpartum pituitary infarction with necrosis that is typically precipitated by an obstetric hemorrhage with severe hypotension. Sheehan syndrome is a rare complication. The damage to the pituitary may affect the secretion of one, several, or all of its hormones. Any of the manifestations of hypopituitarism (e.g., failure to lactate, amenorrhea/oligomenorrhea, hypotension, hyponatremia, hypothyroidism) can occur at any time from the immediate postpartum period to years after delivery. If the patient remains hypotensive after control of hemorrhage and adequate volume replacement, she should be evaluated and treated for adrenal insufficiency immediately; treatment of possible adrenal crisis should not be delayed while diagnostic tests are performed. Glucocorticoids have a role in maintaining peripheral vascular adrenergic tone, and the sudden loss of corticotropin (adrenocorticotropic hormone) secretion, particularly in conjunction with other serious physical stress, can lead to hypotension and shock. Prompt treatment with stress doses of glucocorticoids (e.g., 4 mg dexamethasone by intravenous bolus) is necessary for survival. The workup includes measuring adrenocorticotropic hormone, cortisol, thyroxine, prolactin, and growth hormone levels. The evaluation of other hormonal deficiencies is not urgent and can be deferred until 4 to 6 weeks postpartum.

Feinberg EC, Molitch ME, Endres LK, et al. The incidence of Sheehan's syndrome after obstetric hemorrhage. *Fertil Steril*. 2005;84(4):975-979.

Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics: Normal and Problem Pregnancies*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:955-956.

Matsuwaki T, Khan KN, Inoue T, et al. Evaluation of obstetrical factors related to Sheehan syndrome. *J Obstet Gynaecol Res*. 2014;40(1):46-52.

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Chapter 28
Hypertensive Disorders of Pregnancy

Sharon Abramovitz

A 39-year-old woman gravida 1 para 0 at 29 weeks' gestation was admitted to the hospital because of an elevated blood pressure (BP) (182/111 mm Hg), headache, and proteinuria.

A. Medical Disease and Differential Diagnosis

1. What is the classification of hypertension disorders in pregnancy as defined by the American College of Obstetricians and Gynecologists?
2. What is preeclampsia?
3. What is preeclampsia with severe features?
4. What is eclampsia?
5. What are the risk factors for developing preeclampsia?
6. What is the mortality associated with preeclampsia?
7. Discuss the pathogenesis of preeclampsia.
8. Discuss the pathologic alterations of preeclampsia.
9. Which component of BP best predicts the occurrence of preeclampsia?
10. What is the significance of increased pulse wave velocity (PWV) during pregnancy? How does this relate to birth weight?
11. What are some of the complications associated with preeclampsia?

B. Preoperative Evaluation and Preparation

1. What initial laboratory studies are recommended for patients with preeclampsia?
2. What are the important routine monitors for patients with preeclampsia? When is a central venous pressure (CVP) monitor indicated?
3. What conditions mandate immediate delivery, regardless of the gestational age?
4. Discuss the obstetric management of preeclampsia.
5. In the United States, what drug therapy is the treatment of choice for seizure prophylaxis?
6. Discuss the treatment of magnesium sulfate toxicity.
7. Discuss the mechanism of action of magnesium sulfate.
8. What are the fetal effects of magnesium sulfate therapy?
9. Discuss the treatment of eclampsia.

C. Intraoperative Management

1. What is your choice of analgesia/anesthesia for patients with preeclampsia?
2. What is the advantage of prehydration?
3. Discuss bleeding time and platelet count evaluation during preoperative assessment of a patient with preeclampsia requesting epidural analgesia/anesthesia for labor and delivery.

4. What level of analgesia/anesthesia is required for labor and delivery?

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5. Discuss the commonly used local anesthetics for labor analgesia.
6. Is the addition of epinephrine to local anesthetics advisable in preeclamptic patients?
7. What is the treatment for the abnormal fetal heart rate pattern seen with maternal hypotension after epidural analgesia/anesthesia is instituted?
8. What would you do after an accidental spinal tap? How do you treat postdural puncture headache?
9. How would you manage total spinal anesthesia?
10. Should ergonovine be given to preeclamptic patients?
11. When and how would you give spinal anesthesia?
12. Discuss a general anesthesia technique for the patient with preeclampsia presenting for cesarean delivery.
13. What agents can you use to prevent hypertension during the induction of general anesthesia for cesarean delivery?
14. What is HELLP syndrome?

D. Postoperative Management

1. Discuss the postpartum management of preeclamptic patients.

A. Medical Disease and Differential Diagnosis

A.1. What is the classification of hypertension disorders in pregnancy as defined by the American College of Obstetricians and Gynecologists?

Hypertensive disorders of pregnancy are classified as follows:

- Gestational hypertension
- Preeclampsia
- Preeclampsia without severe features
- Preeclampsia with severe features
- Chronic hypertension preceding pregnancy
- Chronic hypertension with superimposed preeclampsia

American College of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol*. 2013;122:1122-1131.

A.2. What is preeclampsia?

Preeclampsia is a multiorgan disease characterized by the development of hypertension with proteinuria after the 20th week of gestation. It is a disorder affecting approximately 8% of all pregnancies, with most cases occurring during the first pregnancy, and is unique to humans. Preeclampsia is a leading cause of maternal and perinatal morbidity and mortality worldwide, particularly in developing countries. Hypertension is defined as a systolic BP of at least 140 mm Hg or a diastolic BP of at least 90 mm Hg on two occasions at least 4 hours apart in a previously normotensive patient. Proteinuria is defined as 300 mg or more of protein in a 24-hour urine collection, or a protein-creatinine ratio of 0.3 or greater, or 1+ protein on a urine dipstick (if other tests are not readily available because there is variability in this diagnostic test). Edema is no longer part of the diagnostic criteria because it lacks specificity and is found in many healthy pregnant women. In the absence of proteinuria, the diagnosis of preeclampsia can still be made due to the syndromic nature of the disease. Therefore, preeclampsia is diagnosed by the presence of hypertension in association with thrombocytopenia (platelet count less than 100,000 per μL), impaired liver function (elevated blood levels of liver transaminases to twice the normal concentration), the new development of renal insufficiency (elevated serum creatinine greater than 1.1 mg per dL or a doubling of the serum

creatinine in the absence of other renal disease), pulmonary edema, or new-onset cerebral or visual disturbances.

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American College of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol*. 2013;122:1122-1131.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:827-828.

Sibai BM, Stella CL. Diagnosis and management of atypical preeclampsia-eclampsia. *Am J Obstet Gynecol*. 2009;200(5):481.e1-481.e7.

A.3. What is preeclampsia with severe features?

Severe preeclampsia includes at least one of the following features:

- Blood pressure: systolic BP 160 mm Hg or higher or diastolic BP 110 mm Hg or higher on two occasions at least 4 hours apart while the patient is on bedrest
- Thrombocytopenia (platelet count less than 100,000 per μL)
- Serum creatinine concentration greater than 1.1 mg per dL or greater than two times the baseline serum creatinine concentration
- Pulmonary edema
- New-onset cerebral or visual disturbances
- Impaired liver function, indicated by elevated blood concentrations of liver enzymes (twice baseline values) and severe persistent right upper quadrant pain or epigastric pain
- Fetal growth restriction and severe proteinuria (<5 g in 24 hours) are *no* longer considered features of severe preeclampsia

American College of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol*. 2013;122:1122-1131.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:825-827.

A.4. What is eclampsia?

Eclampsia is defined as convulsions and/or coma not caused by coincidental neurologic disease (e.g., epilepsy), which occurs during pregnancy or the puerperium in a woman whose condition also meets the criteria for preeclampsia.

Broughton Pipkin F. The hypertensive disorders of pregnancy. *BMJ*. 1995;311:609-613.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:850-851.

A.5. What are the risk factors for developing preeclampsia?

The risk factors for developing preeclampsia are as follows:

Hypertensive disease

- Previous preeclampsia
- Systolic hypertension during early pregnancy

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- History of chronic hypertension
- Family history of hypertension during pregnancy
- Increase in pulse pressure during the first trimester

Coexisting vascular and endothelial disease

- Diabetes mellitus
- Chronic renal disease
- Systemic lupus erythematosus
- Protein S deficiency
- Activated protein C resistance
- Antiphospholipid antibody syndrome

Obstetric factors

- African American race
- Advanced maternal age greater than 35 years
- Angiotensinogen gene *T235*
- Nulliparity
- Obesity
- Increased trophoblastic mass (e.g., multiple gestation, molar pregnancy)
- Large for gestational age fetus
- Erythroblastosis fetalis
- Polyhydramnios, particularly in young primigravidas

Boxer LM, Malinow AM. Pre-eclampsia and eclampsia. *Curr Opin Anesth*. 1997;10:188-198.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:827-829.

A.6. What is the mortality associated with preeclampsia?

Preeclampsia accounts for 15% to 19% of maternal deaths in the United States and the United Kingdom. It is also accounts for 26% of maternal deaths in Latin America and the Caribbean and 9% of deaths in Africa and Asia.

Berg CJ, Atrash HK, Koonin LM, et al. Pregnancy-related mortality in the United States, 1987-1990. *Obstet Gynecol*. 1996;88:161-167.

Hibbard BM, Anderson MM, Drife JO, et al. *Report on Confidential Enquiries into Maternal Deaths in the United Kingdom, 1991-1993*. London: Her Majesty's Stationery Office; 1996:1-31.

Khan KS, Wojdyla D, Say L, et al. WHO analysis of causes of maternal deaths: a systematic review. *Lancet*. 2006;367:1066-1074.

A.7. Discuss the pathogenesis of preeclampsia.

Preeclampsia is most likely a disease of heterogeneous causes of both maternal and placental origin.

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Immunologic Factors

Immunologic disorders may arise from an abnormal maternal-fetal antigen-antibody response or from the contents of seminal fluids; spermatozoa may cause antibody formation, or prostaglandins may initiate uterine vasoconstriction. The fetus acquires 50% of its genes from the father, which represents in part a paternal allograft that interacts with maternal tissue as the fetal trophoblast migrates into the maternal decidua after implantation. Migration normally occurs in two phases. Trophoblasts displace the muscular structure of the maternal spiral arteries before 20 weeks of gestation, causing their adrenergic denervation and converting them from high-resistance to low-resistance vessels. At the same time, biochemical adaptations occur in the maternal vasculature, with an increased dominance of endothelium-dependent vasodilators, prostacyclin (prostaglandin I [PGI]), and nitric oxide (NO). In preeclampsia, the second wave of trophoblastic migration fails. This failure can result in a high-resistance, low-flow uteroplacental circulation and consequent placental ischemia and hypoxia. These changes may represent an aberrant immunologic mechanism.

Genetic Factors

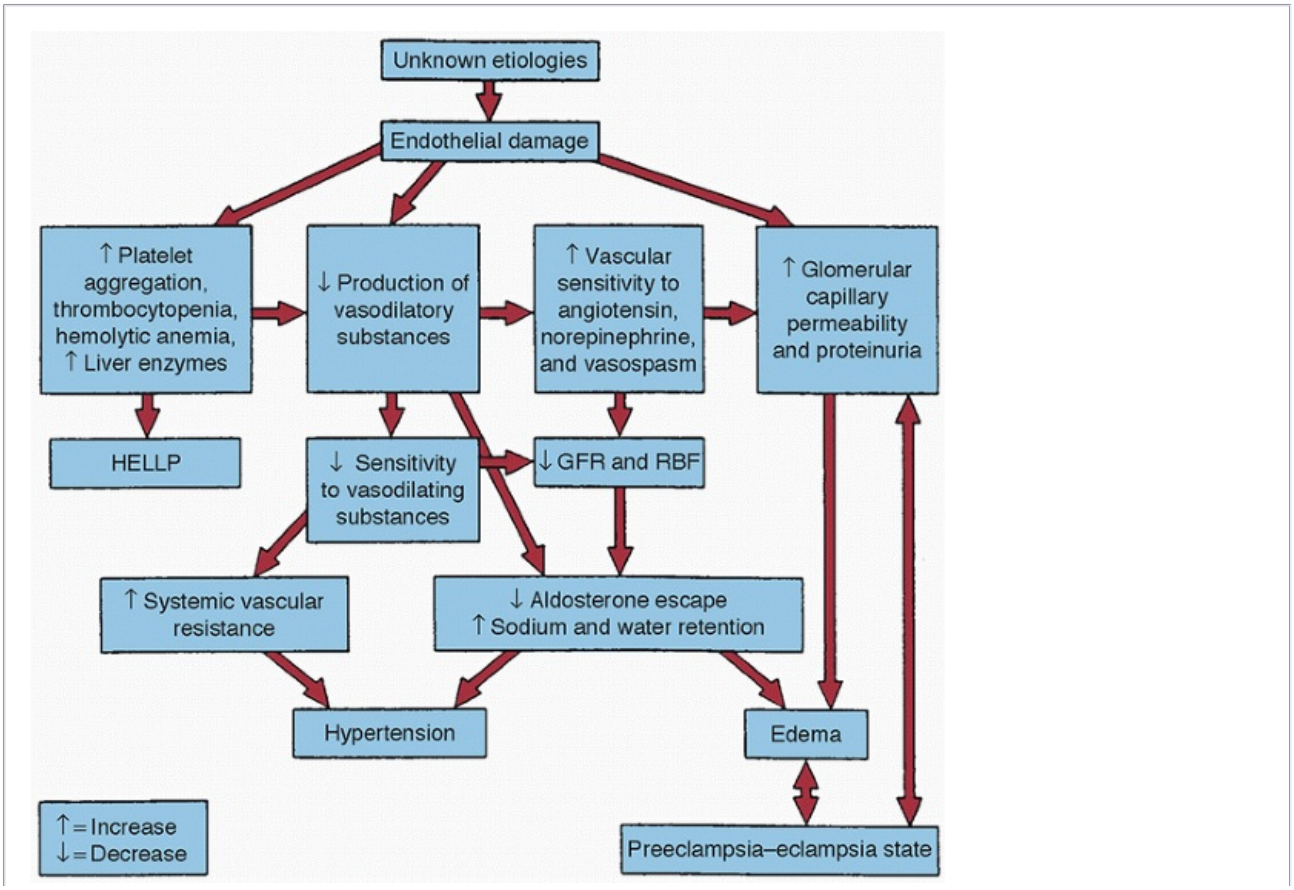
A familial tendency toward preeclampsia exists in some populations, and it may result from a recessive genetic inheritance.

Endothelial Factors

Vascular endothelial damage or dysfunction is the common pathologic feature of preeclampsia and occurs in the placental decidual vessels and renal microvasculature. Endothelial cell dysfunction in response to unknown factors may cause a hormonal imbalance in women with preeclampsia (Fig. 28.1).

The metabolic end products of normal vascular endothelium include PGI_2 and endothelium-derived relaxing factor (EDRF), which is either NO or a related nitrosyl substance.

Both PGI_2 and EDRF are potent vasodilators. In patients with preeclampsia, the failure of the trophoblast to invade the uteroplacental vascular bed may encourage an increased production of free radicals and lipid peroxides by the decidual lymphoid tissue. As a result, an imbalance occurs between the production of the vasoconstrictor thromboxane A_2 (TXA_2), which is derived from platelets, and the production of endothelium-derived PGI_2. This imbalance results in a reduced perfusion of the intervillous space. Some investigators have concluded that hypoxia-induced impairment of NO production by the syncytiotrophoblast results in uteroplacental insufficiency and production of a toxin responsible for the clinical manifestations of preeclampsia.



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FIGURE 28.1 Endothelial cell dysfunction in response to unknown factors may cause a hormonal imbalance in women with pregnancy-induced hypertension. GFR, glomerular filtration rate; HELLP, hemolysis, elevated liver enzymes, low platelets; RBF, renal blood flow. (From Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice.* 3rd ed. Philadelphia, PA: Mosby; 2004:798, with permission.)

It has been shown that production of endothelin 1 (ET-1), which is the most potent endogenous vasoconstrictor and produced mainly by vascular smooth muscle cells as well as by the vascular endothelium, is markedly increased in preeclampsia and correlates inversely with NO production. Therefore, the imbalance between NO and ET-1 may play a significant role in the pathophysiology of preeclampsia.

Fetoplacental blood vessels, namely, the human placental chorionic plate arteries, constrict in response to ET-1. Moreover, there is now some evidence that amniotic concentration of ET-1 is elevated in pregnancies associated with preeclampsia. Margarit et al. found a statistically significant increase in ET-1 concentration in the amniotic fluid of women at 17 weeks' gestation who developed preeclampsia, as compared to those who did not develop preeclampsia. By the second trimester, higher levels of ET-1 have also been shown in the amniotic fluid of women with preterm premature rupture of the membranes.

Platelet Factors

In mild preeclampsia, serotonin (5-HT) released from aggregating platelets interacts with endothelial 5-HT_1 receptors, resulting in the release of prostacyclin and NO (EDRF). The released prostacyclin induces angiotensin II release, improving uteroplacental perfusion. In early-onset severe preeclampsia, damaged uteroplacental vessels cannot respond to 5-HT_1 effects. Instead, serotonin interacts with 5-HT_2 receptors on vascular smooth muscle cells, inducing vasoconstriction. Platelet-derived serotonin also activates 5-HT_2 platelet receptors, establishing a positive feedback loop and intensifying platelet aggregation. The loss of 5-HT_1 receptors prevents stimulation of angiotensin II release (Fig. 28.2).

Calcium

In normal pregnancy, the intracellular free calcium concentration increases slowly, but this increase is significantly greater in the third trimester in women with preeclampsia. The increase in cytoplasmic calcium levels is enhanced by angiotensin II, and the enhancement is greater in women with preeclampsia compared with normotensive women. This response to angiotensin II occurs long before signs of preeclampsia become evident and is a sensitive indicator of its subsequent development.

Coagulation Factors

Platelet activation in preeclampsia is surface-mediated. Women with preeclampsia have an increased tendency toward thromboembolism, which may result in part from an alteration in the plasma ratio between von Willebrand factor and factor VIII coagulant activity.

Fatty Acid Metabolism

Altered handling of fatty acids by the liver is a key factor in the pathogenesis of preeclampsia. Both increased hepatic uptake of free fatty acids and hypertriglyceridemia are seen more frequently in women who develop preeclampsia.

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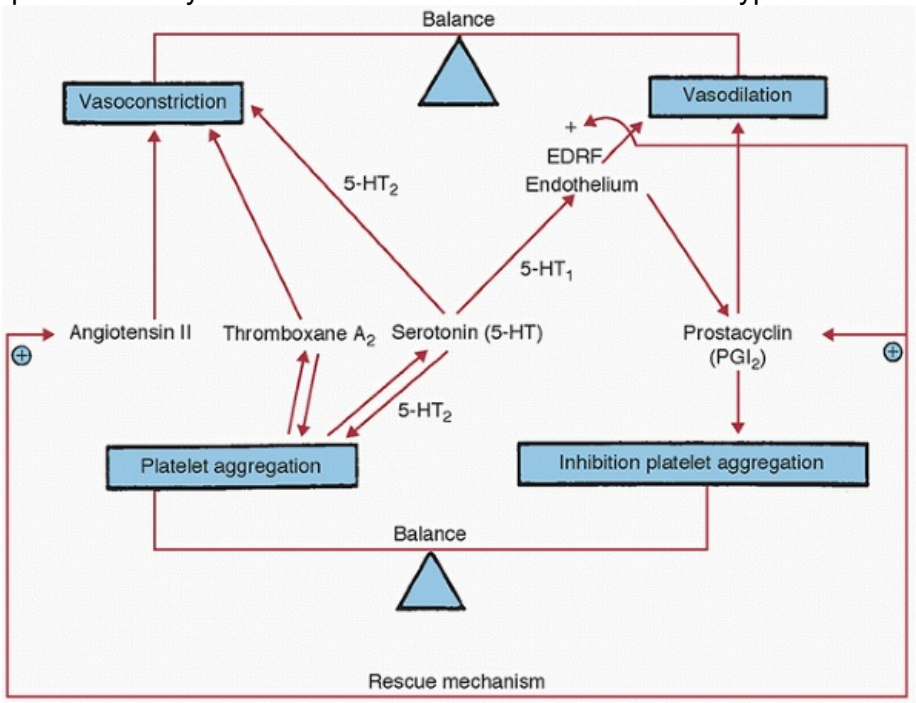


FIGURE 28.2 The loss of 5-HT_1 receptors prevents stimulation of angiotensin II release. EDRF, endothelium-derived relaxing factor. (From Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice.* 3rd ed. Philadelphia, PA: Mosby; 2004:797, with permission.)

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Markers of Angiogenesis

Preeclamptic patients have elevated plasma levels of endoglin and soluble FLT-1, the receptor for vascular endothelial growth factor, throughout gestation. Recent research suggests that these molecules are not just disease markers but are involved in the pathogenesis of preeclampsia.

Baksu B, Davas I, Baksu A, et al. Plasma nitric oxide, endothelin-1 and urinary nitric oxide and cyclic guanosine monophosphate levels in hypertensive pregnant women. *Int J Gynaecol Obstet*. 2005;90(2): 112-117.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:829-833.

Margarit L, Griffiths A, Tsapanos V, et al. Second trimester amniotic fluid endothelin concentration. A possible predictor for pre-eclampsia. *J Obstet Gynaecol*. 2005;25(1):18-20.

Venkatesha S, Toporsian M, Lam C, et al. Soluble endoglin contributes to the pathogenesis of preeclampsia. *Nat Med*. 2006;12:642-649.

A.8. Discuss the pathologic alterations of preeclampsia.

Cardiovascular Changes

- *Blood pressure*. Increase in BP results from an increase in peripheral vascular resistance secondary to a state of sympathetic overactivity. Alternatively, systolic BP increases as a result of increased cardiac output (increased plasma volume—typical of pregnancy) and a noncompliant aorta. In such cases, the systemic vascular resistance (SVR), which is predominantly determined by the smaller arterioles, is not increased but due to aortic stiffness, the ejected stroke volume causes the systolic component to rise significantly.
- *Blood volume*. Reduction in blood volume causes a greater degree of hemoconcentration.

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Hemodynamic Changes

- Three hemodynamic subsets exist:
  - *Hyperdynamic* with increased cardiac output, normal or slightly increased SVR, and normal or slightly decreased blood volume and filling pressures
  - *High SVR* with normal cardiac output and lower filling pressures
  - *Markedly increased SVR* with decreased blood volume and depressed left ventricular function
- Poor correlation between CVP and pulmonary artery (PA) occlusion pressure
  - Decreased colloid oncotic pressure in pregnancy with further reduction in preeclampsia. The low colloid oncotic pressure, coupled with increased vascular permeability and the loss of intravascular fluid and protein into interstitial tissues, increases the risk of pulmonary edema.

Hematologic Changes

- Hypercoagulable state (Table 28.1)
- Platelet activation: Thrombocytopenia occurs in 15% to 30% of women with preeclampsia or eclampsia. Preeclampsia may be associated with a significant defect in *both* platelet function and platelet number. Thrombocytopenia without other coagulation abnormalities but with evidence of hemolysis and increased liver enzymes characterizes HELLP syndrome.

Renal Changes

- Glomerular enlargement results in ischemia, leading to decreased glomerular filtration rate.
- Proteinuria occurs as a result of an increased permeability to most large molecular weight proteins.
- Urate clearance decreases and serum uric acid concentrations increase. Hyperuricemia may provide an early indication of preeclampsia.
- Oliguria parallels the severity of preeclampsia.

TABLE 28.1 Changes That Imply Hypercoagulation in Preeclampsia

↑ Common pathway activity

↓ Fibrinogen

↑ Fibrin-degradation products

D-Dimer positive

↑ Fibrinopeptide A

↑ Factor VIII antigen; factor VIII activity

↓ Antithrombin-III

↑ Antithrombin-III/antithrombin complex

↓ Platelets

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↑ β-Thromboglobulin

↑ Platelet aggregability

↓ Sensitivity to prostacyclin

From Chestnut DH. *Obstetric Anesthesia: Principles and Practice*. 3rd ed. Philadelphia, PA: Mosby; 2004:803, with permission.

Endocrine Changes

In women with preeclampsia, a breakdown of the normal balance between vasodilators (PGI_2, NO) and vasoconstrictors (angiotensin II, TXA_2, serotonin, endothelin) occurs. There is also a decrease in plasma renin concentration and a suppression of the renin-angiotensin-aldosterone system.

Respiratory Changes

- Pharyngeal and laryngeal edema may make airway management difficult, necessitating the use of smaller endotracheal tubes.
- Pulmonary edema occurs in 3% of cases, with some cases occurring postpartum.

Hepatic Changes

- Serum transaminase levels frequently increase in patients with mild preeclampsia.
- Epigastric or subcostal pain is an ominous symptom that is typically caused by distension of the liver capsule by edema or subcapsular or parenchymal bleeding. Hepatic swelling produces epigastric pain.
- Liver rupture is associated with more than 80% mortality.

Neurologic Changes

- The classic manifestations of preeclampsia include severe headache, visual disturbances, central nervous system hyperexcitability, and hyperreflexia.
- The occurrence of seizures indicates eclampsia until proven otherwise. Etiologies of seizures include hypertonic encephalopathy, vasospasm, microinfarctions and punctate hemorrhages, thrombosis, and cerebral edema.
- Postpartum eclampsia may occur up to 10 days after delivery.

Uteroplacental Perfusion

- Uteroplacental perfusion is decreased in preeclampsia with the potential for intrauterine growth retardation.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:833-835.

Pineles BL, Romero R, Montenegro D, et al. Distinct subsets of microRNAs are expressed differentially in the human placentas of patients with preeclampsia. *Am J Obstet Gynecol*. 2007;196:261.e1-261.e6.

Powe CE, Levine RJ, Karumanchi SA. Preeclampsia, a disease of the maternal endothelium: the role of antiangiogenic factors and implications for later cardiovascular disease. *Circulation*. 2011;123:2856-2869.

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A.9. Which component of BP best predicts the occurrence of preeclampsia?

Pregnancy induces several cardiovascular responses and adaptation that include increases in vascular and extravascular volume, higher cardiac output, and marked reduction in peripheral resistance that effectively causes a relatively lower BP by the second trimester of pregnancy. Multiple attempts have been made to correlate first and second trimester systolic, diastolic, and mean arterial pressures (MAPs) with development of preeclampsia. Unfortunately, there is significant variability in the aforementioned components of BP throughout pregnancy, complicated further by factors such as ethnicity, age, nulliparous versus multiparous state, and gestational differences at the time of measurements. In addition, the anxiety component of an office visit (white-coat effect) frequently contributes to variability in measures of BP, limiting their predictability of preeclampsia. Thadhani et al. reported that although systolic, diastolic, and MAP were elevated in women who developed hypertensive disorder of pregnancy as compared to normotensive women, these parameters did not correlate with ensuing preeclampsia. Conversely, elevations in pulse pressure at 7 to 15 weeks of gestation were a significant predictor of preeclampsia but not of gestational hypertension. In fact, for every 1 mm Hg increase in pulse pressure, the associated risk of preeclampsia increased by 6%.

Thadhani R, Ecker JL, Kettyle E, et al. Pulse pressure and risk of preeclampsia: a prospective study. *Obstet Gynecol*. 2001;97:515-520.

A.10. What is the significance of increased pulse wave velocity (PWV) during pregnancy? How does this relate to birth weight?

Similar to increase in pulse pressure, PWV can be a marker of arterial stiffness. In normal pregnancy, arterial stiffness decreases during the first trimester and remains low until the end of pregnancy due to either reduced smooth muscle tone or vessel wall remodeling. However, there is a wide range in arterial stiffness even in normal pregnancy, suggesting a varying degree of cardiovascular adaptation. Maladaptation may lead to retardation in fetal growth as measured by birth weight and by postnatal catch-up growth. Elvan-Taspinar et al. found a significant relation between PWV during the last trimester of pregnancy and fetal birth weight and postnatal catch-up growth independent of MAP. For example, an increase in PWV of 1 m per second was associated with a decrease in birth weight by 17.6%. Similarly, a strong link was found between pulse pressure and birth weight, with an increase of 10 mm Hg in pulse pressure being associated with an 11.8% decrease in weight. Both PWV and pulse pressure appear to offer superior circulatory as well as prognostic information relating to fetal and neonatal outcome.

Elvan-Taspinar A, Franx A, Bots ML, et al. Arterial stiffness and fetal growth in normotensive pregnancy. *Am J Hypertens*. 2005;18:337-341.

Lurbe E, Torró I, Alvarez V, et al. The impact of birth weight on pulse pressure during adolescence. *Blood Press Monit*. 2004;9:187-192.

Spasojevic M, Smith SA, Morris JM, et al. Peripheral arterial pulse wave analysis in women with pre-eclampsia and gestational hypertension. *BJOG*. 2005;112:1475-1478.

A.11. What are some of the complications associated with preeclampsia?

Maternal complications include disseminated intravascular coagulation, congestive heart failure with pulmonary edema, placental abruption, postpartum hemorrhage, acute renal failure, rupture of the liver, cerebrovascular accident, and septic shock. The leading cause of maternal death is intracranial hemorrhage.

Fetal complications include prematurity with respiratory distress, intrauterine growth retardation, oligohydramnios, intracranial hemorrhage, small for gestational age, and aspiration of meconium. The leading cause of intrauterine morbidity and mortality is uteroplacental insufficiency caused by placental infarcts, followed by placental abruption, and chorioamnionitis.

Datta S, ed. *Anesthetic and Obstetric Management of High-Risk Pregnancy* . 3rd ed. New York: Springer; 2004:270-281.

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Ghulmiyyah L, Sibai B . Maternal mortality from preeclampsia/eclampsia. *Semin Perinatol*. 2012;36:56-59.

B. Preoperative Evaluation and Preparation

B.1. What initial laboratory studies are recommended for patients with preeclampsia?

- Complete blood cell count
- Platelet count and aggregation when available
- Coagulation assay including activated partial thromboplastin time, prothrombin time, fibrinogen, D-dimer
- Serum electrolytes
- Blood urea nitrogen, creatinine, and uric acid concentration
- Liver function tests
- Urinalysis, microscopy, 24-hour specimen for protein and creatinine clearance
- Type and screen (crossmatch if antibodies present)

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:835-837.

B.2. What are the important routine monitors for patients with preeclampsia? When is a central venous pressure (CVP) monitor indicated?

Important routine monitors are as follows:

- Noninvasive BP
- Maternal respiratory function assessment with oxygen saturation
- Hourly deep tendon reflexes
- Muscle strength
- Serial magnesium levels
- Foley catheter for assessing urine output
- Tocodynamometer
- Continuous fetal heart rate monitoring
- Consider invasive BP monitoring with an arterial line when severe refractory hypertension is present; when rapid-acting vasodilators, such as sodium nitroprusside (SNP) or nicardipine, are used; or when noninvasive BP measurement proves difficult (e.g., obesity).
- A CVP monitor or a PA catheter may be indicated for the following conditions:
  - Persistent oliguria
  - Difficulty in fluid management therapy in antepartum and/or postpartum period
  - Presence of pulmonary edema

A survey on the use of invasive hemodynamic monitoring among anesthesiologists who care for patients with preeclampsia indicates that central monitoring is used in 7.5% of patients. When invasive hemodynamic monitoring is used, 56% of anesthesiologists use an arterial line, 26% use an arterial line and central monitoring, and 20% use central monitoring only. Also, 92% of respondents use a CVP monitor, whereas only 8% use a PA catheter. The etiology of pulmonary edema, however, may be due to an increase in capillary permeability as well as from diastolic dysfunction, complicating assessment of cardiac function, and volume status. Only in severe forms of preeclampsia is left ventricular

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systolic function markedly reduced. Further, there may be technical difficulties with placing the PA catheter that are both patient-related (awake, anxious, short neck with poorly visible landmarks, coagulopathy) and physician-related (inexperience with central venous catheterization), which may alter the balance between benefit and risk of invasive monitoring. Whenever possible, a bedside transthoracic echocardiogram may be obtained; however, there may be limited windows for imaging due to the gravid uterus—causing distention of the abdomen.

Birnbach DJ, Gatt SP, Datta S, eds. *Textbook of Obstetric Anesthesia* . New York: Churchill Livingstone; 2000:546.

Ross VH, Moore CH, Fragneto RY, et al. Invasive hemodynamic monitoring in the management of PIH: a survey of practicing anesthesiologists. *Anesthesiology*. 2000;92:A89.

B.3. What conditions mandate immediate delivery, regardless of the gestational age?

- Severe hypertension that persists after 24 to 48 hours
- Progressive thrombocytopenia
- Liver dysfunction
- Progressive renal dysfunction (including severe oliguria)
- Premonitory signs of eclampsia
- Evidence of fetal deteriorating status
- Persistent headache or other neurologic sequelae of preeclampsia

Datta S, ed. *Anesthetic and Obstetric Management of High-Risk Pregnancy* . 3rd ed. New York: Springer; 2004:407-408.

Uzan J, Carbonnel M, Piccone O, et al. Pre-eclampsia: pathophysiology, diagnosis, and management. *Vasc Health Risk Manag*. 2011;7:467-474.

B.4. Discuss the obstetric management of preeclampsia.

The goal of therapy is to stabilize the mother and to safely deliver the fetus and placenta.

- Improve intravascular volume.
- Administer seizure prophylaxis with magnesium sulfate.
- Administer antihypertensives for BP control.

Labetalol is a commonly used antihypertensive agent that decreases maternal SVR without increasing maternal heart rate or decreasing cardiac index, uterine blood flow, or fetal heart rate when it is given in a total dose of less than 1 mg per kg. When given in an initial intravenous bolus dose of 10 to 20 mg, it has a faster onset of action than hydralazine, and, if necessary, the dose may be doubled every 10 minutes. It is useful in the management of refractory hypertension. If a second agent must be administered (e.g., hydralazine, SNP, or nicardipine), labetalol helps to prevent reflex tachycardia. It is important to note that the mechanism of hypertension is mediated greatly by circulating catecholamines, making labetalol a preferred antihypertensive agent that will antagonize the vasoconstrictive effects of norepinephrine, in particular. Other agents may reduce the BP as reflected by a peripheral BP monitor; however, unopposed vasoconstriction at the central and at the microcirculatory levels may cause end-organ injury.

Hydralazine is another antihypertensive agent that can be used because of its direct vasodilating effect. The full extent of its effect is evident in 20 minutes; therefore, if sufficient time is not allowed between injections, severe hypotension will be seen. It is used in 5- to 10-mg increments intravenously every 20 to 30 minutes until the diastolic BP is decreased, with a cumulative dose of 20 mg. Hydralazine directly decreases peripheral vascular resistance. Reflex sympathetic activity can result in tachycardia and increased stroke volume and cardiac output. Tachycardia can be treated with labetalol, 10 to 20 mg intravenously. The patient may complain of headache and flushing of the face during therapy.

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Nitroglycerin (NTG) causes vascular smooth muscle relaxation by means of its intracellular degradation to NO. The primary effect of NTG is venodilation, but it is less effective in prehydrated patients. NTG readily crosses the placenta. The drug is most useful for short-term treatment (e.g., to control the response to tracheal intubation). Small doses, 50 to 100 μg, may be given intravenously, or NTG may be given sublingually in a 400-μg metered spray.

SNP relaxes the arterial vessels, thereby reducing afterload. However, SNP also reduces venous return. The drug is most useful for short-term treatment, similar to NTG. Cyanide toxicity is proposed to be more likely with prolonged infusion rates that exceed 4 μg/kg/min over several hours to days; however, Naulty et al. demonstrated that intravenous infusion of nitroprusside solution in pregnant ewes, maintained at a rate sufficient to decrease mean maternal arterial pressure by 20% for 1 hour, resulted in equilibration of maternal and fetal levels of nitroprusside at the 20-minute sample. Five of the eight animals exhibited tachyphylaxis to nitroprusside, and their fetuses died in utero with lethal levels of cyanide. No significant changes were observed in uterine blood flow. There have been attempts to counteract the cyanide toxicity of nitroprusside by coadministration of sodium thiosulfate. Curry et al. administered sodium thiosulfate and nitroprusside to pregnant ewes and only nitroprusside to a control group. Although control ewes and fetuses suffered progressive increases in red

cell cyanide concentrations into the toxic range, experimental ewes and fetuses never developed toxic red cell cyanide levels. These results suggest that coadministration of sodium thiosulfate with SNP to pregnant women at doses currently in use for nonpregnant patients will prevent fetal, as well as maternal, cyanide toxicity. Unfortunately, it is not known whether these findings are transferable to humans, raising major concern over ongoing clinical use of nitroprusside in obstetrics when safer drugs such as nicardipine and labetalol are available.

Nifedipine is a calcium entry blocker that affects predominantly arterial and arteriolar smooth muscle. Common maternal side effects include facial flushing, headache, and tachycardia. Nifedipine rapidly lowers BP after oral or sublingual administration. After an initial dose of 10 mg sublingually, it may be repeated in 30 minutes and subsequently given in a maintenance dose of 10 to 20 mg every 3 to 6 hours. Caution must be exercised in the patient receiving both magnesium sulfate and calcium entry blockers because of the risk of myocardial depression and resultant pulmonary edema.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:837-838.

B.5. In the United States, what drug therapy is the treatment of choice for seizure prophylaxis?

Magnesium sulfate is the initial therapy for seizure prophylaxis. The Eclampsia Trial Collaborative Group compared magnesium sulfate, phenytoin, and diazepam administration for the prevention of recurrent seizures in women with preeclampsia. They found that magnesium sulfate was more effective in preventing recurring seizures than either phenytoin or diazepam.

An initial bolus of 4 to 6 g of magnesium sulfate is administered over 20 minutes and followed with an intravenous infusion of 1 to 2 g per hour. Urine output, respiratory rate, and patellar reflexes are monitored during magnesium therapy. The serum magnesium sulfate concentration should be measured at least 4 hours after initiation of therapy. The therapeutic range for serum magnesium sulfate concentrations is between 4 and 6 mEq per L. Loss of deep tendon reflexes occurs at 10 mEq per L with evidence of prolonged P-Q intervals and widening QRS complexes. Respiratory arrest occurs at 15 mEq per L, and asystole occurs at 20 mEq per L.

Eclampsia Trial Collaborative Group. Which anticonvulsant for women with eclampsia? Evidence from the collaborative eclampsia trial. *Lancet*. 1995;345:1455-1463.

Pauli JM, Repke JT. Preeclampsia: short term and long-term implications. *Obstet Gynecol Clin North Am*. 2015;42(2):299-313.

B.6. Discuss the treatment of magnesium sulfate toxicity.

Magnesium sulfate is excreted by the kidneys. Therefore, urine output must be followed closely and serial serum concentrations of magnesium sulfate must be checked, especially in women with renal dysfunction. If magnesium sulfate toxicity is suspected, the magnesium sulfate infusion should be immediately discontinued. Intravenous calcium gluconate,

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1 g, or calcium chloride, 300 mg, should be administered if needed to antagonize the effects of magnesium sulfate. If respiratory distress occurs, the patient may require endotracheal intubation and mechanical ventilation.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:838-839.

Curry SC, Carlton MV, Raschke RA. Prevention of fetal and maternal cyanide toxicity from nitroprusside with coinfusion of sodium thiosulfate in gravid ewes. *Anesth Analg*. 1997;84:1121-1126.

Naulty J, Cefalo RC, Lewis PE. Fetal toxicity of nitroprusside in the pregnant ewe. *Am J Obstet Gynecol*. 1981;139:708-711.

B.7. Discuss the mechanism of action of magnesium sulfate.

Magnesium has the following effects:

- It is a central nervous system depressant and anticonvulsant.
- It may protect the blood-brain barrier, decrease cerebral edema, or act centrally at *N*-methyl-D-aspartate receptors to raise the seizure threshold.

- It inhibits the release of acetylcholine at the neuromuscular junction, decreases the sensitivity of the motor end plate to acetylcholine, and decreases muscle membrane excitability, thereby potentiating the effects of nondepolarizing and depolarizing muscle relaxants.
- It decreases uterine hyperactivity by its mild relaxant effect on vascular and uterine smooth muscle; it may improve uterine blood flow.
- It is a mild vasodilator in vascular beds (including small-diameter cerebral vessels) by a direct or indirect (calcium-competing) effect, and it has a mild antihypertensive effect.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:838-839.

Euser AG, Cipolla MJ. Magnesium sulfate treatment for the prevention of eclampsia: a brief review. *Stroke*. 2009;40:1169-1175.

B.8. What are the fetal effects of magnesium sulfate therapy?

Magnesium sulfate crosses the placenta. There can be evidence of decreased beat-to-beat variability in the fetal heart rate. Neonatal depression (e.g., respiratory depression and hyporeflexia) also can occur.

Pauli JM, Repke JT. Preeclampsia: short-term and long-term implications. *Obstet Gynecol Clin North Am*. 2015;42(2):299-313.

B.9. Discuss the treatment of eclampsia.

- Stop the convulsions, usually with a benzodiazepine, and administer magnesium sulfate.
- Establish an airway.
- Turn patient to the left side; apply jaw thrust.
- Attempt bag and mask ventilation.
- Insert oropharyngeal airway if necessary.
- Maintain ventilation and oxygenation.

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- Continue bag and mask ventilation.
- Apply pulse oximeter and monitor.
- Maintain circulation.
- Secure intravenous access.
- Check BP at frequent intervals.
- Monitor electrocardiographic (ECG) recordings.
- Administer magnesium sulfate.
- Treat hypertension.
- Deliver the baby expeditiously.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:851-852.

C. Intraoperative Management

C.1. What is your choice of analgesia/anesthesia for patients with preeclampsia?

Most anesthesiologists and obstetricians consider epidural analgesia the safe and preferred form of pain relief for labor and delivery in preeclamptic women. Epidural analgesia provides the following advantages:

- Pain relief that is superior to other analgesic methods
- Attenuation of the exaggerated hypertensive response to pain of preeclamptic women
- Decrease in circulating levels of catecholamines and stress-related hormones, which facilitates BP control
- Improvement of intervillous blood flow in preeclamptic women
- Stable cardiac output
- Preeclamptic women are at increased risk of cesarean delivery compared with normal parturients, and early administration of epidural analgesia for labor facilitates the

subsequent administration of epidural anesthesia for emergent cesarean delivery while avoiding the risks of general anesthesia.

Abboud T, Artal R, Sarkis F, et al. Sympathoadrenal activity, maternal, fetal, and neonatal responses after epidural anesthesia in the preeclamptic patient. *Am J Obstet Gynecol*. 1982;144:915-918.

Pauli JM, Repke JT. Preeclampsia: short-term and long-term implications . *Obstet Gynecol Clin North Am*. 2015;42(2):299-313.

C.2. What is the advantage of prehydration?

Prehydration helps compensate for reductions in preload and afterload during the administration of epidural analgesia/anesthesia. Two studies have investigated the effects of intravenous volume loading with crystalloid on atrial natriuretic peptide (ANP) secretion in preeclamptic women. ANP is a vasodilator secreted from the cardiac atria in response to an acute volume load, and this response is more pronounced in preeclamptic women. ANP has properties that counteract vasospasm and improve renal elimination of excess extracellular fluid. These studies support the use of volume expansion before administration of regional anesthesia in preeclamptic women.

However, in current practice, lower concentrations of local anesthetics combined with an opioid are used for labor analgesia, and fluid preloading is of less clinical relevance. One still needs to be vigilant to the risk of pulmonary edema in the severely preeclamptic patient, as the incidence of global diastolic dysfunction, although usually mild, is about 40%.

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Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:843-845.

Melchiorre K, Sutherland GR, Baltabaeva A, et al. Maternal cardiac dysfunction and remodeling in women with preeclampsia at term. *Hypertension*. 2011;57:85-93.

C.3. Discuss bleeding time and platelet count evaluation during preoperative assessment of a patient with preeclampsia requesting epidural analgesia/anesthesia for labor and delivery.

The bleeding time does not specifically measure platelet function, and it can be abnormal in a number of coagulation disorders, such as factor deficiencies. No evidence suggests that the skin bleeding time predicts the potential for bleeding from a traumatized epidural vein in a woman with severe preeclampsia. Therefore, the bleeding time should not be used to measure platelet function. A specific platelet count that predicts the risk of complications from regional anesthesia has not been determined. The *trend* in platelet count is important to note, as preeclampsia is a dynamic disorder, and a rapid decrease in platelet count in a short interval may warrant concern.

Many anesthesiologists will place an epidural anesthetic at a platelet count of 80,000 per μL and some at lower platelet counts. The patient must be individualized and a thorough bleeding history, along with the trend in platelet count, should always be considered. If the platelet count is below 100,000 per μL, serial platelet counts as well as the prothrombin time, partial thromboplastin time, and fibrinogen levels should be measured.

Abramovitz S, Beilin Y. Thrombocytopenia, low molecular weight heparin, and obstetric anesthesia. *Anesthesiol Clin North America*. 2003;21:99-109.

Laskin S, Payne B, Hutcheon JA, et al. The role of platelet counts in the assessment of inpatient women with preeclampsia. *J Obstet Gynaecol Can*. 2011;33:900-908.

C.4. What level of analgesia/anesthesia is required for labor and delivery?

- First stage of labor: T10-L1
- Second stage of labor: S2-S4

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:412-415.

C.5. Discuss the commonly used local anesthetics for labor analgesia.

Bupivacaine, ropivacaine, and levobupivacaine (amide local anesthetics) are commonly used because they provide potent analgesia. They provide analgesia with less motor block than an equipotent concentration of lidocaine. Moreover, dilute solutions cause less hypotension than more concentrated solutions.

Bupivacaine is four times more potent than lidocaine. It is 90% to 95% bound to maternal plasma protein. It is known to be more cardiotoxic than lidocaine. The mechanism relates to its action on cardiac sodium channels. Bupivacaine and lidocaine both block sodium channels to the nerves and to the heart. They are similar because they both cause a rapid block of cardiac sodium channels on depolarization. They differ in their recovery from block. The lidocaine block is complete within less than 1 second, whereas bupivacaine takes five times longer. Bupivacaine is a “fast-in, slow-out” agent. Its main advantage is that it has a longer duration and a weak motor block when given in analgesic concentrations.

Ropivacaine is a homolog of mepivacaine and bupivacaine, but it is formulated as a single levorotatory isomer rather than as a racemic mixture. It appears to be less cardiotoxic than bupivacaine.

Levobupivacaine is also a single levorotatory isomer formulation of a local anesthetic. Levobupivacaine appears to be less cardiotoxic than bupivacaine.

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2-Chloroprocaine is an ester type of local anesthetic. It is hydrolyzed by plasma cholinesterase, and it has a rapid metabolism, allowing for a very quick onset of action.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:261-265.

C.6. Is the addition of epinephrine to local anesthetics advisable in preeclamptic patients?

Clinical evidence supports the safety of epidural administration of an epinephrine-containing local anesthetic in preeclamptic women. However, care must be taken when using epinephrinecontaining local anesthetic solutions in severe preeclamptic women as inadvertent intravascular injection may result in acute severe hypertension.

Dror A, Abboud TK, Moore J, et al. Maternal hemodynamic responses to epinephrine-containing local anesthetics in mild pre-eclampsia. *Reg Anesth*. 1988;13:107-111.

Heller PJ, Goodman C. Use of local anesthetics with epinephrine for epidural anesthesia in preeclampsia. *Anesthesiology*. 1986;65:224-226.

C.7. What is the treatment for the abnormal fetal heart rate pattern seen with maternal hypotension after epidural analgesia/anesthesia is instituted?

- Administration of oxygen with face mask
- Left uterine displacement
- Increased hydration
- Elevation of lower extremities to facilitate venous return
- Administration of small increments of phenylephrine, 50 to 100 μg, or ephedrine, 2.5 to 5 mg, intravenously, if the BP falls more than 20% of baseline

Vercauteren M. Obstetric spinal analgesia and anesthesia. *Curr Opin Anesthesiol*. 2003;16:503-507.

C.8. What would you do after an accidental spinal tap? How do you treat postdural puncture headache?

Accidental dural puncture can be managed with one of two options. First, the epidural needle may be repositioned in another interspace. Local anesthetic must be administered slowly because now there is a direct communication with the intrathecal space through the dural hole, and thereby, a more profound analgesic/anesthetic block may appear. The incidence of a postdural puncture headache after an accidental wet tap with an epidural needle is more than 50%. After delivery of the fetus, the catheter should be removed. Intravenous and oral caffeinated beverages should be encouraged. Intravenous caffeine and oral analgesics may be used as well. If symptoms worsen (e.g., tinnitus, blurry vision, neck pain, difficulty sitting or standing), one should consider an epidural blood patch. Immediate relief occurs in almost 90% of patients on first attempt. Transient side effects include backache and neck pain. Second, an epidural catheter (20 gauge) can be inserted intrathecally for use as a continuous spinal catheter. After delivery, one can remove the catheter and follow the guidelines as listed earlier, or one can consider maintaining the intrathecal catheter in place for 24 hours to allow for an inflammatory reaction to develop around the intrathecal catheter. This inflammatory

reaction may decrease the leakage of cerebrospinal fluid and thereby the incidence of postdural puncture headache.

Gaiser R. Postdural puncture headache. *Curr Opin Anaesthesiol*. 2006;19:249-253.

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C.9. How would you manage total spinal anesthesia?

- High spinal anesthesia may occur several minutes after an epidural injection of local anesthetic, especially if the injection is into the subarachnoid or subdural space. It is vitally important to communicate with the patient. Agitation, dyspnea, and difficulty speaking may indicate the onset of total spinal anesthesia.
- Avoid aortocaval compression.
- Administer 100% oxygen.
- Provide positive pressure ventilation if necessary, preferably through an endotracheal tube.
- Monitor maternal BP, ECG recordings, and fetal heart rate.
- Support maternal circulation with intravenous fluids and vasopressors as needed. Give epinephrine if needed.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:487-488.

C.10. Should ergonovine be given to preeclamptic patients?

Preeclampsia is a relative contraindication to the use of ergot alkaloids because of the risk of inducing a hypertension crisis. In preeclamptic patients, uterine atony unresponsive to oxytocin may be treated with 15-methylprostaglandin $F_{2\alpha}$.

Suresh M, Segal BS, Preston RL, et al, eds. *Shnider and Levinson's Anesthesia for Obstetrics*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2013:159-163.

C.11. When and how would you give spinal anesthesia?

Spinal anesthesia may be used for cesarean delivery, even in a patient with preeclampsia with severe features. Hyperbaric bupivacaine 0.75% in a dose of 11.25 to 12 mg with or without fentanyl, 15 to 20 μg, and morphine, 100 to 200 μg, may be given.

Advantages of spinal anesthesia in patients with preeclampsia with severe features include the following:

- Avoidance of general anesthesia and risks of difficulty with an edematous airway
- Elimination of risk of severe hypertensive response to laryngoscopy and endotracheal intubation, which can result in intracranial hemorrhage
- More reliable anesthesia than with an epidural anesthetic technique
- Smaller needle size than an epidural and therefore possibly less risk of trauma to epidural veins

One study by Aya et al. noted that the risk of hypotension was almost six times less in severely preeclamptic women than in healthy pregnant women receiving spinal anesthesia for elective cesarean section. In these preeclamptic patients, spinal anesthesia may cause a higher incidence than epidural anesthesia; however, this hypotension is typically easily treatable and short-lived and has not been linked to clinically significant differences in maternal or neonatal outcomes.

Aya AG, Mangin R, Vialles N, et al. Patients with severe preeclampsia experience less hypotension during spinal anesthesia for elective cesarean delivery than healthy parturients: a prospective cohort comparison. *Anesth Analg*. 2003;97:867-872.

Henke VG, Bateman BT, Leffert LR. Focused review: spinal anesthesia in severe preeclampsia. *Anesth Analg*. 2013;117:686-693.

C.12. Discuss a general anesthesia technique for the patient with preeclampsia presenting for cesarean delivery.

- Aspiration prophylaxis. Acceptable methods include 30 mL of an oral nonparticulate antacid, and/or an H_2-blocker intravenously, and possibly metoclopramide, 10 mg intravenously.

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- Preoxygenation and denitrogenation with 100% oxygen through face mask
- Induction of anesthesia with cricoid pressure and either propofol and/or etomidate
- Succinylcholine, 1.5 mg per kg, for effective intubation conditions
- Use a smaller endotracheal tube (6.0 or 6.5 mm internal diameter) because of airway edema.
- May consider use of nondepolarizing muscle relaxants for maintenance of neuromuscular block once the patient has demonstrated recovery from succinylcholine; magnesium sulfate potentiates the effects of both depolarizing and nondepolarizing muscle relaxants.
- Use two-thirds of the minimum alveolar concentration of inhalation agent of the nonpregnant adult to ensure an adequate depth of anesthesia.
- Continue magnesium sulfate administration during intraoperative and postoperative periods.
- Consider arterial line placement before induction in patients with preeclampsia with severe features for continuous BP measurement. The transient but severe hypertension that accompanies tracheal intubation in preeclamptic women can significantly increase maternal intracranial pressure, with the attendant risks of cerebrovascular accident.
- Antihypertensive drugs can be given as required.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:846-848.

C.13. What agents can you use to prevent hypertension during the induction of general anesthesia for cesarean delivery?

Before induction, labetalol, 5- to 10-mg increments, NTG, 50 to 100 *μ*g increments; or SNP, 50-*μ*g increments, can be used to attenuate the pressor response to laryngoscopy and intubation. Also, the short-acting opioid remifentanil can be used.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:846-848.

C.14. What is HELLP syndrome?

HELLP syndrome is a severe form of preeclampsia characterized by hemolysis (*H*), elevated liver enzymes (*EL*), and low platelets (*LP*). It can occur antepartum or postpartum. Delivery represents the only definitive treatment of HELLP syndrome. HELLP syndrome is associated with maternal and neonatal morbidity and mortality. Hemolysis is defined by an abnormal peripheral blood smear and an increased bilirubin level (1.2 mg per dL or greater). Elevated liver enzymes are defined as an increased serum glutamic-oxaloacetic transaminase (aspartate aminotransferase) of at least 70 U per L and a lactate dehydrogenase level of more than 600 U per L. A low platelet count is generally defined as a count of less than 100,000 per *μ*L. Patients with HELLP syndrome have a high incidence of serious maternal complications including disseminated intravascular coagulation, placental abruption, need for blood transfusion, pleural effusion, acute renal failure, and wound infection.

Audibert F, Friedman SA, Frangieh AY, et al. Clinical utility of strict diagnostic criteria for the HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. *Am J Obstet Gynecol*. 1996;175:460-464.

Pauli JM, Repke JT. Preeclampsia: short-term and long-term implications. *Obstet Gynecol Clin North Am*. 2015;42(2):299-313.

D. Postoperative Management

D.1. Discuss the postpartum management of preeclamptic patients.

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- Provide adequate analgesia.
- Maintain strict intake/output for at least 24 hours postpartum or until diuresis develops.
- Continue magnesium sulfate for at least 24 hours postpartum or until evidence of diuresis.
- Maintain hemodynamic control with antihypertensives if necessary.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:849-50.

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Chapter 29
Breech Presentation, Fetal Distress, and Mitral Stenosis

Jill Fong

A 25-year-old unregistered primigravida at 38 weeks of gestation presented to the labor room contracting. The patient had a history of rheumatic fever with no subsequent medical follow-up. On physical examination, she had a diastolic murmur and an opening snap. She reported having shortness of breath when climbing two flights of stairs. She was attached to an external fetal heart rate (FHR) monitor and tocodynamometer; recurrent variable decelerations without any beat-to-beat variability were noted. Simultaneously, the patient was found to have ruptured membranes, meconium-stained amniotic fluid, a fetal foot in her vagina, and a prolapsed umbilical cord. She was rushed to the operating room for an emergency cesarean section. Her blood pressure was 100/60 mm Hg; pulse rate, 100 beats per minute; and respiratory rate, 18 breaths per minute.

A. Medical Disease and Differential Diagnosis

1. How are fetal lie, presentation, and position defined and determined?
2. What is the approximate frequency of the various lies and presentations at or near term?
3. What are the different types of breech presentation, and what is their incidence?
4. What is the cause of breech presentation?
5. What are the perinatal problems associated with breech presentation?
6. What is the usual obstetrical management for patients with breech presentation?
7. What is the incidence of heart disease in pregnancy and the mortality rate associated with maternal cardiac disease?
8. What classifications may help predict an individual pregnant woman's cardiac risk?
9. What are the cardiovascular changes of pregnancy?
10. What changes may normally occur in heart sounds during pregnancy?
11. What are the normal electrocardiographic and echocardiographic changes seen during pregnancy?
12. What causes rheumatic heart disease?
13. What are the physiologic consequences of mitral stenosis?
14. What are the auscultatory findings associated with mitral stenosis?
15. What may be seen on the electrocardiogram (ECG) in patients with mitral stenosis?
16. What are the echocardiographic findings associated with mitral stenosis?
17. What is the effect of the physiologic changes of pregnancy on patients with mitral stenosis?
18. If mitral stenosis is first recognized during pregnancy and symptoms develop, how would you treat the patient?
19. What are the determinants of fetal oxygenation?
20. What are the determinants of uterine blood flow?

B. Preoperative Evaluation and Preparation

1. How is fetal well-being assessed during labor?
2. How are FHR and maternal contractions monitored?
3. What is the normal FHR with beat-to-beat variability?
4. What are periodic decelerations?

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5. How accurate is FHR monitoring in predicting fetal well-being?
6. In the fetus with a nonreassuring FHR pattern, what other modalities can be used to assess fetal well-being?
7. What is the significance of meconium-stained amniotic fluid?
8. What is meconium aspiration syndrome?
9. What are the usual noninvasive tests used to evaluate the pregnant cardiac patient?
10. What preoperative medications would you give this patient?

C. Intraoperative Management

1. What monitors would you use in this functional New York Heart Association (NYHA) class II patient during her cesarean section?
2. When would you use invasive monitoring in a pregnant patient with cardiac disease?
3. What are the hemodynamic goals of intraoperative management of the pregnant patient with mitral stenosis?
4. What anesthetic technique would you use for this emergency cesarean section?
5. What technique could you use for general anesthesia in this patient?
6. If you had unexpectedly been unable to intubate this patient, how would you have managed the airway?
7. Would this patient benefit from the use of β-blockers?
8. What is the effect of the inhalation agents on uterine contractility?
9. What is the Apgar scoring system?
10. What is the significance of Apgar scores?
11. At birth, what should be done to minimize an infant's risk of meconium aspiration syndrome?
12. The Apgar score of the newborn was 3 at 1 minute. How would you treat the newborn?
13. Blood gases are sent immediately after delivery. What are the normal values for umbilical vein and artery blood gases?

D. Postoperative Management

1. Immediately after the baby was delivered, the mother's oxygen saturation decreased. What is the differential diagnosis?

A. Medical Disease and Differential Diagnosis

A.1. How are fetal lie, presentation, and position defined and determined?

- Fetal lie describes the position of the long axis of the fetus in relative to the long axis of the mother. Longitudinal, transverse, and oblique lies exist. Longitudinal lies are either cephalic or pelvic (breech) depending on which fetal structure enters the maternal pelvis. Transverse lies are either back up or back down with the long axis of the fetus perpendicular (90 degrees) to the mother's long axis. An oblique lie results when the long axis of the fetus is at an acute angle to that of the mother. It is usually only transitory and converts to a transverse or longitudinal lie when labor begins.
- Presentation describes the part of the fetus that is lowermost in the pelvis: cephalic, breech, or shoulder. Cephalic presentations are further subdivided into vertex, brow, and face presentations.

- Position of the presenting part is described as a relationship between a certain pole of the fetal presenting part and the maternal surrounding pelvis.
- Fetal lie, presentation, and position can often be determined by manual pelvic and abdominal examination. Ultrasonography is also useful, particularly, when palpation is inconclusive, as can occur with maternal obesity, multiple gestations, placenta previa, and hydramnios.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:433-

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A.2. What is the approximate frequency of the various lies and presentations at or near term?

Longitudinal lie, >99%, including cephalic presentation, 97%; breech presentation, 3% to 4%; transverse lie, 0.3%; compound presentation, 0.1%; face presentation, 0.05%; and brow presentation, 0.01%.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:434.

A.3. What are the different types of breech presentation, and what is their incidence?

- *Frank breech*: Both fetal lower extremities are flexed at the hips and extended at the knees. The incidence is approximately 60% (48% to 73%) of breech presentations.
- *Complete breech*: The knees are flexed, as are the hips. The incidence is approximately 10% (4.6% to 11.5%).
- *Incomplete or footling breech*: One or both hips are extended and a foot or knee hangs below the breech. The incidence is approximately 30% (12% to 38%).

Gabbe SG, Niebyl JR, Simpson JL, et al, eds. *Obstetrics: Normal and Problem Pregnancies*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2012:396-402.

A.4. What is the cause of breech presentation?

The etiology of breech is unknown, but certain factors are associated with this presentation including prematurity, hydramnios, uterine relaxation associated with high parity, multiple fetuses, oligohydramnios, hydrocephaly, anencephaly, uterine anomalies, pelvic tumors, placenta previa, cornual-fundal placenta implantation, and previous breech delivery. Ford et al. found that the rate of breech recurrence after a previous breech pregnancy was 9.9%, and after two prior breech deliveries, the incidence of another breech presentation was 27.5%. After a prior cesarean delivery, a twofold increase in the incidence of breech presentation has been reported.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:559-560.

Ford JB, Roberts CL, Nassar N, et al. Recurrence of breech presentation in consecutive pregnancies. *BJOG*. 2010;117(7):830-836.

A.5. What are the perinatal problems associated with breech presentation?

There is an increased incidence of prolapsed cord, perinatal morbidity and mortality resulting from difficult delivery, preterm delivery, fetal anomalies, placenta previa, and uterine anomalies.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:561.

A.6. What is the usual obstetrical management for patients with breech presentation?

An external cephalic version is attempted to convert the breech to a vertex presentation in nonlaboring patients who are candidates for vaginal deliveries. In general, the American College of Obstetricians and Gynecologists (ACOG) recommends that external version should be considered in patients when a breech presentation is recognized prior to labor at or after 36 weeks' gestation. The reported success rates vary from 35% to 86%. Successful version is more commonly associated with multiparity, abundant amniotic fluid, a non-engaged presenting part, fetal size ranging from

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2,500 to 3,000 g, a posterior placenta, and non-obesity. Tocolysis has been shown to be variably effective in improving version success rates; there is

more evidence to support betamimetic tocolysis than the use of nifedipine or nitroglycerin. Epidural anesthesia during version has been shown by Schorr et al. and Mancuso et al. to improve the success rate of external cephalic version. While others have found no improvement in version success associated with neuraxial analgesia/anesthesia, Collaris and Oei found that maternal and fetal complications increased when conduction anesthesia had been used, and they concluded that the decreased maternal pain associated with these versions encouraged an overzealous application of force. A meta-analysis of six randomized trials involving 508 attempted versions found that spinal or epidural anesthesia improved the rate of success to 59.7% compared to 37.6% for those receiving intravenous or no analgesia. According to ACOG in 2014, there is evidence that success may be enhanced by regional anesthesia. If the version is successful, labor and vaginal delivery may proceed.

The 2006, and reaffirmed in 2012, recommendation from ACOG for breech delivery of the singleton fetus states “the decision regarding mode of delivery should depend on the experience of the health care provider,” and “planned vaginal delivery of a term singleton breech fetus may be reasonable under hospital-specific protocol guidelines.” Cesarean delivery is commonly used in the following circumstances: lack of operator experience, incomplete or footling breech, hyperextended fetal head, fetal macrosomia, unfavorable pelvic shape, severe fetal growth retardation, fetal anomaly incompatible with vaginal delivery, healthy preterm fetus with maternal labor or with indicated delivery, previous perinatal death/trauma, maternal cesarean section request, and possibly previous cesarean delivery. The availability of skilled operators to safely deliver breech fetuses vaginally seems to be declining at least in Australia. The rates of planned vaginal delivery attempts, at least in Dublin, Ireland, are also declining.

American College of Obstetricians and Gynecologists. External cephalic version. ACOG Practice Bulletin Number 13 February 2000. *Obstet Gynecol*. 2000;95(2). Reaffirmed 2012.

American College of Obstetricians and Gynecologists, Society for Maternal-Fetal Medicine. Obstetric care consensus no. 1: safe prevention of the primary cesarean delivery. *Obstet Gynecol*. 2014;123(3):693-711.

American College of Obstetricians and Gynecologists Committee on Obstetric Practice. ACOG Committee Opinion No. 340. Mode of term singleton breech delivery. *Obstet Gynecol*. 2006;108(1):235-237. Reaffirmed 2012.

Collaris RJ, Oei SG. External cephalic version: a safe procedure? A systematic review of version related risks. *Acta Obstet Gynecol Scand*. 2004;83:511-518.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:558, 562, 570-541.

Goetzinger KR, Harper LM, Tuuli MG, et al. Effect of regional anesthesia on the success rate of external cephalic version: a systematic review and meta-analysis. *Obstet Gynecol*. 2011;118(5):1137-1144.

Mancuso KM, Yancey MK, Murphy JA, et al. Epidural anesthesia for cephalic version: a randomized trial. *Obstet Gynecol*. 2000;95(5):648.

Schorr SJ, Speights SE, Rose EL, et al. A randomized trial of epidural anesthesia to improve external cephalic version success. *Am J Obstet Gynecol*. 1997;177:1133.

A.7. What is the incidence of heart disease in pregnancy and the mortality rate associated with maternal cardiac disease?

The incidence of cardiac disease is around 1% and is now the leading cause of indirect maternal deaths accounting for 20% of the deaths. Worldwide, rheumatic fever is the main cause of the cardiac valvular disease encountered during pregnancy. Congenital heart disease, not rheumatic heart disease, is now the major cause of heart disease in pregnancy in the developed world. In the developing world and in immigrants to developed countries, rheumatic heart disease

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continues to be a major problem. Small et al. also found that cardiovascular disease was a leading obstetrical cause for intensive care unit admission.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:881.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:958, 973.

Small MJ, James AH, Kershaw T, et al. Near-miss maternal mortality: cardiac dysfunction as the principal cause of obstetric intensive care unit admission. *Obstet Gynecol.* 2012;119(2 pt 1):250-255.

A.8. What classifications may help predict an individual pregnant woman's cardiac risk?

The NYHA classification of a complete diagnosis of cardiovascular disease is not widely used now. The grading of dyspnea and/or fatigue resulting from heart failure is, however, often still classified using the old functional NYHA classification.

- *Class I*: no limitation of physical activity
- *Class II*: slight limitation of physical activity; symptoms with ordinary activity
- *Class III*: marked limitation of physical activity; symptoms with less than ordinary activity
- *Class IV*: unable to carry on any physical activity without discomfort; symptoms may be present at rest

On the basis of an analysis of 562 pregnant patients with heart disease, Siu et al. expanded on the NYHA classification and developed a system for predicting complications during pregnancy. Their predictors of cardiac complications included the following:

1. Prior heart failure, arrhythmia, transient ischemic attack, or stroke
2. A baseline NYHA III or IV classification or cyanosis
3. A left-sided heart obstruction defined as a mitral valve area less than 2 cm2, aortic valve area less than 1.5 cm2, or an echocardiographically demonstrated peak left ventricular outflow tract gradient exceeding 30 mm Hg
4. Less than 40% ejection fraction

Their cardiac disease in pregnancy (CARPREG) scoring system helps predict maternal cardiac events. Each predictor is 1 point. With one of these factors, the risk of sustained arrhythmia, pulmonary edema, stroke, or cardiac death was increased, and if two or more factors existed, the risk was enhanced. The cardiac complication rate associated with 0 point is 5%, with 1 point is 27%, and with ≥2 points is 75%. There were no maternal deaths in patients in NYHA class I or II. Similarly, Stangl et al. found that pregnant patients with acquired and congenital cardiac disease were at increased risk of maternal and fetal morbidity and mortality if they had a left ventricular ejection fraction <50%, an NYHA class >II, a peak left ventricular outflow gradient >60 mm Hg, or were cyanotic. The CARPREG risk score has been validated in several studies and appears to be a valuable tool to predict maternal risk in acquired and congenital heart disease. Drenthen et al. investigated populations with congenital heart disease that has yet to be validated by other studies and outlined created a ZAHARA point system for predicting maternal cardiovascular events.

The European Task Force recommends that maternal risk assessment be based on the World Health Organization risk classification for cardiovascular disease in pregnancy (Table 29.1).

Maternal cardiac disease is associated with a 20% to 28% neonatal complication rate; neonatal and maternal adverse events are highly correlated. In women with cardiac disease, maternal predictors of increased neonatal adverse events include a baseline NYHA class >II, cyanosis, smoking during pregnancy, left-sided heart obstruction, multiple gestations, oral anticoagulation during pregnancy, and mechanical valve prosthesis.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:976-977.

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Drenthen W, Boersma E, Balci A, et al. Predictors of pregnancy complications in women with congenital heart disease. *Eur Heart J*. 2010;31(17):2124-2132.

Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, et al. ESC guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). *Eur Heart J*. 2011;32(24):3147-3197.

Siu SC, Sermer M, Colman JM, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. *Circulation*. 2001;104(5):515-521.

Stangl V, Schad J, Gossing G, et al. Maternal heart disease and pregnancy outcome: a single-centre experience. *Eur J Heart Fail*. 2008;10(9):855-860.

TABLE 29.1 Modified World Health Organization (WHO) Risk Classification for Cardiovascular Disease in Pregnancy

WHO Class I: no increased mortality risk; no/mild increase morbidity	• Uncomplicated, small or mild - Pulmonary stenosis - Patent ductus arteriosus - Mitral valve prolapse • Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage). • Atrial or ventricular ectopic beats, isolated
WHO II: small increased mortality risk; moderate increase morbidity	• Unoperated atrial or ventricular septal defect • Repaired tetralogy of Fallot • Most arrhythmias
WHO II-III (depends on individual)	• Mild left ventricular impairment • Hypertrophic cardiomyopathy • Native or tissue valvular heart disease not considered WHO I or IV • Marfan syndrome without aortic dilation • Aorta <45 mm in aortic disease associated with bicuspid aortic valve • Repaired coarctation
WHO III: significant increase mortality risk; severe increase morbidity	• Mechanical valve • Systemic right ventricle • Fontan circulation • Cyanotic heart disease (unrepaired) • Other complex congenital heart disease • Aortic dilatation 40-45 mm in Marfan syndrome • Aortic dilatation 45-50 mm in aortic disease associated with bicuspid aortic valve

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WHO IV: extremely high-risk mortality/morbidity; pregnancy contraindicated; discuss termination	• Pulmonary arterial hypertension of any cause • Severe systemic ventricular dysfunction (LVEF <30%, NYHA III-IV) • Previous peripartum cardiomyopathy with any residual impairment of left ventricular function • Severe mitral stenosis, severe symptomatic aortic stenosis • Marfan syndrome with aorta dilated >45 mm • Aortic dilatation >50 mm in aortic disease associated with bicuspid aortic valve • Native severe coarctation

LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Modified from Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. *Heart*. 2006;92(10):1520-1525; Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, et al. ESC guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). *Eur Heart J*. 2011;32(24):3147-3197.

A.9. What are the cardiovascular changes of pregnancy?

During the first trimester of pregnancy, the cardiac output increases to between 40% and 50% above the normal nonpregnant level and plateaus at approximately 28 weeks of gestation. It remains fairly stable until the stresses imposed by labor increase it further. The increase in cardiac output is due to a 30% increase in stroke volume and a 15% increase in heart rate. Blood pressure, however, is not elevated because peripheral vascular resistance decreases. Central venous pressure, pulmonary capillary wedge pressure, pulmonary artery diastolic pressure, and left ventricular stroke work index are unchanged when compared to nonpregnant values.

During labor, cardiac output increases approximately 15% with uterine contractions during the latent phase, 30% in the active phase, and 45% in the expulsive phase when compared to prelabor values. The greatest increase in cardiac output occurs immediately postpartum when it increases an average of 80% above prelabor values. Cardiac output and heart rate decline to prelabor values within 1 hour of delivery, and by approximately 24 hours, mean blood pressure and stroke volume return to their prelabor values. In the first 3 to 6 months

after delivery, the cardiovascular changes of pregnancy resolve. It can take a year, however, for the residual effects of cardiovascular remodeling to subside.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:59-60, 974.

Walsh RA, Fang JC, Fuster V, eds. *Hurst's The Heart: Manual of Cardiology* . 13th ed. New York: McGraw-Hill; 2013:628-629.

A.10. What changes may normally occur in heart sounds during pregnancy?

In a study of 50 normal pregnant women at varying stages in pregnancy, a phonocardiographic study found that the first heart sound might have an exaggerated split with increased loudness of both components. In up to 84% of pregnant patients, a third heart sound is also evident. In 16% of pregnant women, a fourth heart sound may be heard, but it typically disappears by term. Functional systolic murmurs, which disappear shortly after delivery, occur in more than 90% of pregnant women. Soft transient diastolic murmurs occur in 18% of these women, and 10% have continuous murmurs apparently arising from the breast vasculature. These murmurs alone, therefore, are not indicative of organic heart disease. Similarly, venous distention, tachycardia, edema, and breathlessness may be seen with pregnancy and not be a sign of heart disease. Audible diastolic murmurs on auscultation are uncommon, however, and warrant further investigation.

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Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:16. Walsh RA, Fang JC, Fuster V, eds. *Hurst's The Heart: Manual of Cardiology*. 13th ed. New York: McGraw-Hill; 2013:628-631.

A.11. What are the normal electrocardiographic and echocardiographic changes seen during pregnancy?

Premature atrial and ventricular contractions can occur. The QRS axis may shift to the right during the first trimester and then to the left, -15 degrees, in the third trimester. A true left axis deviation, -30 degrees, implies heart disease. In lead III, inverted P waves and small Q waves may be seen that disappear with inspiration. Some ST-segment depression and flattening or inverting of the T waves may occur. ST elevations, however, do not occur normally during pregnancy and should be considered pathologic.

Normal echocardiographic findings include an increase in atrial diameters bilaterally. Left ventricular wall mass is increased. Left ventricular function is unchanged or slightly improved. During end-diastole and end-systole, the left and right ventricular chamber sizes are increased; left ventricular mass increases. The annuli of the pulmonary, tricuspid, and mitral valves dilate progressively, and term pregnant women may have mild tricuspid, pulmonic, and/or much more infrequently mitral regurgitation. A small pericardial effusion may develop as well.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:16, 961, 964-965.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:976.

Desai DK, Moodley J, Naidoo D. Echocardiographic assessment of cardiovascular hemodynamics in normal pregnancy. *Obstet Gynecol*. 2004;104(1):20-29.

Walsh RA, Fang JC, Fuster V, eds. *Hurst's The Heart: Manual of Cardiology* . 13th ed. New York: McGraw-Hill; 2013:632.

A.12. What causes rheumatic heart disease?

Rheumatic heart disease may occur in patients who have had acute rheumatic fever (ARF). ARF is an immune-mediated illness that may develop after some group A streptococcal infections. It predominantly affects the heart and joints and may lead to chronic rheumatic heart disease. In individuals who appear to be genetically susceptible, ARF may follow an untreated pharyngeal group A streptococcal infection. ARF occurs most commonly in 5- to 15-year-old children and occurs most commonly in the winter or spring. It is much less common in developed countries than it was a few decades ago. Treatment of ARF includes

an anti-inflammatory agent for those with arthritis and/or mild carditis, an agent such as phenobarbital, diazepam, haloperidol, etc. for those with chorea, and a prophylactic antibiotic. Long-term antibiotic prophylaxis is indicated because ARF frequently recurs with subsequent group A streptococcal infections. The duration of this secondary prophylaxis against recurrent rheumatic fever depends on the presence or absence of carditis and/or valvular disease.

The diagnosis of ARF is a clinical one, and the manifestations are extremely variable. There are no specific laboratory tests to confirm the diagnosis, and the exact pathogenetic mechanism is unknown. The diagnosis is made using the original Jones criteria and the 1992 American Heart Association committee update. In addition to the requirement of supporting evidence of an antecedent group A streptococcal tonsillopharyngitis infection, there are five major criteria: carditis, polyarthritis, Sydenham chorea, erythema marginatum, and subcutaneous nodules. Several minor criteria exist. The presence of one major and two minor or two major criteria are needed for the diagnosis.

Rheumatic heart disease is the only long-term sequela of ARF. With the improved ability to prevent recurrent attacks, the prognosis of these patients has improved greatly. An individual's prognosis is related directly to the severity of cardiac involvement during the acute phase. On 10-year follow-up after ARF, only 6% of patients with no history of carditis had heart murmurs. Heart disease occurred, however, in 30%, 40%, and 68% of the patients who had apical systolic murmurs,

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basal diastolic murmurs, and pericarditis and/or congestive heart failure, respectively, during the initial attack. With the use of echocardiography and based on screening 5,800 randomly selected schoolchildren in Colombia and Mozambique, studies have found that the prevalence of rheumatic heart disease in developing countries is about 10-fold greater than that recognized by conventional screening.

In almost all adults, mitral stenosis is caused by a previous rheumatic carditis. Approximately 60% of the patients with rheumatic mitral valve disease report no history of rheumatic fever or chorea. In about 40% of all patients with rheumatic heart disease, an isolated mitral stenosis occurs. Mitral valve insufficiency and aortic valve stenosis and insufficiency can also occur in these patients.

Bennett JE, Dolin R, Blaser MJ, eds. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 8th ed. Philadelphia, PA: Saunders/Elsevier; 2015:2300.e3-2309.e3.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 10th ed. Philadelphia, PA: Saunders/Elsevier; 2015:1834-1842.

Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Thorac Cardiovasc Surg*. 2014;148(1):e1-e132.

Walsh RA, Fang JC, Fuster V, eds. *Hurst's The Heart: Manual of Cardiology* . 13th ed. New York: McGraw-Hill; 2013:380.

A.13. What are the physiologic consequences of mitral stenosis?

The normal mitral valve orifice area is 4 to 6 cm^2. With mitral stenosis, the valve area is reduced. The pathophysiology of mitral stenosis results from the obstruction of blood flow from the left atrium into the left ventricle. When the valve area reaches 2 cm^2, cardiovascular hemodynamics become impaired. The American Heart Association and American College of Cardiology classify the severity of valvular heart disease (VHD) as stage A, patients with risk factors for developing VHD; stage B, patients with progressive asymptomatic mild to moderately severe VHD; stage C, asymptomatic patients who meet the criteria for severe VHD: Those with compensated left or right ventricles are C1, whereas those with a decompensated ventricle are C2; stage D, patients with severe VHD and symptoms. With mitral stenosis, a valve area ≤1.5 cm^2 is considered moderate mitral stenosis. As the valves cross-sectional area decreases further to 1 cm^2, it is considered severe, and mean left atrial pressure increases to at least 25 mm Hg to maintain an adequate cardiac output. Left ventricular diastolic pressure is usually normal. Pulmonary venous and capillary pressures increase, leading to exertional dyspnea. If pulmonary capillary pressure exceeds blood oncotic pressure, pulmonary edema can develop. Pulmonary hypertension can result from elevated left atrial pressure and pulmonary arteriolar constriction. If severe pulmonary hypertension develops, right-sided

heart failure can occur. Factors that may increase pulmonary pressure include tachycardia, increased cardiac output, and atrial fibrillation.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 10th ed. Philadelphia, PA: Saunders/Elsevier; 2015:1446-1523.

Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Thorac Cardiovasc Surg*. 2014;148(1):e1-e132.

Walsh RA, Fang JC, Fuster V, eds. *Hurst's The Heart: Manual of Cardiology* . 13th ed. New York: McGraw-Hill; 2013:380-381.

A.14. What are the auscultatory findings associated with mitral stenosis?

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The first heart sound is increased, and a presystolic murmur can be heard. There may be an opening snap that is usually the loudest at the apex. A diastolic rumbling murmur may be best heard at the apex with the patient in the left lateral decubitus position. As pulmonary arterial pressure increases, P2 becomes accentuated and can be heard at the mitral and aortic areas. Signs of severe pulmonary hypertension include a single, accentuated S2, a systolic tricuspid regurgitation murmur, a Graham Steell murmur indicating pulmonic regurgitation, and a right ventricle-generated S4.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 10th ed. Philadelphia, PA: Saunders/Elsevier; 2015:1446-1523.

Walsh RA, Fang JC, Fuster V, eds. *Hurst's The Heart: Manual of Cardiology* . 13th ed. New York: McGraw-Hill; 2013:380-381.

A.15. What may be seen on the electrocardiogram (ECG) in patients with mitral stenosis?

There may be broadened diphasic P waves in lead V_1 with a larger negative terminal component that is indicative of left atrial enlargement. There may be signs of right ventricular hypertrophy if pulmonary hypertension is marked. Atrial fibrillation may be present.

Walsh RA, Fang JC, Fuster V, eds. *Hurst's The Heart: Manual of Cardiology* . 13th ed. New York: McGraw-Hill; 2013:383.

A.16. What are the echocardiographic findings associated with mitral stenosis?

Two-dimensional (2D) echocardiography and Doppler ultrasonography are the mainstays of diagnosis and characterization of mitral stenosis. On 2D echo, the hallmark of mitral stenosis is thickening and restriction of motion of both mitral valve leaflets with the main process being fibrosis and fusion of the leaflets tips and proximal chordae. Early on, due to inflammation and leaflet tip thickening that restricts tip but not leaflet motion, a characteristic “doming” of the valve occurs during diastole and the anterior leaflet has a “hockey-stick” configuration (Fig. 29.1). As the stenosis progresses, the body of the leaflet may become involved, and calcification can occur within the leaflets and on the subvalvular apparatus including the chordae and papillary muscle tips. Left atrial enlargement can be seen. Pulmonary valve motion abnormalities and right ventricular enlargement may signify pulmonary hypertension. In addition to reduced excursion and thickening of the leaflets, M-mode echocardiography shows a decrease in the closure rate of the anterior mitral leaflet during early diastole; this results in a reduced E-F slope. M-mode and 2D echocardiography do not reliably predict the severity of mitral stenosis. In addition to determining the anatomic extent and severity of the lesion, Doppler echocardiography can assess the physiologic significance of the lesion. Doppler studies can provide an estimate of valve area that is within ±0.4 cm^2 of those obtained by cardiac catheterization. During pregnancy, however, mitral valve area calculations by Doppler may be inaccurate. Transesophageal echocardiography is helpful in assessing atrial thrombi. Three-dimensional echocardiography is increasingly playing a role in assessing mitral valve morphology and severity.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 10th ed. Philadelphia, PA: Saunders/Elsevier; 2015:1446-1523.

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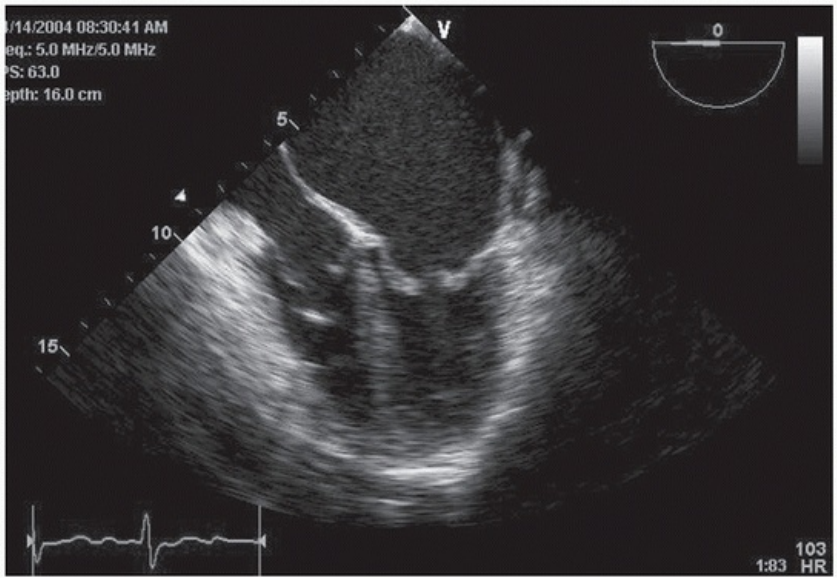


FIGURE 29.1 Two-dimensional echocardiography of the mitral valve showing severe mitral stenosis with the typical "hockeystick" appearance.

A.17. What is the effect of the physiologic changes of pregnancy on patients with mitral stenosis?

The increased physiologic cardiovascular load of pregnancy can cause patients to deteriorate and advance from one NYHA classification to another. The increased cardiac output, tachycardia, and fluid retention increase the pressure gradient across the stenotic valve. Hameed et al. found that more than half of NYHA class I and II patients with mitral stenosis had worsening clinical symptomatology during pregnancy. The incidence of maternal and fetal complications was related to the severity of the mitral stenosis. Similarly, Silversides et al. found the incidence of maternal cardiac complications with mild mitral stenosis to be lower (26%) than those occurring with moderate (38%) and severe (67%) disease. Maternal and perinatal outcomes depend mainly on maternal functional status during pregnancy. Maternal mortality and morbidity is understandably increased in parturients with NYHA III and IV classified mitral stenosis.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:981-982.

Hameed A, Karaalp IS, Tummala PP, et al. The effect of valvular heart disease on maternal and fetal outcome of pregnancy. *J Am Coll Cardiol*. 2001;37(3):893-899.

Silversides CK, Colman JM, Sermer M, et al. Cardiac risk in pregnant women with rheumatic mitral stenosis. *Am J Cardiol*. 2003;91(11):1382-1385.

A.18. If mitral stenosis is first recognized during pregnancy and symptoms develop, how would you treat the patient?

Heart rate reduction and a decreased left atrial pressure are the standard therapeutic goals for women with moderate to severe mitral stenosis. Therefore, *β*-adrenergic receptor blockade is the cornerstone of medical therapy in the symptomatic patient. It is useful in preventing tachycardia and prolonging diastolic filling time, which can result in a marked improvement of symptoms. Atrial fibrillation or flutter should be treated aggressively; a rapid ventricular response compromises diastolic flow time and can lead to pulmonary edema. Verapamil intravenously and/or cardioversion should be used to immediately treat a rapid ventricular response from new onset atrial fibrillation. For chronic atrial fibrillation, digoxin, a *β*-adrenergic receptor blocker, or a calcium channel blocker can be given. Atrial fibrillation not only increases the risk of pulmonary edema but also increases the likelihood of a thromboembolic event. If symptoms of pulmonary congestion develop, salt restriction and cautious use of diuretics can decrease left atrial pressure by decreasing blood volume. Avoidance of

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hypovolemia and decreased uteroplacental perfusion are, however, essential. Patients with persistent atrial fibrillation should be anticoagulated. Hameed et al. suggest that patients with severe mitral stenosis should receive antithrombotic therapy even if they are in sinus rhythm because of the potential for thrombotic events.

If symptoms are uncontrolled by medical therapy, the mitral valve should be repaired or replaced. Percutaneous balloon valvuloplasty can be done using echocardiography or with appropriate radiation shielding of the fetus if radiographic imaging is required; it has a low morbidity rate for the mother and the fetus and has a favorable long-term results when performed in NYHA functional class III and IV patients. If a contraindication to balloon valvuloplasty exists, a surgical commissurotomy or valve replacement should be done and is usually well tolerated by the mother, as well as a comparable nonpregnant woman, but fetal loss exceeds 10%.

Esteves CA, Munoz JS, Braga S, et al. Immediate and long-term follow-up of percutaneous balloon mitral valvuloplasty in pregnant patients with mitral stenosis. *Am J Cardiol*. 2006;98(6):812-816.

Hameed A, Akhter M, Bitar F, et al. Left atrial thrombosis in pregnant women with mitral stenosis and sinus rhythm. *Am J Obstet Gynecol*. 2005;193(2):501-504.

Mann DL, Zipes DP, Libby P, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* . 10th ed. Philadelphia, PA: Saunders/Elsevier; 2015:1755-1770.

Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Thorac Cardiovasc Surg*. 2014;148(1):e1-e132.

Sutton SW, Duncan MA, Chase VA, et al. Cardiopulmonary bypass and mitral valve replacement during pregnancy. *Perfusion*. 2005;20(6):359-368.

Walsh RA, Fang JC, Fuster V, eds. *Hurst's The Heart: Manual of Cardiology* . 13th ed. New York: McGraw-Hill; 2013:638.

A.19. What are the determinants of fetal oxygenation?

Fetal oxygenation is dependent on uteroplacental blood flow, maternal to fetal oxygen partial pressure gradient, maternal to fetal hemoglobin oxygen affinity, placental diffusion capacity, placental vascular geometry, and placental oxygen consumption.

Carter AM. Evolution of factors affecting placental oxygen transfer. *Placenta*. 2009;30(suppl A):S19-S25.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:62-63.

A.20. What are the determinants of uterine blood flow?

Uterine blood flow is derived from the Ohm's law, which states that pressure equals flow multiplied by resistance. Therefore, uterine blood flow is shown as follows:

$$\text{Uterine blood flow} = \frac{\text{uterine artery pressure} - \text{uterine venous pressure}}{\text{uterine artery resistance}}$$

Normally, 10% of maternal cardiac output goes to the uterus. Of this, the placenta receives nearly 90%, and the myometrium receives the rest at term. Uterine blood flow is directly related to maternal blood pressure; the uterine vessels do not autoregulate.

Datta S, Kodali BS, Segal S. *Obstetric Anesthesia Handbook*. 5th ed. New York: Springer; 2010:65.

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Gabbe SG, Niebyl JR, Simpson JL, et al, eds. *Obstetrics: Normal and Problem Pregnancies*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:28-29.

B. Preoperative Evaluation and Preparation

B.1. How is fetal well-being assessed during labor?

Fetal well-being is dependent on an intact uteroplacental unit. Simultaneous monitoring of FHR and uterine contractions aids in the detection of fetal distress.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:473-474, 497-498.

B.2. How are FHR and maternal contractions monitored?

FHR can be monitored noninvasively using the Doppler technique or invasively using a fetal scalp electrode. Uterine contractions may be monitored noninvasively by a tocodynamometer, which measures the tightening of maternal abdominal muscles, or invasively by a transcervical pressure catheter hooked to a strain gauge.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:473-474, 497-498.

B.3. What is the normal FHR with beat-to-beat variability?

Interpretation of FHR patterns can be confusing because of the lack of uniformity on definitions and nomenclature. During a 10-minute tracing segment, the baseline FHR is the approximate mean rate rounded to 5 beats per minute increments. In the third trimester, the normal mean baseline FHR is 120 to 160 beats per minute with beat-to-beat variability. Internationally, some recommend that 110 beats per minute be the lower limit of normal. A baseline FHR <110 beats per minute is termed *bradycardia* and >160 beats per minute is called *tachycardia*. Normal beat-to-beat variability is 6 to 25 beats per minute.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:475-482.

B.4. What are periodic decelerations?

Periodic FHR patterns refer to changes in baseline FHR in relation to uterine contractions. An acceleration is an increase and a deceleration is a decrease in FHR from its baseline. In the United States, periodic decelerations in FHR fall into the following three categories—early, late, or variable—depending on their shape and timing with respect to maternal contractions (Fig. 29.2).

- Early decelerations are uniform FHR decreases that coincide with the onset, peak, and end of uterine contraction. This is a probably vagal response caused by fetal head compression and is not associated with fetal hypoxia, academia, or low Apgar scores.
- Late decelerations are a gradual decrease in FHR that begins after the onset of a contraction and lasts beyond the end of the contraction. They can indicate uteroplacental insufficiency and require prompt evaluation and treatment.
- Variable decelerations occur variably and usually abruptly in relationship to contractions. The decrease must last between >15 seconds to 2 minutes and must have an amplitude of ≥15 beats per minute. They are FHR reflexes that reflect fetal blood pressure changes due to umbilical cord compression or changes in fetal oxygenation. The difficulty for obstetricians is in determining when variable decelerations are pathologic. According to the ACOG, recurrent variable decelerations with minimal to moderate variability are indeterminate, but those without variability are abnormal.

A prolonged deceleration is an isolated deceleration from baseline that lasts 2 or more minutes but less than 10 minutes.

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These are difficult to interpret, and management is based on bedside clinical judgment.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:482-487.

B.5. How accurate is FHR monitoring in predicting fetal well-being?

Uncertainty about diagnosing fetal distress from FHR patterns has given rise to the descriptions of these patterns as reassuring or nonreassuring. After more than 50 years of FHR pattern interpretation, there is no consensus about interpretation and management of FHR patterns. The National Institute of Child Health and Human Development Workshop's threetiered FHR pattern classification system has been recommended by ACOG. Based on this system, category I is considered normal and includes a baseline FHR rate of 110 to 160 beats per minute, moderate beat-to-beat variability, and no late or variable decelerations; early decelerations and accelerations may or may not be present. Category III is considered abnormal and includes FHR patterns that have absent baseline FHR variability and either recurrent late

decelerations, recurrent variable decelerations, or bradycardia; sinusoidal patterns are also abnormal. Category II is indeterminate and includes all FHR tracings that are not categorized in category I or III. FHR patterns that do not fall into the aforementioned classifications of normal or abnormal represent an appreciable fraction of nonreassuring FHR tracings. Cahill et al. retrospectively found that none of the three categories had a significant association with neonatal blood academia (pH ≤7.10). *Reduced beat-to-beat variability is generally believed to be the single most reliable sign of fetal compromise.* These fetal assessments are subjective clinical judgments and are inevitably and knowingly open to imperfection. Management options depend upon whether or not the cause of the fetal insult can be identified and corrected.

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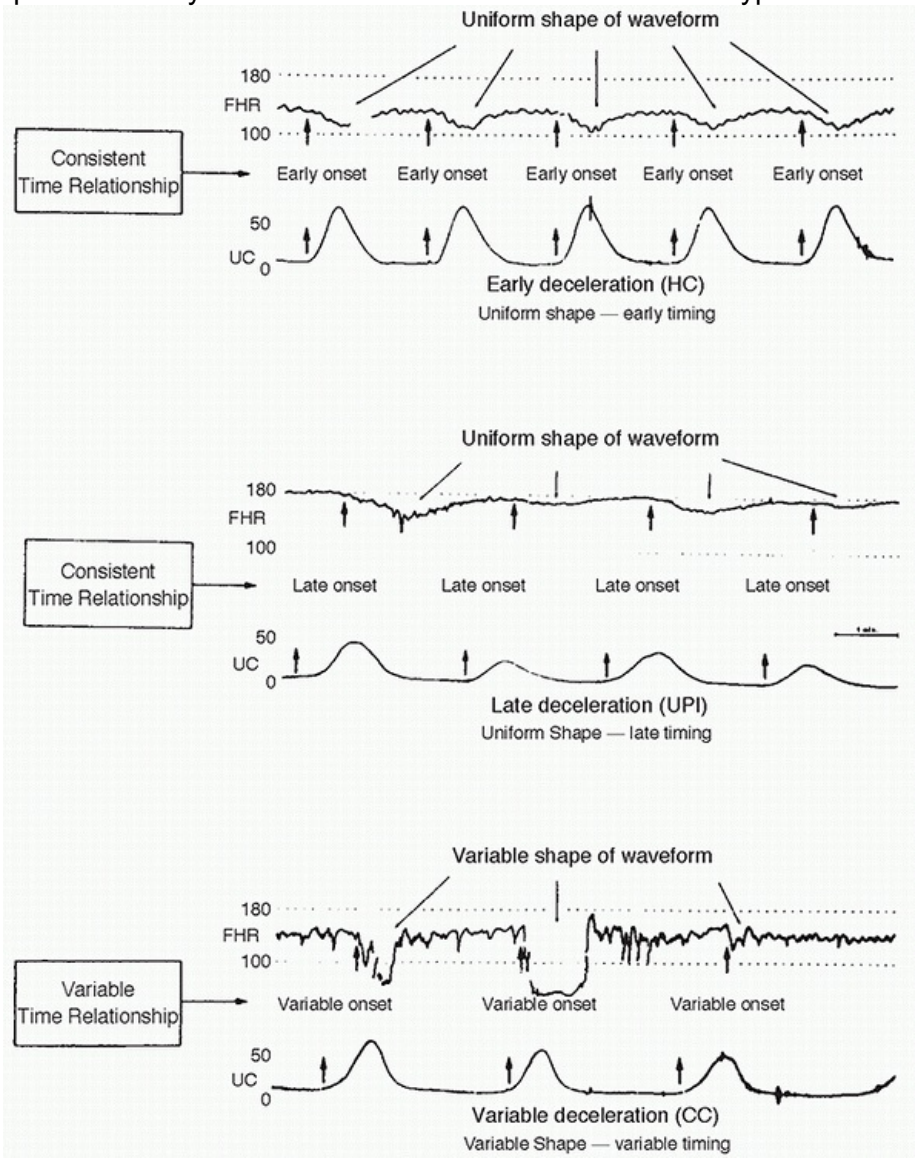


FIGURE 29.2 Fetal heart rate (FHR) decelerations in relation to the time of onset of uterine contractions (UCs). CC, cord compression; HC, head compression; UPI, uteroplacental insufficiency. (From Hon EH. *An Atlas of Fetal Heart Rate Patterns*. New Haven, CT: Harty Press; 1968, with permission.)

Cahill AG, Roehl KA, Odibo AO, et al. Association and prediction of neonatal acidemia. *Am J Obstet Gynecol*. 2012;207(3):206.e1-206.e8.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:491-493.

Macones GA, Hankins GD, Spong CY, et al. The 2008 National Institute of Child Health and Human Development workshop report on electronic fetal monitoring: update on definitions, interpretations, and research guidelines. *Obstet Gynecol*. 2008;112(3):661-666.

B.6. In the fetus with a nonreassuring FHR pattern, what other modalities can be used to assess fetal well-being?

Intrapartum fetal stimulation and fetal scalp capillary blood pH are additional methods to assess fetal well-being. In the fetus with a nonreassuring FHR tracing, any spontaneous or induced (scalp or vibroacoustic stimulation) FHR accelerations may indicate the absence of acidosis but are less than perfect. Fetal capillary scalp pH is now uncommonly

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used. According to the ACOG, fetal outcome cannot be predicted by either normal or abnormal scalp pH results. Currently, fetal electrocardiography is still being investigated while fetal pulse oximetry and intrapartum Doppler velocimetry have been abandoned. In a parturient with a breech fetus, any technique that requires access to the fetal head would not be applicable.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:489-490.

Skupski DW, Rosenberg CR, Eglington GS. Intrapartum fetal stimulation tests: a meta-analysis. *Obstet Gynecol*. 2002;99(1):129-134.

B.7. What is the significance of meconium-stained amniotic fluid?

Although meconium staining occurs in 12% to 22% of all deliveries, most of the infants are not depressed; there is a high false-positive rate and low sensitivity for acidemia. The physiology of meconium passage and its adverse sequelae are incompletely understood. Three theories have been suggested to explain the passage of meconium by the fetus, and the wide differences in the proposed theories may help explain the tenuous connection between meconium detection and infant mortality. The pathologic explanation proposes that in response to hypoxia, the fetus passes meconium and that meconium, therefore, signals fetal compromise. Alternatively, in utero passage of meconium may indicate normal gastrointestinal tract maturation under neural control. A third alternative suggests that passage of meconium follows vagal stimulation from common but transient umbilical cord entrapment and resultant peristalsis.

Ramin et al. suggest meconium becomes an environmental hazard when fetal acidemia occurs rather than meconium release being solely a marker of preexisting fetal compromise. Importantly, because acidemia occurs acutely, meconium aspiration is unpredictable and likely unpreventable. Greenwood et al. looked at women with clear amniotic fluid and emphasized that clear fluid is an unreliable sign of fetal well-being.

Evidence is accumulating that many infants with meconium aspiration syndrome have suffered hypoxia before birth. Blackwell et al. found that 60% of the infants with meconium aspiration syndrome had umbilical artery blood pH greater than or equal to 7.20; this suggests that this syndrome was unrelated to the neonates' condition at delivery. Meconium aspiration syndrome is more likely when meconium is thick, the pregnancy is postterm, or the fetus is growth restricted.

Blackwell SC, Moldenhauer J, Hassan SS, et al. Meconium aspiration syndrome in term neonates with normal acid-base status at delivery: is it different? *Am J Obstet Gynecol*. 2001;184(7):1422-1425.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:493-494, 638.

Greenwood C, Lalchandani S, MacQuillan K, et al. Meconium passed in labor: how reassuring is clear amniotic fluid? *Obstet Gynecol*. 2003;102(1):89-93.

Ramin KD, Leveno KJ, Kelly MA, et al. Amniotic fluid meconium: a fetal environmental hazard. *Obstet Gynecol*. 1996;87(2):181-184.

B.8. What is meconium aspiration syndrome?

Of the 8% to 20% of births with meconium-stained amniotic fluid, 2% to 9% of the infants develop meconium aspiration pneumonia. Of these infants, 30% require mechanical ventilation. Mortality rates depend on the severity of meconium aspiration syndrome. The pathophysiology is complex and includes hypoxemia due to airway obstruction, surfactant inactivation or dysfunction, chemical pneumonitis with a release of inflammatory and vasoconstrictive mediators, and persistent pulmonary hypertension of the newborn with right-toleft extrapulmonary shunting.

Meconium aspiration syndrome is characterized by respiratory distress with a marked mismatch of ventilation to perfusion. Ventilatory support is given when needed. Pneumothorax and/or pneumomediastinum are complications. With severe disease, pulmonary hypertension leading to persistent fetal circulation can occur. The use of surfactant and inhaled

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nitric oxide has led to a decrease in mortality and the need for extracorporeal membrane oxygenation.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:638.

Swarnam K, Soraisham AS, Sivanandan S. Advances in the management of meconium aspiration syndrome. *Int J Pediatr*. 2012;2012:359571.

B.9. What are the usual noninvasive tests used to evaluate the pregnant cardiac patient?

Physical examination, exercise tolerance test, ECG, pulse oximeter oxygen saturation, Holter monitoring, and echocardiography with Doppler flow studies may all be useful in evaluating these patients. Cardiac magnetic resonance imaging is generally safe in pregnant women, but contrast dye should not be used. Tests using radiation should be avoided unless absolutely necessary. If a radiologic test is needed, delaying it until as late as possible in the pregnancy and protective fetal radiation shielding would be best. The risk of fetal anomalies is low with less than 5 rads (0.05 Gray) of radiation exposure. Radiation exposure with a chest radiograph is approximately 10 millirads, and the fetal exposure is only about 0.07 millirads (0.0007 mGray).

Brent RL. Saving lives and changing family histories: appropriate counseling of pregnant women and men and women of reproductive age, concerning the risk of diagnostic radiation exposures during and before pregnancy. *Am J Obstet Gynecol*. 2009;200(1):4-24.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:930-934.

Walsh RA, Fang JC, Fuster V, eds. *Hurst's The Heart: Manual of Cardiology* . 13th ed. New York: McGraw-Hill; 2013:632.

B.10. What preoperative medications would you give this patient?

Recommendations for antibiotic prophylaxis against endocarditis are dependent on the cardiac lesion and the procedure being performed. Prophylaxis has been overused. As recommended by the American Heart Association and endorsed by the ACOG, prophylaxis for bacterial endocarditis should be administered intrapartum to women at risk only in the presence of suspected bacteremia or active pelvic infection. In patients with acquired valvular dysfunction, endocarditis prophylaxis is not recommended for cesarean section or uncomplicated vaginal delivery. The AHA does recommend predental procedure prophylaxis for patients with prosthetic valves, prior endocarditis, unrepaired or incompletely repaired cyanotic heart disease or during the first 6 months after complete repair, and valvulopathy after heart transplant. Only a few antibiotic regimens are recommended by the ACOG for prophylaxis if needed based on the above AHA guidelines. Ampicillin 2 g intravenously (IV), cefazolin 1 g IV, or ceftriaxone 1 g IV should be given 30 to 60 minutes before the procedure. If the patient has an allergy to these antibiotics, clindamycin 600 mg IV should be given.

However, prophylactic antibiotics are given to patients having cesarean sections to prevent postcesarean section endometritis, febrile morbidity, and wound infections. In the past, the antibiotic was given after cord clamping. Currently, ACOG recommends that a prophylactic antibiotic, a first-generation cephalosporin, such as cefazolin, be given within 1 hour of surgical incision. Studies exist that show that this timing decreases postcesarean section maternal infections without adverse neonatal effects.

Pregnant patients are considered to be at an increased risk for aspiration of gastric contents. Gastric fluid volume and pH are not different in the pregnant patient versus their nonpregnant counterparts. Pregnancy itself does not decrease gastric emptying, but during labor, gastric motility does decrease. The increased risk for aspiration is thought to be due to the parturient's decrease in lower esophageal sphincter tone and an increased risk of having difficulty with intubation. Based on the chemical and physical nature of the aspirate and the volume, the risk of aspiration pneumonitis exists. With a nonparticulate aspirate, historically, patients

were considered to be at risk for aspiration pneumonitis if greater than 0.4 mL per kg of fluid with a pH of less than 2.5 was aspirated. The volume guideline has been called into question. The goal of prophylactic therapy, however, remains the

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same. Ideally, the pH level should be greater than 2.5, and potential volume of the aspirate should be minimized. Although the exact time at which the risk increases is unclear, it seems prudent to consider the pregnant patient to be at increased risk for aspiration of gastric contents after 16 to 20 weeks' gestation. In this patient for emergency cesarean, an oral nonparticulate antacid, such as 15 to 30 mL of 0.3 M sodium citrate, given immediately before induction reduces the risk of developing aspiration pneumonitis. H_2-receptor antagonists (ranitidine and famotidine) and metoclopramide may also decrease this risk but require more time, at least 30 to 40 minutes, to be effective. These drugs may be given after the anesthetic induction if time does not allow for preinduction dosing. Avoiding general anesthesia is the most effective way to prevent the risk of aspiration.

American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 120: use of prophylactic antibiotics in labor and delivery. *Obstet Gynecol*. 2011;117(6):1472-1483.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:33, 554, 660, 976-977.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:991.

Tita AT, Rouse DJ, Blackwell S, et al. Emerging concepts in antibiotic prophylaxis for cesarean section: a systematic review. *Obstet Gynecol*. 2009;113(3):675-682.

Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation*. 2007;116:887-896.

C. Intraoperative Management

C.1. What monitors would you use in this functional New York Heart Association (NYHA) class II patient during her cesarean section?

Pregnant cardiac patients should be monitored with an ECG, blood pressure monitoring, pulse oximetry, temperature monitor, and urinary catheter. In addition, end-tidal carbon dioxide and neuromuscular blockade monitoring is recommended if general anesthesia is used. In addition, electroencephalogram-processing monitors may be used, but it is unclear if they can reduce the incidence of intraoperative awareness during general anesthesia for cesarean section.

The use of FHR monitoring before and after induction of anesthesia for cesarean delivery is controversial. ACOG has recommended that FHR monitoring before a scheduled cesarean delivery be individualized, but the National Collaboration Centre for Women's and Children's Health in the United Kingdom has stated that during induction of neuraxial anesthesia until the beginning of abdominal skin preparation, FHR should be monitored. In the emergency cesarean section, continuous FHR monitoring may be useful because changes of FHR for better or worse may change the clinical interventions implemented.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:552-553.

C.2. When would you use invasive monitoring in a pregnant patient with cardiac disease?

NYHA class I and II patients do not routinely require invasive hemodynamic monitoring. However, the parturient in class III or IV is often monitored with a pulmonary artery catheter; echocardiographic monitoring may also be used instead of or in addition to invasive monitoring. An arterial line may be placed if serial blood gas determinations and/or continuous blood pressure monitoring seems warranted. The hemodynamic monitoring should be continued for at least 24 hours postdelivery since the sudden increase in preload immediately after delivery can precipitate pulmonary edema.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:982.

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C.3. What are the hemodynamic goals of intraoperative management of the pregnant patient with mitral stenosis?

- Avoid tachycardia.
- Maintain sinus rhythm.
- Avoid marked decrease in systemic vascular resistance.
- Avoid marked increase in central blood volume.
- Avoid increase in pulmonary vascular resistance.

Increased heart rate should be avoided because decrease in the amount of diastolic time for blood to flow across the stenotic mitral valve can lead to pulmonary edema and a decreased cardiac output. Atrial fibrillation with a rapid ventricular response similarly can result in cardiac decompensation, and the loss of atrial contraction is detrimental. Marked decrease in systemic vascular resistance should be avoided because compensatory increase in heart rate can result. Elevation of pulmonary vascular resistance, which can occur with hypercarbia, hypoxia, and acidosis, is poorly tolerated by these patients.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:970, 985.

C.4. What anesthetic technique would you use for this emergency cesarean section?

The choices of anesthetic techniques for cesarean section are regional, spinal or epidural, or general anesthesia. In this case, a general anesthetic would be the anesthetic of choice. General anesthesia has a rapid onset, which is necessary because of the abnormal FHR tracing and the inability to free the compressed prolapsed umbilical cord. In addition, if the patient has not been adequately hydrated with an IV crystalloid solution before a rapid regional anesthetic induction, the resulting decrease in systemic vascular resistance, hypotension, and reflex tachycardia might exacerbate fetal distress and lead to maternal cardiac decompensation in the patient with mitral stenosis. In the non-emergent setting, patients with mitral stenosis do well with epidural anesthesia for their vaginal delivery or cesarean section. Combined spinal-epidural analgesia has also been used successfully in these patients during vaginal delivery.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:970, 985.

C.5. What technique could you use for general anesthesia in this patient?

- IV crystalloid solution through a large-bore cannula (if not already present) should be used.
- Place the patient on the table in the supine position with left lateral tilt to avoid aortocaval compression.
- Preoxygenate the mother and place monitors on her quickly. Preoxygenation may be accomplished by allowing her to breathe 100% oxygen by face mask for 3 to 5 minutes or instructing her to take four maximally deep inspirations, that is, vital capacity breaths, if time is limited.
- After a team “time-out” and abdominal preparation and draping, perform a rapid sequence induction using thiopental sodium, 4 mg per kg, or etomidate, 0.2 to 0.3 mg per kg, and succinylcholine, 1 mg per kg. Thiopental sodium is not readily available in the United States. Propofol, 2.4 mg per kg, is often used for induction of general anesthesia for cesarean delivery but should be avoided in this patient due to its hypotensive effects. Ketamine should be avoided because it could increase her heart rate. Pregnant women do not experience severe fasciculations; therefore, a defasciculating dose of nondepolarizing muscle relaxant is not recommended. Depending on the severity, mitral stenosis patients may benefit from a β-adrenergic receptor antagonist, such as esmolol, or a modest dose of opioid before or during induction of general anesthesia. Based on the severity of the maternal cardiac condition, the induction medications should be selected to facilitate a favorable maternal outcome. Remember, however, to inform the neonatologist in the delivery room about the medications that the mother has received. If hypotension occurs,

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phenylephrine, not ephedrine, is the vasopressor of choice because it does not cause tachycardia.

- Endotracheal intubation: Mucosal swelling and capillary engorgement can make intubation more difficult. A smaller endotracheal tube, such as a 7-mm internal diameter tube, should be used. The value of using cricoid pressure has been questioned. Classically, cricoid pressure is maintained until the endotracheal tube cuff is inflated and the position is checked. In human cadavers, cricoid pressure effectively prevented regurgitation with gastric pressures as high as 50 to 94 cm H_2O. Smith et al. found that cricoid pressure in awake volunteers led to airway displacement and did not reliably produce midline esophageal compression; they concluded that its protective effect against passive reflux was limited and that it might make intubation more difficult. However, Rice et al. report that the cricoid pressure compresses the hypopharynx leading to effective compression of the conduit between the stomach and the pharynx.
- Maintenance of anesthesia before the baby is delivered may involve the following: N_2O with at least 50% oxygen, volatile anesthetic agent (e.g., 1% sevoflurane), and muscle relaxant as needed (vecuronium, cisatracurium, or rocuronium). Isoflurane and desflurane probably should be avoided in this patient because they may cause tachycardia. Additionally, if a patient has mitral stenosis with pulmonary hypertension, N_2O should be avoided because it increases pulmonary vascular resistance. Once again, the anesthetic technique has to be tailored to the severity of the patient's underlying condition. Eucapnia should be maintained.
- Maintenance of anesthesia after the baby is delivered no longer requires fetal consideration. A narcotic technique can be implemented using, for instance, fentanyl, midazolam, muscle relaxant, and oxygen with or without N_2O and/or 0.75 to one minimum alveolar concentration (MAC) of a volatile halogenated anesthetic agent. The MAC of volatile halogenated agents is decreased by up to 40% in pregnant patients. MAC is a spinal nociceptive reflex involving both sensory and motor components; the decrease in MAC has been interpreted to mean that pregnant patients have a decreased inhalational anesthetic requirement. Ueyama et al. have questioned this interpretation. In a small study of 30 patients, they found no difference in bispectral index (BIS) values between cesarean section patients and nonpregnant gynecologic patients undergoing sevoflurane general anesthesia and concluded that pregnancy does not enhance the hypnotic effect of sevoflurane on the brain. However, according to Zand et al., the BIS is not reliable for monitoring depth of anesthesia during cesarean section. Regardless of the anesthetic agents chosen, the aim is to achieve a satisfactory balance between hemodynamic stability, maternal amnesia, adequate postpartum uterine tone, and as little neonatal depression as possible.
- After the delivery of newborn, an intravenous oxytocin infusion should be given; any bolus administration of oxytocin, methylergonovine, or 15-methyl prostaglandin $F_{2\alpha}$ can increase pulmonary vascular resistance.
- Tracheal extubation is done after her protective laryngeal reflexes have returned and the patient has regained consciousness.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:31, 570-575, 970.

de Souza DG, Doar LH, Mehta SH, et al. Aspiration prophylaxis and rapid sequence induction for elective cesarean delivery: time to reassess old dogma? *Anesth Analg*. 2010;110(5):1503-1505.

Norris MC, Dewan DM. Preoxygenation for cesarean section: a comparison of two techniques. *Anesthesiology*. 1985;62:827-829.

Rice MJ, Mancuso AA, Gibbs C, et al. Cricoid pressure results in compression of the postcricoid hypopharynx: the esophageal position is irrelevant. *Anesth Analg*. 2009;109(5):1546-1552.

Schulte-Sasse U, Hess W, Tarnow J. Pulmonary vascular response to nitrous oxide in patients with normal and high pulmonary vascular resistance. *Anesthesiology*. 1982;57(1):9-13.

Smith KJ, Dobranowski J, Yip G, et al. Cricoid pressure displaces the esophagus: an observational study using magnetic resonance imaging. *Anesthesiology*. 2003;99(1):60-64.

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Ueyama H, Hagihira S, Takashina M, et al. Pregnancy does not enhance volatile anesthetic sensitivity on the brain: an electroencephalographic analysis study. *Anesthesiology*. 2010;113:577-584.

Zand F, Hadavi SM, Chohedri A, et al. Survey on the adequacy of depth of anesthesia with bispectral index and isolated forearm technique in elective Caesarean section under general anaesthesia with sevoflurane. *Br J Anaesth*. 2014;112(5):871-878.

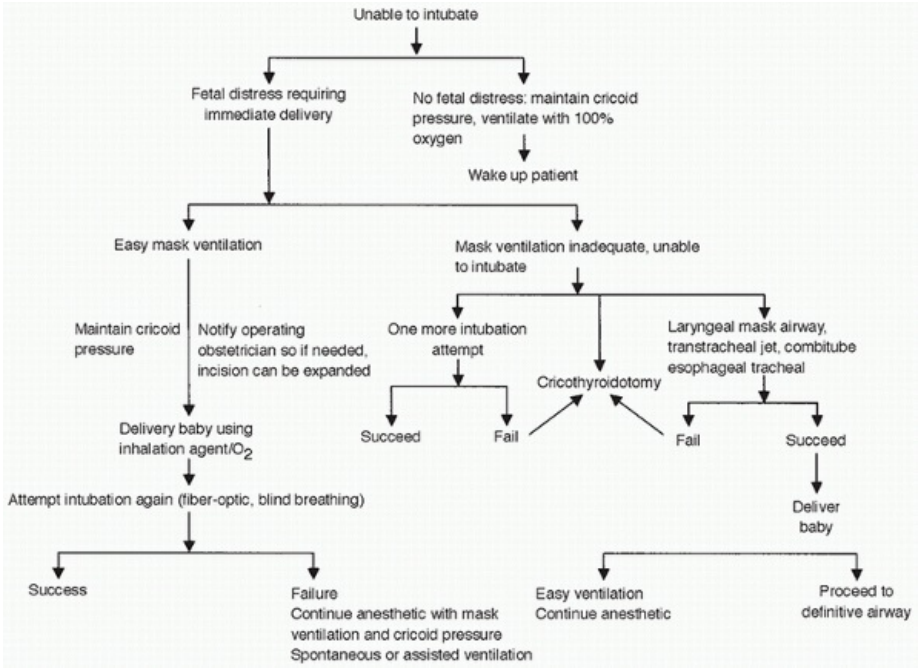


FIGURE 29.3 Algorithm for management of difficult intubation. If the surgeon infiltrates region with local anesthetic, it will decrease your general anesthetic requirement.

C.6. If you had unexpectedly been unable to intubate this patient, how would you have managed the airway?

Figure 29.3 shows one way to deal with the failed intubation in the obstetric patient with an unrecognized difficult airway. However, other anesthetic techniques may be used. For instance, some would let the patient breathe spontaneously, and others would administer muscle relaxants while continuing mask ventilation. Additionally, some prefer video versus direct laryngoscopy for additional intubation attempts. Remember that like face mask ventilation, the laryngeal mask airway does not prevent aspiration. The mother's life should not be endangered to deliver a distressed fetus. Calling for help promptly when difficulties arise is wise.

American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for the management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of Difficult Airway. *Anesthesiology*. 2003;98(5):1269-1277.

American Society of Anesthesiologists Task Force on Obstetric Anesthesia. Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia. *Anesthesiology*. 2007;106(4):843-863.

Frerk C, Mitchell VS, McNarry AF, et al. Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults. *Br J Anaesth*. 2015;115:827-848. http://m.bja.oxfordjournals.org/content/early/2015/11/05/bja.aev371.full.pdf. Accessed December 15, 2015.

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C.7. Would this patient benefit from the use of β-blockers?

Since this patient is asymptomatic, β-blockade is unnecessary. Should compromising tachycardia occur, β-blockade with drugs such as propranolol, atenolol, or esmolol may be useful, as may digoxin, a calcium channel blocker, and/or cardioversion depending on her dysrhythmia. Al Kasab et al. have shown that pregnant patients with symptomatic mitral stenosis who receive β-blockade with propranolol or atenolol to attenuate tachycardia have a significant decrease in the incidence of pulmonary edema with no adverse neonatal side effects.

al Kasab SM, Sabag T, al Zaibag M, et al. Beta-adrenergic receptor blockage in the management of pregnant women with mitral stenosis. *Am J Obstet Gynecol*. 1990;163:37-40.

TABLE 29.2 Apgar Scoring System

		SCORE		
MNEMONIC	**SIGN**	**0**	**1**	**2**
A	Appearance (color)	Blue, pale	Body pink, extremities blue	Pink
P	Pulse	Absent	<100/min	>100/min
G	Grimace (reflex irritability; response to catheter in the nose)	Absent	Grimace	Cough, sneeze
A	Activity (muscle tone)	Limp	Some extremity flexion	Active motion
R	Respiratory effect	Absent	Slow, irregular	Good cry

C.8. What is the effect of the inhalation agents on uterine contractility?

If less than one MAC of a potent volatile inhalation agent such as isoflurane or sevoflurane is used, there is no increase in blood loss or decrease in uterine contractility because at these low concentrations, the uterus still responds to oxytocin. At higher concentrations, the uterine contractility is decreased and blood loss is increased.

Tjeuw MT, Yao FS, van Poznak A. Depressant effects of anesthetics on isolated human gravid and non-gravid uterine muscle. *Chinese Med J (Engl)*. 1986;99(3):235-242.

Warren TM, Datta S, Ostheimer GW, et al. Comparison of the maternal and neonatal effects of halothane, enflurane, and isoflurane for cesarean delivery. *Anesth Analg*. 1983;62:516-520.

C.9. What is the Apgar scoring system?

The Apgar scoring system is used in the delivery to assess the neonate's condition at 1 minute and 5 minutes. Each of five categories is given a rating of 0 to 2, and the final score at each time is the sum of the individual category scores. Ten points is the best possible neonatal Apgar score (Table 29.2).

Apgar V. A proposal for a new method of evaluation of the newborn infant. *Curr Res Anesth Analg* . 1953;32:260-

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267.

C.10. What is the significance of Apgar scores?

Overall, Apgar scores qualitatively measure basic neurologic reflexes and correlate with generalized neonatal depression. In depressed neonates, Apgar scores may be continued every 5 minutes until a 20-minute score is assessed. The 1-minute Apgar score identifies if immediate resuscitation is needed, and the 5-minute score is useful to evaluate the effectiveness of any resuscitative measures especially if the score changes during this time interval. In term neonates, Casey et al. found that the risk of neonatal death was approximately 1 in 5,000 for those with 5-minute Apgar scores of 7 to 10, whereas the mortality rate was 1 in 4 with Apgar scores of 3 or less; in preterm neonates, low Apgar scores were comparably predictive. Adverse neurologic outcomes, however, correlate poorly with a 5-minute Apgar score of 3. Apgar scores only loosely correlate with acidosis and asphyxia. Apgar scores aid in predicting mortality but poorly predict morbidity; the longer the Apgar score is low, the higher the neonatal mortality. Apgar scores may be influenced by many factors including, but not limited to, prematurity, fetal anomalies, infection, and maternal medications.

Casey BM, McIntire DD, Leveno KJ. The continuing value of the Apgar score for the assessment of newborn infants. *N Engl J Med*. 2001;344(7):467-471.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:627-628.

Silverman F, Suidan J, Wasserman J, et al. The Apgar score: is it enough? *Obstet Gynecol*. 1985;66(3):331-336.

C.11. At birth, what should be done to minimize an infant's risk of meconium aspiration syndrome?

In the past, obstetricians suctioned the mouth and nose of the newborn before the infant's first breath and the delivery of its shoulders. Currently, the American Heart Association and American Academy of Pediatrics as well as the ACOG recommend against this practice of routine oropharyngeal and nasopharyngeal suctioning in the presence of meconium-stained fluid based on the work by Vain et al. Similarly, experts also recommend that vigorous newborns with meconium exposure not be intubated and suctioned. Depressed newborns, however, should be intubated and be suctioned directly via the endotracheal tube to remove any aspirated meconium from below the glottis. Exogenous surfactant and/or inhaled nitric oxide administration to infants with meconium aspiration syndrome on ventilatory support has decreased the need for extracorporeal membrane oxygenation support.

American Heart Association, American Academy of Pediatrics. 2005 American Heart Association (AHA) guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) of pediatric and neonatal patients: neonatal resuscitation guidelines. *Pediatrics*. 2006;117(5):e1029-e1038.

Committee on Obstetric Practice, American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 379: management of delivery of a newborn with meconium-stained amniotic fluid. *Obstet Gynecol*. 2007;110(3):739.

Polin RA, Carlo WA. Surfactant replacement therapy for preterm and term neonates with respiratory distress. *Pediatrics*. 2014;133(1):156-163.

Vain NE, Szyld EG, Prudent LM, et al. Oropharyngeal and nasopharyngeal suctioning of meconiumstained neonates before delivery of their shoulders: multicentre, randomized controlled trial. *Lancet*. 2004;364(9434):597-602.

C.12. The Apgar score of the newborn was 3 at 1 minute. How would you treat the newborn?

In the first 30 seconds after delivery, initial care includes providing warmth, clearing his or her airway, and drying and

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stimulating the newborn. If the infant's heart rate is <100 beats per minute or the infant is gasping or apneic, positive pressure ventilation and preductal pulse oximetry, that is, right upper extremity, should be instituted after the first minute of life. Over the last few decades, the standard practice of starting with 100% oxygen whenever supplemental oxygen is needed has been challenged because of increasing evidence that hyperoxia may cause tissue and organ injury. It is currently suggested that infants >30 weeks' gestation be initially resuscitated with room air via bag-mask positive pressure ventilation, and for those ≤30 weeks, a 30% oxygen concentration can be used. If, however, the infant's heart rate is <60 beats per minute after 90 seconds of resuscitation, the oxygen concentration should be increased to 100% until the heart rate recovers to a normal range, that is, >100 beats per minute. In the immediate neonatal period, pulse oximetry should be used if resuscitation is anticipated, more than a few breaths of positive pressure ventilation are needed, cyanosis persists, or supplementary oxygen is utilized. For term infants born at sea level, target preductal SpO_2 levels based on the time after delivery are the following:

- 1 minute, 60% to 65%
- 2 minutes, 65% to 70%
- 3 minutes, 70% to 75%
- 4 minutes, 75% to 80%
- 5 minutes, 80% to 85%
- 10 minutes, 85% to 95%

Although target data on SpO_2 levels for preterm neonates and term infants born at different altitudes are lacking, the above levels are thought to be reasonably usable in these patient populations.

Intubation is needed if tracheal suctioning for meconium is required in a depressed, nonvigorous neonate, bag-mask ventilation is ineffective or prolonged, or chest compressions are being done. Chest compressions should be done if the infant's heart rate stays below 60 beats per minute despite adequate ventilation for 30 seconds. Rarely are drugs needed

during neonatal resuscitation, but if the heart rate remains <60 beats per minute despite adequate ventilation and chest compressions, intravenous epinephrine, 0.01 to 0.03 mg per kg, should be given. Umbilical vein catheterization is the quickest way to gain intravenous access and should be done. Event-appropriate fluids and drugs should be administered.

Dawson JA, Vento M, Finer NN, et al. Managing oxygen therapy during delivery room stabilization of preterm infants. *J Pediatr*. 2012;160(1):158-161.

Kattwinkel J, Perlman JM, Aziz K, et al. Neonatal resuscitation: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Pediatrics*. 2010;126(5): e1400-e1413.

Kattwinkel J, Perlman JM, Aziz K, et al. Part 15: neonatal resuscitation: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2010;122(18 suppl 3):S909-S919.

Perlman JM, Wyllie J, Kattwinkel J, et al. Neonatal resuscitation: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Pediatrics*. 2010;126(5):e1319-e1344.

Rook D, Schierbeek H, Vento M, et al. Resuscitation of preterm infants with different inspired oxygen fractions. *J Pediatr*. 2014;164(6):1322.e3-1326.e3.

C.13. Blood gases are sent immediately after delivery. What are the normal values for umbilical vein and artery blood gases?

In normal term infants, the blood gases are as follows:

Umbilical artery

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- pH, 7.27 ± 0.069
- PCO_2, 50.3 ± 11.1 mm Hg
- PO_2, 22.0 ± 3.6 mm Hg
- Bicarbonate, 22.3 ± 2.5 mEq per L

Umbilical vein

- pH, 7.35 ± 0.05
- PCO_2, 38.2 ± 5.6 mm Hg
- PO_2, 29.2 ± 5.9 mm Hg
- Bicarbonate, 20.4 ± 2.1 mEq per L

Fetal conditions are reflected in the umbilical artery blood gas values, and umbilical vein blood gas determinations represent uteroplacental and maternal conditions. Ideally, both samples are collected. The ACOG recommends that cord blood gas measurements be obtained in the following circumstances: cesarean section for fetal compromise, a low 5-minute Apgar score, severe fetal growth restriction, abnormalities in FHR tracings, maternal thyroid disease, an intrapartum maternal fever, and/or multiple gestation. If any derangements exist, it is important to determine the metabolic versus respiratory contributions to the abnormalities. In 2003, the American Academy of Pediatrics and the ACOG defined metabolic acidosis as umbilical arterial pH <7.0 and a base deficit of at least 12 mmol per L. Umbilical cord blood gas and pH measurements alone, however, are poorly predictive of immediate or longterm adverse neurologic outcome, but they do provide objective evidence of fetal metabolic state at birth.

A 2014 ACOG task force on neonatal encephalopathy and neurologic outcome outlined criteria to help determine the likelihood that an acute peripartum or intrapartum event contributes to a neonatal hypoxic-ischemic encephalopathy (HIE). The neonatal signs that they found to be consistent with an acute event are an Apgar score of <5 at 5 and 10 minutes, a fetal umbilical arterial pH <7.0 and/or a base deficit of at least 12 mmol per L, acute brain injury on brain magnetic resonance imaging (MRI) or spectroscopy (MRS) consistent with HIE, and the presence of multisystem organ failure consistent with HIE. The contributing factors that they identified as consistent with an acute peripartum or intrapartum event were a sentinel hypoxic or ischemic event occurring immediately before or during delivery, abnormal FHR monitor patterns consistent with such an acute event, brain imaging studies

consistent such an etiology, and no evidence of other proximal or distal factors that could be contributing. They also concluded that of the several types of cerebral palsy that occur, acute peripartum ischemia only results in the spastic quadriplegic type.

American College of Obstetricians and Gynecologists, American Academy of Pediatrics. *Neonatal Encephalopathy and Cerebral Palsy: Defining the Pathogenesis and Pathophysiology*. Washington, DC: American College of Obstetricians and Gynecologists; 2003.

American College of Obstetricians and Gynecologists Committee on Obstetric Practice. ACOG Committee Opinion No. 348, November 2006: umbilical cord blood gas and acid-base analysis. *Obstet Gynecol*. 2006;108(5):1319-1322.

American College of Obstetricians and Gynecologists' Task Force on Neonatal Encephalopathy. Executive summary: neonatal encephalopathy and neurologic outcome, second edition. *Obstet Gynecol*. 2014;123(4):896-901.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:628-631, 639-640.

Phelan JP, Korst LM, Martin GI. Application of criteria developed by the Task Force on Neonatal Encephalopathy and Cerebral Palsy to acutely asphyxiated neonates. *Obstet Gynecol*. 2011;118(4):824-830.

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D. Postoperative Management

D.1. Immediately after the baby was delivered, the mother's oxygen saturation decreased. What is the differential diagnosis?

The following may be likely causes of hypoxemia in this parturient:

- Mechanical problems with the endotracheal tube
- Cardiac decompensation with pulmonary edema
- Pulmonary venous embolism: air, amniotic, and thrombotic

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:928.

Fong J, Gadalla F, Pierri MK, et al. Are Doppler-detected venous emboli during cesarean section air emboli? *Anesth Analg*. 1990;71(3):254-257.

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Chapter 30
Appendectomy for a Pregnant Patient

Farida Gadalla

A 25-year-old woman at 32 weeks' gestation presented to the emergency room with vague right-sided abdominal pain. She had lost her appetite and had two episodes of vomiting. Temperature was 37.5°C (99.5°F); pulse rate, 100 beats per minute; hematocrit, 34%; and white blood cell count, 15,000 per μL.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis for this patient?
2. How would you attempt to make the diagnosis of acute appendicitis clinically?
3. What is the incidence of appendicitis during pregnancy?
4. Is the incidence of gangrenous appendix higher in pregnant than in nonpregnant women? Why?
5. What is Alder's sign?
6. What is the incidence of perforation of the appendix, and in which trimester is it most likely to occur?
7. What is the incidence of surgery during pregnancy?
8. What are the main concerns associated with nonobstetric surgery in the pregnant patient?
9. What are the factors influencing teratogenicity in mammals? Discuss the teratogenicity of anesthetic agents in humans.
10. Discuss the U.S. Food and Drug Administration (FDA) fetal risk categories for therapeutic agents and classify the most commonly used anesthetic agents.
11. How would you prevent intrauterine fetal asphyxia?
12. Although this patient presented with an acute abdomen, what is another reason for nonobstetric surgical intervention in the pregnant patient? What are the risks to the mother and the fetus due to trauma?

B. Preoperative Evaluation and Preparation

1. What would you discuss with this patient preoperatively?
2. Is there a difference in the aim of anesthesia for delivery and for nonobstetric surgery in a pregnant patient?
3. How would you premedicate this patient?

C. Intraoperative Management

1. What factors would alter your anesthetic technique from that used for a nonpregnant patient?
2. Describe your technique and dosage if you choose epidural anesthesia.
3. If the patient is in need of supplemental medication, what would be your choice?
4. What vasopressor would you choose to improve uteroplacental perfusion?

5. When this patient arrived in the operating room, she was panic-stricken and desired a general anesthetic. Describe your technique.
6. Does any controversy exist surrounding the use of nitrous oxide?
7. What is the incidence of fetal loss and what factors influence it?
8. If the patient were having surgery on her hand, what would you do differently?
9. What would you expect to see on the fetal monitor during a sevoflurane-nitrous oxide-oxygen anesthetic?

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10. The surgeon schedules the procedure to be performed laparoscopically. Does this pose any problems?

D. Postoperative Management

1. When would you extubate this patient?
2. What monitors would you use postoperatively?
3. What other precautions would you take postoperatively?
4. What is the incidence of preterm delivery following nonobstetric surgery during pregnancy?
5. The next day, the patient went into premature labor having “failed” tocolytic therapy. She now needed a cesarean section for prematurity and breech presentation. She required another general anesthetic. In what way would your technique differ from your previous anesthetic technique?

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis for this patient?

The differential diagnosis includes the following:

Medical conditions

- Sickle cell disease
- Porphyria
- Glomerulonephritis
- Pyelonephritis
- Pneumonia
- Withdrawal from drug addiction

Obstetric conditions

- Labor
- Abruptio placentae
- Chorioamnionitis

Gynecologic conditions

- Salpingitis
- Degenerating myoma
- Ovarian cyst or tumor, either torted or ruptured
- Tubo-ovarian abscess

Surgical conditions

- Appendicitis
- Cholecystitis
- Pancreatitis
- Mesenteric adenitis
- Intestinal obstruction
- Maternal trauma

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:358-379.

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Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2353-2356.

A.2. How would you attempt to make the diagnosis of acute appendicitis clinically?

Diagnosis is based on a detailed history and the following symptoms:

- Vague abdominal pain, variable in position because of the growing uterus
- Anorexia
- Vomiting

The signs are the following:

- Abdominal tenderness
- Rebound pain
- Abdominal guarding
- Rectal tenderness
- Mildly elevated temperature, 37°C to 38°C (98.6°F to 100.4°F)
- Mildly elevated pulse rate
- An increase in white blood cell count, which is generally higher in pregnant patients compared to nonpregnant patients

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:358-379.

Kumamoto K, Imaizumi H, Hokama N, et al. Recent trends of acute appendicitis during pregnancy [published online ahead of print February 27, 2015]. *Surg Today*. doi:10.1007/s00595-015-1139-x.

A.3. What is the incidence of appendicitis during pregnancy?

Between 0.75% and 2% of pregnant women will require emergency nonobstetric surgery for acute appendicitis, cholecystitis, maternal trauma, and cancer. Appendicitis is the most common surgical emergency during pregnancy. The incidence varies from 1:350 to 1:10,000. Appendicitis is the reason for approximately 25% of operative indications for nonobstetric surgery during pregnancy. In epidemiologic studies, the reduced incidence of appendicitis in pregnant women compared to matched controls suggests a protective effect of pregnancy, especially in the third trimester.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:358-379.

Kumamoto K, Imaizumi H, Hokama N, et al. Recent trends of acute appendicitis during pregnancy [published online ahead of print February 27, 2015]. *Surg Today*. doi:10.1007/s00595-015-1139-x.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2353-2356.

A.4. Is the incidence of gangrenous appendix higher in pregnant than in nonpregnant women? Why?

It has been suggested that the incidence of gangrenous appendix has been reported to be higher during pregnancy because the enlarging uterus pushes the appendix away from the abdominal wall (Fig. 30.1), thereby causing the

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diseased appendix to produce little pain. This will delay the diagnosis and allow time for the appendix to become gangrenous. Recent studies using magnetic resonance imaging (MRI) have confirmed that the appendix is displaced upward to a mean distance of 45 mm above the iliac crest at term. This will frequently result in flank pain instead of the typical right lower quadrant pain as the presenting symptom in some women. Another factor contributing to the delay in diagnosis of a nonobstetric abdominal crisis is that useful diagnostic procedures such as radiography and laparoscopy are postponed because of concern for the fetus. Recent epidemiologic data, however, show no higher incidence of perforated appendix in pregnant women compared to matched controls.

Andersson RE, Lambe M. Incidence of appendicitis during pregnancy. *Int J Epidemiol*. 2001;30(6):1281-1285.

Kumamoto K, Imaizumi H, Hokama N, et al. Recent trends of acute appendicitis during pregnancy [published online ahead of print February 27, 2015]. *Surg Today*. doi:10.1007/s00595-015-1139-x.

Pates JA, Avendiano TC, Zaretsky MV, et al. The appendix in pregnancy: confirming historical observations with a contemporary modality. *J Reprod Med*. 2008;53:711-713.

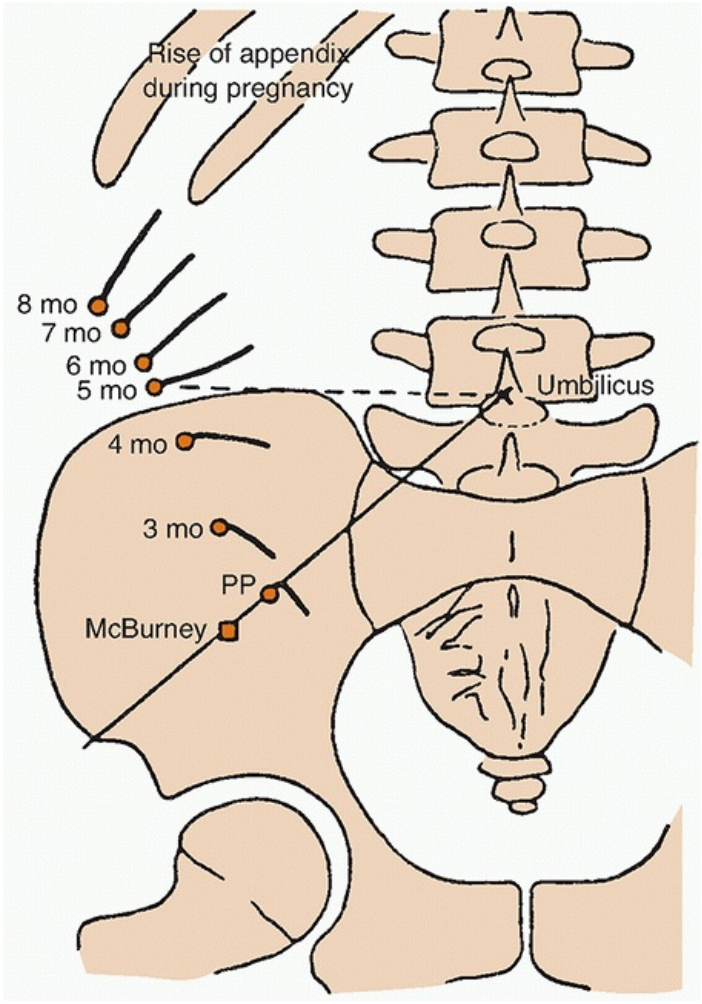


FIGURE 30.1 Changes in position and direction of the appendix during pregnancy. McBurney, McBurney's point; PP, prepregnancy. (Adapted from Baer JL, Reis RA, Arens RA. Appendicitis in pregnancy with changes in position and axis of normal appendix in pregnancy. *JAMA*. 1932;98:1359.)

A.5. What is Alder's sign?

Alder's sign is a clinical sign used to differentiate between uterine and appendiceal pain.

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The pain is localized with the patient supine. The patient then lies on her left side. If the area of pain shifts to the left, it is presumed to be uterine. According to one study, the Alder's sign was positive in 36% of cases.

Alders N. A sign for differentiating uterine from extrauterine complications of pregnancy and puerperium. *Br Med J*. 1951;2:1194-1195.

Augustin G. *Acute Abdomen During Pregnancy*. New York: Springer; 2014:3-34.

A.6. What is the incidence of perforation of the appendix, and in which trimester is it most likely to occur?

The incidence of perforation of the appendix is approximately 15%. Thirty percent of these occur in the first and second trimesters and 70% during the third trimester. The perforation rates for first, second, and third trimesters tend to be 8.7%, 12.1%, and 26.1%, respectively.

Augustin G. *Acute Abdomen During Pregnancy*. New York: Springer; 2014:3-34.

A.7. What is the incidence of surgery during pregnancy?

The incidence of surgery is estimated at between 0.75% and 2.2%. Most common causes are acute appendicitis, acute cholecystitis, maternal trauma, and cancer.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2353-2356.

Reitman E, Flood P. Anaesthetic considerations for a non-obstetric surgery during pregnancy. *Br J Anaesth*. 2011;107(suppl 1):i72-i78.

A.8. What are the main concerns associated with nonobstetric surgery in the pregnant patient?

The main concerns are maternal and fetal safety. To ensure maternal safety, awareness of the physiologic changes of the parturient is of great importance. Special care should be taken to prevent aspiration pneumonitis especially after midgestation. Failed intubation is as much a risk during early pregnancy with nonobstetric surgery as it is during cesarean delivery. Faster uptake of anesthetics and a decrease in minimum alveolar concentration (MAC) for volatile anesthetics may render patients unconscious rapidly and at lower doses.

At as early as 8 weeks of gestation, most of the increase in cardiac output, increase in stroke volume, and decrease in vascular resistance are apparent and continue to midterm. At 32 weeks, this patient is also at risk of supine hypotensive syndrome. For fetal safety, it is essential to avoid teratogenic anesthetic agents and intrauterine fetal asphyxia. Maintenance of adequate maternal oxygenation, oxygen-carrying capacity, and uteroplacental perfusion are critical to fetal well-being.

Augustin G. *Acute Abdomen During Pregnancy*. New York: Springer; 2014:3-34.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:358-379.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2353-2356.

A.9. What are the factors influencing teratogenicity in mammals? Discuss

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the teratogenicity of anesthetic agents in humans.

The factors influencing teratogenicity are genetic factors, nature, and dose of the anesthetic agent used, access of the agent to the fetus, and fetal developmental stage.

In this case, teratogenicity is unlikely because the most susceptible time in the human is that of organogenesis between the 15th and the 30th day after conception; susceptibility declines thereafter to the 50th day. Almost all anesthetics are teratogenic in some animals. Before implantation of the ovum, teratogenicity leads to abortion. Later, malformation, functional deficiencies, and even death can occur. However, no documented reports are found of teratogenicity or increase in birth defects in humans ascribed to any anesthetic agent used during pregnancy. Evidence does not support any increase in congenital birth defects in pregnant patients receiving anesthesia irrespective of the type of anesthetics.

In 2007, the Anesthetic and Life Support Drugs Advisory Committee of the FDA concluded after reviewing the data that "there are not adequate data to extrapolate the animal findings to humans." Swedish registries have validated the findings that anesthetics do not result in increased birth defects. In a consensus statement in the *NewEngland Journal of Medicine* in 2000, no anesthetic agents were listed as definitively causative of fetal malformations. Nevertheless, most anesthesiologists adhere to the use of only time-tested anesthetics, rather than new agents in the pregnant patient, especially in the first trimester of pregnancy.

Augustin G. *Acute Abdomen During Pregnancy*. New York: Springer; 2014:3-34.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:358-379.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2353-2356.

A.10. Discuss the U.S. Food and Drug Administration (FDA) fetal risk categories for therapeutic agents and classify the most commonly used anesthetic agents.

The final rule in content and labeling for human prescription drug and biologic products for pregnancy and lactation requires the removal of the pregnancy categories A, B, C, D, and X formerly proposed in its registers in 1979 and 2008. This rule is effective June 30, 2015. The final rule requires that the labeling includes a summary of the risks of using a drug during pregnancy and lactation, a discussion of the data supporting that summary, and relevant information to help health care providers make prescribing decisions and counsel women about the use of drugs during pregnancy and lactation.

The new rule requires the following:

- The inclusion of a general statement about background risk, specifically "All pregnancies have a background risk of birth defect, loss, or other adverse outcome regardless of drug exposure. The fetal risk summary below describes (name of drug)'s potential to increase the risk of developmental abnormalities above the background risk."
- Under the subheading "Fetal Risk Summary," the labeling to contain a risk conclusion and a narrative description of the risk(s) (if the risk conclusion is based on human data)
- The fetal risk summary to characterize the likelihood that the drug increases the risk of developmental abnormalities and other risks in humans
- If data demonstrate that a drug is not systemically absorbed, the fetal risk summary contains only the following statement: (Name of drug) is not absorbed systemically from (part of body) and cannot be detected in the blood. Maternal use is not expected to result in fetal exposure to the drug.
- When both human and animal data are available, that risk conclusions based on human data be presented before risk conclusions based on animal data; that a risk conclusion based on human data be followed by a narrative description of the risks
- When human data are sufficient to reasonably determine the likelihood that the drug increases the risk of fetal developmental abnormalities or specific developmental abnormalities, the labeling to contain one of two risk conclusions: Human data do not indicate that (*name of drug*) increases the risk of (*type of developmental abnormality*

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or specific developmental abnormality) or Human data indicate that (*name of drug*) increases the risk of (*type of developmental abnormality or specific developmental abnormality*)

- When human data are available but not sufficient to reasonably determine the drug's effects on fetal developmental abnormalities, the labeling to characterize the likelihood that the drug increases the risk of developmental abnormalities as low, moderate, or high
- When the data on which the risk conclusion is based are animal data, the fetal risk summary characterizes the likelihood that the drug increases the risk of developmental abnormalities using one of the following risk conclusions: not predicted to increase the risk, low likelihood of increased risk, moderate likelihood of increased risk, high likelihood of increased risk, or insufficient animal data on which to assess the likelihood of increased risk
- When human data are available, that in addition to the risk conclusion(s), the fetal risk summary be followed by a brief narrative description of the risks of developmental abnormalities as well as on other relevant risks associated with the drug

As stated earlier, there is not enough evidence that the animal data related to anesthetics is translatable to humans.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:358-379.

Department of Health and Human Services, Food and Drug Administration. Pregnancy, lactation, and reproductive potential: labeling for human prescription drug and biological products. *Fed Reg*. 2014;79(233):72064-72103.

A.11. How would you prevent intrauterine fetal asphyxia?

It is essential to maintain maternal homeostasis to ensure fetal well-being. Fetal oxygenation is directly dependent on maternal oxygen tension, oxygen saturation, hemoglobin content, oxygen affinity, and uteroplacental perfusion. Maternal hypoxia will result in fetal hypoxia

and, if uncorrected, fetal abnormalities or death. Factors that decrease uterine blood flow must be avoided. Uterine blood flow is determined by uterine vascular resistance and uterine perfusion pressure. Uterine blood flow may be decreased by the following: maternal hypotension, stress (which releases maternal catecholamines), pain, anxiety, hypoxia, hypercarbia, hyperventilation, positive pressure ventilation, and pressor agents.

The following principles govern the administration of anesthesia to parturients:

- Delay elective surgery until after delivery.
- Try to avoid surgery during the first trimester.
- Use regional anesthesia when feasible.
- Attach greater importance to anesthetic management than to agents used.
- Change anesthetic management to conform to changes in maternal physiology.

Augustin G. *Acute Abdomen During Pregnancy*. New York: Springer; 2014:3-34.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:358-379.

Mhuireachtaigh RN, O'Gorman DA. Anesthesia in pregnant patients for nonobstetric surgery. *J Clin Anesth*. 2006;18:60-66.

A.12. Although this patient presented with an acute abdomen, what is another reason for nonobstetric surgical intervention in the pregnant patient? What are the risks to the mother and the fetus due to trauma?

Trauma occurs in 6% to 8% of all pregnancies and ranks first among nonobstetric causes of maternal death. Most

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common causes of trauma during pregnancy are motor vehicle accidents, falls and slips, and domestic violence. In a recent systematic review, the following incidence and prevalence was noted.

- Motor vehicle accidents—207 per 100,000 live births
- Falls and slips—48.9 per 100,000 live births
- Domestic violence—8,307 per 100,000 live births

Maternal mortality and fetal mortality are 1.4 per 100,000 and 3.7 per 100,000 pregnancies, respectively.

Death rates and complications are higher in mothers at term compared to prenatal women. Maternal complications are due to uterine rupture, placental abruption, and premature rupture of membranes. Fetal complications are due to these factors as well as due to premature and stillbirths.

Primary goal in treatment is to stabilize the mother because fetal well-being depends on that. Aggressive resuscitation is recommended. Uterus should be displaced to one side, and initial evaluation should be based on trauma guidelines for nonpregnant patients. Emergent delivery may be necessary. Radiographic studies, if indicated, should be done. Ultrasound, MRI, and computed tomography (CT) scans may be necessary. Radiation exposure of the baby with CT scan (3.5 rads per study) should be weighed against maternal safety.

Brown S, Mozurkewich E. Trauma during pregnancy. *Obstet Gynecol Clin North Am*. 2013;40(1):47-57.

Mendez-Figueroa H, Dahlke JD, Vrees RA, et al. Trauma in pregnancy: an updated systematic review. *Am J Obstet Gynecol*. 2013;209(1):1-10.

B. Preoperative Evaluation and Preparation

B.1. What would you discuss with this patient preoperatively?

It is important to discuss her options concerning regional versus general anesthesia, emphasizing that, statistically, the fetal outcome is similar, but regional anesthesia is the technique of choice for the mother whenever possible.

However, in this case, if the appendectomy is planned laparoscopically, general anesthesia with controlled airway is the better option. Some studies suggest that laparoscopic appendectomy is associated with a significantly higher fetal loss compared to open

appendectomy (5.6% vs. 3%) especially in second and third trimester, and this may favor open approach.

Swedish registry of 2 million births over a 20-year period compared the fetal outcomes between 2,233 laparoscopic and 2,491 open cases and found no difference between the two groups.

Both groups were associated with a higher risk of low birth weight and growth restriction in the infant.

Augustin G. *Acute Abdomen During Pregnancy*. New York: Springer; 2014:3-34.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:258-275.

Kumamoto K, Imaizumi H, Hokama N, et al. Recent trends of acute appendicitis during pregnancy [published online ahead of print February 27, 2015]. *Surg Today*. doi:10.1007/s00595-015-1139-x.

Walsh CA, Tang T, Walsh SR. Laparoscopic versus open appendectomy in pregnancy: a systemic review. *Int J Surg*. 2008;6(4):339-344.

B.2. Is there a difference in the aim of anesthesia for delivery and for nonobstetric surgery in a pregnant patient?

Yes. The aim of obstetric anesthesia is to permit pain-free labor and delivery without interfering with the progress of labor,

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whereas the aim of surgical anesthesia is to provide maternal anesthesia without stimulating uterine activity and precipitating premature labor. Second, obstetric anesthesia should provide maternal analgesia without fetal neurologic depression and delayed neonatal breathing. Surgical anesthesia, on the other hand, is designed to maintain uteroplacental perfusion but without consideration for fetal neurologic or respiratory depression.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:258-275.

B.3. How would you premedicate this patient?

Premedication may be avoided by reassurance and support. If necessary, barbiturates can be given for sedation. Glycopyrrolate, which does not cross the placental barrier, can be used as a vagolytic and antisialagogue.

A nonparticulate antacid, such as 30 mL of 0.3 M sodium citrate, is given about 30 minutes before surgery to prevent aspiration pneumonitis, and an H_2-receptor antagonist may also be given.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:374.

C. Intraoperative Management

C.1. What factors would alter your anesthetic technique from that used for a nonpregnant patient?

The anatomic and physiologic changes of pregnancy alter the anesthetic technique in the following systems:

Cardiovascular system

- Increased blood volume (more increase in plasma than in red blood cell count)
- Increased cardiac output (stroke volume and heart rate)
- Decreased peripheral resistance
- Decreased mean arterial blood pressure
- Vena caval and aortic compression in the supine position as shown in Figure 30.2. Therefore, the pregnant patient should be tilted by a wedge under her right hip.

Respiratory system

- Increased minute ventilation
- Increased oxygen consumption
- Decreased functional residual capacity as shown in Figure 30.3

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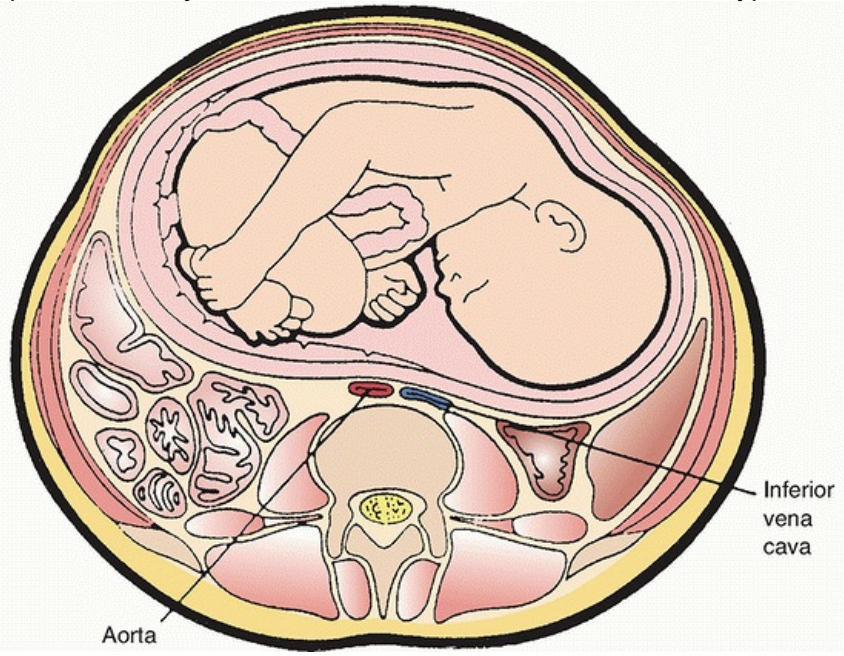


FIGURE 30.2 The pregnant uterus compressing the aorta and the inferior vena cava (aortocaval compression) in supine position. (Adapted from Ostheimer GW. *Regional Anesthesia Techniques in Obstetrics*. New York: Breon Laboratories; 1980.)

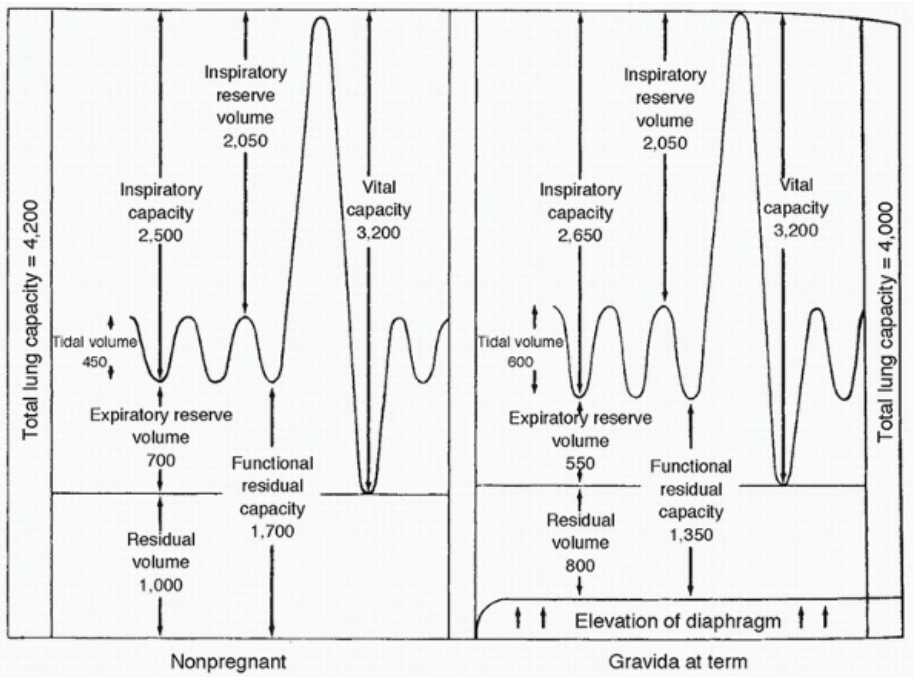


FIGURE 30.3 Pulmonary volumes and capacities during pregnancy. (From Bonica JJ. *Principles and Practice of Obstetric Analgesia and Anesthesia*. Philadelphia, PA: FA Davis Co; 1967, with permission.)

Gastrointestinal system

- Decreased gastrointestinal motility and increased gastric emptying time
- Decreased volume of gastrointestinal secretions
- Increased gastric acidity

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- Decreased lower esophageal tone because of increased progesterone level. For these reasons, a pregnant patient beyond the first trimester should always be considered as having a full stomach and must be considered at risk for regurgitation and aspiration.

Central nervous system

- Decreased MAC of inhaled anesthetics
- Increased sensitivity to local anesthesia
- Decreased volume of epidural anesthetic required because of engorgement of epidural veins and consequent decrease in size of epidural space

Skin and mucous membranes

- More friable mucous membranes and engorged mucosal capillaries (therefore, avoid insertion of nasal airways, nasotracheal, and nasogastric tubes)

Metabolic

- Increase in oxygen consumption by 20%

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:15-36, 358-379.

C.2. Describe your technique and dosage if you choose epidural anesthesia.

The patient is placed on her side or in the sitting position for epidural placement. Adequate hydration is achieved with intravenous fluids. The epidural block is placed at L2-L3 or L3-L4 using the loss-of-resistance or hanging-drop technique. After testing for inadvertent spinal or intravascular placement, the local anesthetic is given in divided doses to attain a T4 level. This takes between one-half and two-thirds of the dose used for a nonpregnant patient (between 18- and 24-mL average volume). An inadvertent spinal injection is detected by the rapid onset of a solid motor block following a 2- to 5-mL test dose, and an intravascular injection is evidenced by signs of systemic toxicity (e.g., dizziness, tinnitus, circumoral numbness, metallic taste).

The patient is once again placed in the left lateral decubitus position, oxygen is delivered by nasal cannula, and her blood pressure is monitored closely.

The choices of local anesthetics are either 2% lidocaine, 0.5% bupivacaine, or 0.5% to 0.75% ropivacaine. These agents afford good analgesia with a degree of motor blockade that provides muscular relaxation. The addition of epidural fentanyl promotes a quicker onset and more solid block.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:172, 229-260.

C.3. If the patient is in need of supplemental medication, what would be your choice?

It is best to use the narcotics that have been tried by time and appear to be safe, such as morphine and fentanyl. Small doses of ketamine (0.25 mg per kg intravenously) may also be given.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:55-74, 353.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2328-2358.

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C.4. What vasopressor would you choose to improve uteroplacental perfusion?

Ephedrine was considered the safest vasopressor because it increases mean arterial pressure and uterine artery blood flow without a concomitant decrease in uteroplacental perfusion. The overall increase in cardiac output from the *β*-adrenergic stimulation of ephedrine will

maintain uterine artery perfusion and compensate for its mild adrenergic vasoconstriction. Currently, the ban on pure *α*-agonists has been lifted because a number of current studies involving the use of both ephedrine and phenylephrine to treat maternal hypotension during spinal anesthesia for cesarean section show that phenylephrine does not adversely affect neonatal outcome and decreases the incidence of fetal acidosis.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:55-74, 303-325.

Lee A, Ngan Kee WD, Gin T. A quantitative, systematic review of randomized controlled trials of ephedrine versus phenylephrine for the management of hypotension during spinal anesthesia for cesarean delivery. *Anesth Analg*. 2002;94(4):920-926.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2353-2356.

Ngan Kee WD, Khaw KS, Tan PE, et al. Placental transfer and fetal metabolic effects of phenylephrine and ephedrine during spinal anesthesia for cesarean delivery. *Anesthesiology*. 2009;111(3):506-512.

C.5. When this patient arrived in the operating room, she was panic-stricken and desired a general anesthetic. Describe your technique.

- Check the adequacy of the intravenous cannula.
- Oxygenate for at least 3 minutes to ensure denitrogenation in the lungs and to avoid maternal and fetal hypoxemia during induction and intubation.
- Carry out induction using a rapid sequence induction intubation technique (propofol, succinylcholine, and intubation using a cuffed endotracheal tube with a 7-mm internal diameter or less).
- Carry out maintenance using agents with a long history of safety, including morphine, fentanyl, succinylcholine, nondepolarizing muscle relaxants, sevoflurane, and desflurane. The inhalation anesthetics have the added advantage of relaxing the uterus in the hope of preventing premature labor.
- Avoid hyperventilation and hypoventilation.
- Extubate the trachea when the patient is awake and has regained laryngeal reflexes.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:55-74, 275, 303-325.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2353-2356.

C.6. Does any controversy exist surrounding the use of nitrous oxide?

Yes, especially during early pregnancy. This is because nitrous oxide inhibits methionine synthase, potentially affecting DNA synthesis. Neuronal apoptosis and learning impairment observed in animals after exposure to nitrous oxide remain to be determined in humans.

Nitrous oxide also increases adrenergic tone and decreases uterine blood flow. This, however, can be prevented by the addition of a volatile agent. Therefore, nitrous oxide may be used as a component of the inhalational anesthetic. Although

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used in United Kingdom for a long time, there is a recent resurgence in interest in using nitrous oxide analgesia in the United States.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:55-74, 303-325, 347.

Collins MR, Starr SA, Bishop JT, et al. Nitrous oxide for labor analgesia: expanding analgesic options for women in the United States. *Rev Obstetr and Gynecol*. 2012;5(3-4):e126-e131.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2353-2356.

C.7. What is the incidence of fetal loss and what factors influence it?

Prenatal loss may be caused by premature labor, but it can also be caused by generalized peritonitis and sepsis. Fetal loss is related more to the severity of the disease than to the surgical procedure or the anesthetic. The perinatal mortality rate in cases of prematurity because of

generalized peritonitis is 200 to 350 per 1,000. The perinatal mortality rate for nonperforated appendicitis is approximately 50 per 1,000 women.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:55-74, 303-325.

C.8. If the patient were having surgery on her hand, what would you do differently?

Initially, offer the patient the choice of a brachial plexus block or an intravenous regional technique. It is possible to monitor the fetal heart during surgery and to monitor for uterine contractions using a tocodynamometer. Continuous fetal heart monitoring using transabdominal Doppler is possible at approximately 18 weeks' gestation.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:358-379.

C.9. What would you expect to see on the fetal monitor during a sevoflurane-nitrous oxide-oxygen anesthetic?

One would expect to see a decrease in beat-to-beat variability during anesthesia using inhalation agents.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:55-74, 303-325, 352.

C.10. The surgeon schedules the procedure to be performed laparoscopically. Does this pose any problems?

Laparoscopy has been performed during pregnancy both for diagnostic and procedural surgery. CO_2 pneumoperitoneum can cause fetal respiratory acidosis. This leads to the recommendation of maintaining low intra-abdominal pressure, limiting the duration of surgery, and using arterial blood gas analysis. However, capnography is adequate to guide ventilation during laparoscopic surgery. End-tidal CO_2 should be maintained at approximately 32 mm Hg. Fetal outcomes were similar in patients undergoing laparoscopy versus laparotomy in pregnancies between 4 and 20 weeks of surgery.

Augustin G. *Acute Abdomen During Pregnancy*. New York: Springer; 2014:3-34.

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Bhavani-Shankar K, Steinbrook RA, Brooks DC, et al. Arterial to end-tidal carbon dioxide pressure difference during laparoscopic surgery in pregnancy. *Anesthesiology*. 2000;93:370-373.

Reedy MB, Källén B, Kuehl TJ. Laparoscopy during pregnancy: a study of five fetal outcome parameters with use of the Swedish Health Registry. *Am J Obstet Gynecol*. 1997;177(3):673-679.

Walsh CA, Tang T, Walsh SR. Laparoscopic versus open appendectomy in pregnancy: a systemic review. *Int J Surg*. 2008;6(4):339-344.

D. Postoperative Management

D.1. When would you extubate this patient?

The patient can be extubated when she is fully awake, in control of her airway reflexes, and able to avoid pulmonary aspiration.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:358-379.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2328-2356.

D.2. What monitors would you use postoperatively?

- Electrocardiogram
- Pulse oximeter
- Urinary catheter (to be discontinued within 24 hours, unless specifically indicated)
- Intermittent blood pressure and temperature monitoring

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- Tocodynamometer to detect premature labor
- Fetal heart monitor to ensure fetal well-being

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:358-379.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2353-2356.

D.3. What other precautions would you take postoperatively?

- Provide adequate hydration.
- Continue left uterine displacement.
- Administer supplemental oxygen.

Many obstetricians use heavy sedation plus a course of β-agonist drugs to prevent premature labor. It is recommended that pregnant patients should be observed on the obstetric floor for a minimum of 12 hours following nonobstetric surgery. Magnesium sulfate is given intravenously if preterm labor occurs.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:358-379.

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D.4. What is the incidence of preterm delivery following nonobstetric surgery during pregnancy?

In a study of 778 women who underwent appendectomy while pregnant, 22% delivered during the following week if surgery occurred between 24 and 36 weeks' gestation. There is an increased risk of low birth weight infants (less than 2,500 g) and premature labor before 37 weeks.

Augustin G. *Acute Abdomen During Pr*egnancy. New York: Springer; 2014:3-34.

Mazza RI, Källén B. Appendectomy during pregnancy: a Swedish registry study of 778 cases. *Obstet Gynecol*. 1991;77:835-840.

D.5. The next day, the patient went into premature labor having "failed" tocolytic therapy. She now needed a cesarean section for prematurity and breech presentation. She required another general anesthetic. In what way would your technique differ from your previous anesthetic technique?

- Magnesium sulfate will prevent the muscle fasciculations that normally occur following the administration of succinylcholine.
- Use smaller doses of muscle relaxants since magnesium sulfate potentiates their effects.
- Avoid the use of narcotics until after delivery and then stop the inhalation agent and begin using a narcotic technique.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014:358-379.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2328-2358.

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Chapter 31
Hemophilia and Coagulation Disorders

Thomas J. Graetz

George J. Despotis

A 46-year-old man with hemophilia A and HIV-positive was scheduled for elective elbow synovectomy with resection of the radial head because of limited, painful range of motion.

A. Medical Disease and Differential Diagnosis

1. What are the differences between hemophilia A, B, and C?
2. Describe the typical presentation history and pathophysiology associated with von Willebrand disease (vWD).
3. What plasma protein is important in maintaining normal levels of factor VIII?
4. What is the difference between platelet adhesion, platelet activation, and platelet aggregation at sites of vascular injury?
5. Describe the physiologic events that occur following endothelial interruption in the blood vessel.
6. What prevents the extension of a clot beyond the site of injury?
7. Describe the procoagulant factors involved in the extrinsic, intrinsic, and common coagulation cascade.
8. Describe the levels of factor VIII necessary for hemostasis.
9. Describe the various laboratory tests that evaluate the coagulation cascade and the specific components measured by each.
10. Would there be any differences in preoperative factor replacement therapy between a patient with hemophilia A and hemophilia B? If so, describe the difference.

B. Preoperative Evaluation and Preparation

1. What steps would you take to normalize this patient's coagulation status before surgery?
2. What is meant by 1 unit of factor VIII clotting activity, and how much does 1 unit of factor VIII clotting activity per kilogram of body weight increase factor VIII concentrations?
3. Would you administer factor VIII using a bolus or infusion technique?
4. Can a hemophiliac patient fail to mount an appropriate coagulation response following factor VIII infusion?
5. If a patient with hemophilia does not respond to a bolus injection of factor VIII, can an infusion technique be effective?
6. How much factor VIII activity is present in fresh frozen plasma (FFP)? What are the risks associated with administration of FFP?

7. What are the indications for the administration of FFP?
8. How is cryoprecipitate prepared? What are the components in cryoprecipitate? How much factor VIII activity is present in cryoprecipitate? What are the indications for cryoprecipitate?
9. Describe the advantages and disadvantages of the products that are available for transfusion of factor VIII activity.
10. What is the role of desmopressin D-arginine vasopressin (DDAVP) for hemostatic management in this patient?
11. What is the role of antifibrinolytic therapy in the perioperative period for the patient with hemophilia? What are examples of antifibrinolytics used in treatment of hemophilia?
12. Is there a role for recombinant activated factor VII (rFVIIa) in the treatment of hemophilia?

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13. What is the mechanism of action and dosing of rFVIIa?

C. Intraoperative Management

1. Is it safe to administer an intramuscular injection to this patient before surgery?
2. Would an axillary block be appropriate for this patient?
3. If general anesthesia is used as a technique, would it be safe to intubate the patient's trachea?
4. Would you use any special precautions for this patient who is positive for HIV?
5. What special considerations should be taken in choosing anesthetic drugs for this patient?
6. During an operative procedure, if the surgeon indicates that significant blood loss is occurring, would you transfuse this patient with packed red blood cells (RBCs) or whole blood?
7. During the transfusion of the first unit of whole blood, the patient's temperature rose from 36.8°C to 37.9°C (98.24°F to 100.22°F). What immediate steps should be taken by the anesthesiologist at this time?
8. Does giving blood intraoperatively increase the potential for the development of factor VIII inhibitors?
9. Can factor VIII be safely administered to patients who have developed circulating inhibitors?
10. The surgeon has requested the use of a tourniquet to minimize surgical bleeding. What are the physiologic and hemodynamic responses to tourniquet use?
11. Is it appropriate to suction the endotracheal tube and oropharynx of this patient before extubation?

D. Postoperative Management

1. What special consideration should be given to postoperative pain management for this patient?
2. What steps should be taken to enhance the coagulation status of this patient in the postoperative period while at home?
3. Can this patient be treated with factor VIII supplements using home infusion?

A. Medical Disease and Differential Diagnosis

A.1. What are the differences between hemophilia A, B, and C?

Hemophilia, one of the oldest known genetic disorders, can be classified into types A, B, or C. Hemophilia A (congenital factor VIII deficiency) is the most common form, accounting for 85% of all patients with hemophilia. It involves reduced protein levels related either to reduced protein synthesis or accelerated clearance related to a neutralizing acquired factor VIII inhibitor (i.e., either related to exposure to animal sources of factor VIII or

spontaneous development of an autoantibody to factor VIII that occurs in 1:1,000,000 individuals). It is an X-linked recessive disorder and therefore occurs predominately in men and on occasion in homozygous women. Approximately 30% of patients have no family history of this disease; presumably, their disease is caused by a new somatic mutation that results in reduced hepatic protein synthesis. The clinical disease severity (i.e., bleeding diathesis) generally directly correlates both with the factor VIII activity level as well as the presence and efficacy of a neutralizing inhibitor. Patients with less than 1% activity generally express a severe form of the disease, which may manifest as spontaneous bleeding into joints, muscles, and vital organs and involve life-threatening bleeding events (e.g., central nervous system [CNS], retroperitoneum). Patients with between 6% and 40% activity generally have mild disease and may go undiagnosed until they face hemostatic stress. A screening test for hemophilia A is the activated partial thromboplastin time (aPTT), which will be prolonged in all patients except those with mild disease depending on the sensitivity of the coagulation methods/reagents used. Measuring factor VIII activity will generally provide a diagnosis, but reproducibly normal levels do not exclude carrier status because factor VIII concentrations may become elevated in times of stress. Genetic testing provides a definitive diagnosis in the setting of an inherited disorder of protein synthesis.

Patients with hemophilia B present with either deficient or defective factor IX; this entity represents approximately 14% of hemophilia patients. This X-linked genetic disorder has an inheritance pattern and clinical features that are similar to those of hemophilia A but can be diagnosed by measuring both the concentration and function of factor IX. Factor IX is a vitamin K-dependent factor.

The remaining 1% of hemophiliac patients have a deficiency in factor XI and is classified as hemophilia C, an autosomal

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disorder that is extremely rare except in Ashkenazi Jews. Hemophilia C can be distinguished from A and B by the absence of bleeding into joints and muscles. In addition, the degree of factor XI deficiency may not predict a patient's bleeding tendency in the postoperative period.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:408-442.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

A.2. Describe the typical presentation history and pathophysiology associated with von Willebrand disease (vWD).

vWD is the most common congenital bleeding disorder; it is characterized by either protein deficiency and/or defects in von Willebrand factor (vWF). vWF plays a role in hemostasis by catalyzing the binding of platelets to the subendothelium (i.e., via glycoprotein [GP] Ib receptors) or to other platelets (i.e., via GP IIb/IIIa receptors) and additionally acting as the predominate carrier for factor VIII. vWF is synthesized by endothelial cells, but there is substantial posttranslational modification of the protein monomers within the Golgi apparatus that leads to high molecular weight (HMW) and very high molecular weight (VHMW) forms that have the highest capacity to activate platelets. The most common form of the disease (i.e., type 1) is inherited as an autosomal dominant trait and has an incidence cited as high as 2% to 3% of northern European populations while probably is 0.1% in the general population. Patients with vWD can have a prolonged bleeding time (BT), which is rarely performed, as well as other test abnormalities (e.g., increased aPTT or prolonged platelet function analyzer [PFA]-100 values). vWD manifests clinically as bruising, epistaxis, mucocutaneous bleeding, and menorrhagia in women. Because vWD is an assortment of various forms (e.g., type 1, 2, and 3 as outlined in Table 31.1), there is frequently heterogeneity in its clinical manifestations and relative risk of bleeding. The diagnosis may be suggested by the patient's history of a bleeding diathesis and the presence of a prolonged BT, prolonged aPTT (i.e., in 50% of patients), or abnormal PFA-100 result despite a normal platelet count and no drug effect. Laboratory analysis is useful for classifying the types and subtypes of vWD to guide therapy. Acquired forms of vWD have also been described, associated with lymphoproliferative disease, tumors, cardiac valvular lesions, as well as others. Six different

vWD types and subtypes exist (type 1, type 2A, type 2B, type 2N, type 2M, and type 3). Type 1 and type 3 represent quantitative deficiency of normal vWF related to either modest (type 1) or severe (type 3) reductions in vWF levels due to reduced synthesis. Type 2 includes qualitative defects that are subdivided based on the levels and function of HMW forms of vWF and the corresponding mechanistic defects on platelet adhesion, platelet activation/aggregation, or factor VIII binding. Type 1 vWD represents most afflicted patients (e.g., 85%) and is marked by decreased levels of normal vWF. First-line treatment for type 1 disease is with desmopressin (L-deamino-8-D-arginine-vasopressin [DDAVP]). DDAVP has been shown to frequently normalize vWF and factor VIII levels due to release of vWF from the endothelium as well as other hemostatic factors (i.e., tissue plasminogen activator [tPA], prostacyclin, etc.). Type 2A vWD represents 15% to 30% of type 2 patients and is a qualitative defect in platelet-vWF platelet adhesion. Accordingly, vWF protein levels can be normal, but the absence of HMW vWF multimers results in reduced platelet activation, as reflected by reduced ristocetin induced cofactor activity. Type 2B vWD represents that subset of patients with enhanced affinity for platelet GP Ib, related to a structural abnormality in HMW forms of vWF that result in a more pronounced degree of platelet activation leading to spontaneous platelet aggregation and resultant thrombocytopenia. In these patients, thrombocytopenia may be aggravated by administration of desmopressin. Subtype 2B can be assessed by evaluating the exaggerated response to an antibiotic ristocetin, which stimulates the binding of vWF to platelet GP Ib and resultant platelet aggregation. In the absence of HMW forms of vWF, no agglutination will occur with the ristocetin cofactor activity assay. In type 2N, there is a decreased affinity of vWF for factor VIII based on the absence of the factor VIII binding receptors on vWF. These patients are often misdiagnosed as having hemophilia A. In type 2M, there is a decrease in vWF-dependent platelet adhesion due to an abnormality of HMW multimers. Type 3 vWD is inherited in a recessive fashion and represents virtually complete absence of vWF, and many of these patients die in utero on within a few days after birth. DDAVP is not beneficial in type 3 because these patients have no endogenous production of vWF. Type 2B and type 3 are extremely rare. It is important to distinguish the subtypes of vWD because the use of DDAVP in type 2B may cause worsening of the degree of thrombocytopenia. DDAVP does not increase vWF in type 3 because there are no stores of vWF in endothelial cells.

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TABLE 31.1 von Willebrand Disease: Diagnosis, Classification, and Response to Desmopressin D-Arginine Vasopressin (DDAVP)

TYPE	RCoA	vWFAg	PLATELET COUNT	RIPA	FVIII	DDAVP EFFECTIVE	MULTIMER PATTER
1	↓	↓	NL	NL or ↓	NL or ↓	Yes	Uniform decrease with all multimers present
2A (15%)	↓	NL or ↓	NL	NL or ↓	NL	+/−	Decreased large multimers
2B (5%)	↓	NL or ↓	NL or ↓	↑	NL	No	Decreased large multimers
2M (<1%)	↓	NL or ↓	NL	NL or ↓	NL	No	Uniform decrease with all multimers present
2N (3%)	NL	NL	NL	NL	↓	No	Normal
3 (1%)	↓↓	↓↓	NL	↓↓	↓↓	No	Undetectable

FVIII, factor VIII; NL, normal; RCoA, ristocetin cofactor activity; RIPA, ristocetin-induced platelet aggregation; vWFAg, von Willebrand factor activity.

From Sadler JE, Budde U, Eikenboom JC, et al. Update on the pathophysiology and classification of von Willebrand disease: a report of the subcommittee on von Willebrand factor. *J Thromb Haemost*. 2006;4(10):2103-2114.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:408-442.

Favaloro EJ, Bodó I, Israels SJ, et al. von Willebrand disease and platelet disorders. *Haemophilia*. 2014;20(suppl 4):59-64.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

A.3. What plasma protein is important in maintaining normal levels of factor VIII?

Binding of factor VIII to vWF is required for optimal factor VIII survival and for transport of factor VIII to areas of endothelial injury to enable approximation with factor IX (i.e., the factor VIII and IX complex leads to activation of factor X

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on the platelet surface). Factor VIII is one of the largest and least stable coagulation factors. It forms a noncovalent complex with vWF. By binding factor VIII, vWF reduces the inactivation of factor VIII by protein C. The half-life of factor VIII is about 2 hours in the absence of vWF. vWF only binds factor VIII prior to cleavage by thrombin to activated factor VIII (fVIIIa). Although vWF is important in maintaining adequate levels of factor VIII, less than 10% of vWF multimers bind factor VIII.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:442.

Berntorp E, Shapiro AD. Modern haemophilia care. *Lancet*. 2012;379(9824):1447-1456.

Bolton-Maggs PHB, Pasi KJ. Haemophilias A and B. *Lancet*. 2003;361(9371):1801-1809.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Lenting PJ, Casari C, Christophe OD, et al. von Willebrand factor: the old, the new and the unknown. *J Thromb Haemost*. 2012;10(12):2428-2437.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

A.4. What is the difference between platelet adhesion, platelet activation, and platelet aggregation at sites of vascular injury?

Platelet adhesion occurs via interaction of collagen-bound HMW vWF at subendothelial sites of injury with platelet GP Ib-V-IX and platelet GP VI. Not only does GP VI play a role in adhesion, but it is also the major agonist for initial platelet activation and granule release. Platelet activation via collagen is independent of thrombin activation. Tissue factor (TF) is another stimulus for activation of platelets that are exposed to vascular subendothelium. When platelets are activated to a certain threshold, the release reaction ensues which involves release of alpha and dense granule contents (i.e., thromboxane A2 and adenosine diphosphate [ADP]), which are agonists for expression of additional surface receptors for further platelet activation and ultimately aggregation. Platelet aggregation involves cross-linking of platelets to each other (clumping) using the critical GP IIb/IIIa receptors that are bound by either vWF or fibrinogen. The degree of platelet aggregation is also influenced by varying shear rates in vascular beds and more importantly the local concentration of thrombin.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:410, 432.

Furie B, Furie BC. Mechanisms of thrombus formation. *N Engl J Med*. 2008;359(9):938-949.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

A.5. Describe the physiologic events that occur following endothelial interruption in the blood vessel.

The small size of platelets relative to other blood components, such as red or white cells, results in their slower transit in the blood vessel with resultant margination. Platelet diffusivity or margination is the process in which the faster moving, larger cellular components within blood push the platelets toward the walls of the blood vessel; accordingly, in the setting of anemia, reduced margination of platelets may result in a lower concentration of platelets in close proximity to the vessel wall. As a result of margination, platelets are in contact with the surface of the blood vessel and can immediately respond

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to potential endothelial defects. Any endothelial break exposes platelets to subendothelial structures, including collagens and other proteins that activated the hemostatic system (e.g., TF), which promote adhesion between GP Ib receptors on platelets to the subendothelium as well as generation of thrombin. In addition to the generation of thrombin, platelet adhesion also initiates platelet activation, in which the shape of the platelet is altered and the contents of the cytoplasmic granule are

released. The substances inside the alpha and dense granules include factors such as ADP and serotonin, and factor Va, which further promote platelet activation and aggregation. The platelet plug formed in this process provides initial hemostasis. The degree of platelet activation, release, and ultimate aggregation is in large part predicated by the concentration of thrombin (IIa) in the local milieu. The final stage of platelet plug formation is driven by IIa mediated expression of IIb/IIIa receptors that enables fibrinogen (fibrin) and vWF to crosslink platelets (aggregation). Thrombin also converts fibrinogen to fibrin to strengthen the platelet matrix. Finally, activation of factor XIII produces cross-polymerization of the loose fibrin to produce a firm and stable platelet—coagulation factor cross-linked matrix resulting in a clot.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:410-414.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

A.6. What prevents the extension of a clot beyond the site of injury?

Localization of coagulation and control of primary/secondary hemostasis are controlled by many factors. Circulating heparin or endothelial glycosaminoglycans and low levels of thrombin can result in release of tissue factor pathway inhibitor (TFPI) which inhibits TF activation of factor X. Additionally, lower levels of factor IIa result in activation of protein C (along with its cofactor protein S) which inactivate activated factors Va and VIIIa along the endothelium via thrombomodulin, which along with other coagulation inhibiting substances are present on the intact endothelial glycocalyx. The heparin-antithrombin complex binds and inhibits activated clotting factors, including factors XIIa, XIa, IXa, Xa, and IIa. Finally, the intact endothelial surface secretes many mediators, which have a platelet-inhibiting (e.g., triphosphate dephosphorylases, prostacyclin or PGI2, nitric oxide) or clot-lysing effect (e.g., tPA). tPA initiates the physiologic process of fibrinolysis and digests factors V/VIII and fibrinogen and fibrin resulting in fibrin degradation (split) products (fibrin split products [FSPs]) and D-dimers (cross-linked fibrin), respectively, which are removed by the liver via mononuclear phagocyte system. Accumulation of these by-products (FSPs and D-dimer) in the setting of substantial liver dysfunction can lead to abnormal hemostasis secondary to platelet dysfunction.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:412-414.

Johnston-Cox HA, Ravid K. Adenosine and blood platelets. *Purinergic Signal*. 2011;7(3):357-365.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

A.7. Describe the procoagulant factors involved in the extrinsic, intrinsic, and common coagulation cascade.

After an extended period of time, when normal blood is placed in an empty test tube, a clot will form without adding any agents. The clotting factors involved in this process were originally classified as the “intrinsic” factors because everything necessary for blood to clot was “intrinsic” to the test tube. The “extrinsic” path is another potent stimulus for thrombin formation and is initiated by exposure of tissue thromboplastin (TF) to factor VIIa. The extrinsic and intrinsic pathways

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converge as the both result in activation of factor X to form the common pathway.

This classic separation of procoagulant factors into extrinsic, intrinsic, and common coagulation cascades, although a convenient framework, is not necessarily the most ideal way to describe the hemostatic system because of the crosstalk of many factors other than coagulation proteins (e.g., endothelium, platelets, and leukocytes). In fact, the current paradigm of coagulation uses a cell-based model and takes into account many in vivo pathways and, importantly, the contribution of the endothelium and the cellular components. Although the classic intrinsic and extrinsic coagulation pathways do lead to the formation and activation

of thrombin (and hence the amplification of coagulation), its failure to take into account the cellular components, which play a vital role in hemostasis, limits their usefulness in a complete understanding of the hemostatic system.

The cell-based theory consists of three stages: initiation, amplification, and propagation. Each stage represents a different aspect of hemostasis at a cellular level, with a pivotal point predicated on a spike or “burst” in the concentration of thrombin that ultimately results in the formation of a stable clot. An appreciation of thrombin's role in the coagulation cascade is critical, and the coagulation cascade is the reason that the majority of all therapeutic anticoagulation strategies are directed at the inhibition of either Xa and/or thrombin. In addition to the effects of thrombin activation secondary to platelet adhesion, the initiation phase of the cell-based model is marked by the exposure of TF to circulating factor VIIa that leads to generation of thrombin as the essential step. This thrombin generation leads to amplification via factor XI and the generation of even more thrombin, thereby activating the other two phases, serving as a potent catalyst for hemostasis. An understanding of these mechanisms helps to illustrate how the drug NovoSeven (activated factor VII) is such an effective hemostatic agent predominately related to its ability to lead to thrombin generation. This agent is ideally suited for settings that involve local sites of injury which express TF (e.g., localized, not traumatic CNS bleeds). Untoward events can occur in situations (e.g., disseminated intravascular coagulation [DIC], extracorporeal devices) that potentially involve the presence of high systemic levels of TF, which can lead to systemic activation of thrombin and resultant thrombosis. The classic coagulation cascade is shown in Figure 31.1.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:408-442.

Furie B, Furie BC. Mechanisms of thrombus formation. *N Engl J Med*. 2008;359(9):938-949.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Hoffman M, Monroe DM III. A cell-based model of hemostasis. *Thromb Haemost*. 2001;85:958-965.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

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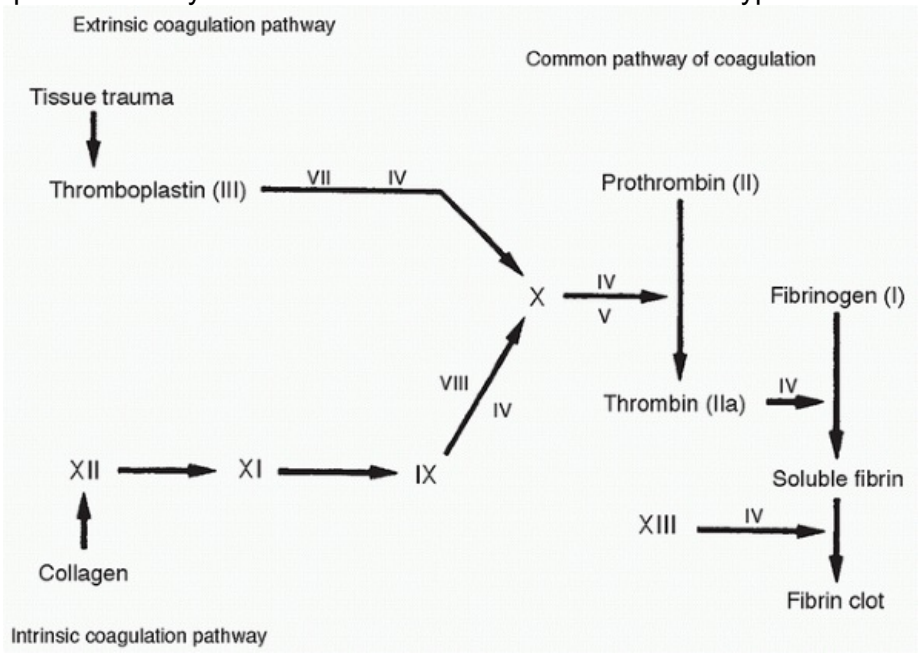


FIGURE 31.1 Schematic diagram of the procoagulant phase of coagulation depicting the cascade sequence in three steps, designated as the intrinsic, extrinsic, and common coagulation pathways. (From Stoelting RK, Dierdorf SF, McCammon RL, eds. *Anesthesia and Co-existing Disease*. 2nd ed. New York: Churchill Livingstone; 1988:577, with permission.)

TABLE 31.2 Levels of Factor VIII Necessary for Hemostasis

CLINICAL PRESENTATION	FACTOR VIII CONCENTRATION (% OF NORMAL)
Severe and/or life-threatening spontaneous bleeding	<1
Spontaneous mild hemorrhage (e.g., low-grade hematemesis or mild dermal bleeding or epistaxis)	1-3
Moderate trauma	4-8
Hemarthrosis and deep skeletal muscle hemorrhage	10-15
Major surgery or any significant or life-threatening bleeding (e.g., spontaneous or injury-related CNS bleeding)	>30, depending on location, closer to 100

CNS, central nervous system.

A.8. Describe the levels of factor VIII necessary for hemostasis.

The levels of factor VIII necessary for hemostasis are described in Table 31.2. When lifethreatening airway or neurologic bleeding has occurred, factor VIII levels of 100% or 1 U per mL should be achieved. Similarly, when major surgery is anticipated, correction to 100% factor VIII levels should be done preoperatively and maintained for some interval

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postoperatively (see section D.2).

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Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Jamco RL, McClean WE, Terrin JM, et al. A prospective study of patterns of bleeding in boys with hemophilia. *Haemophilia*. 1996;2:202-206.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

A.9. Describe the various laboratory tests that evaluate the coagulation cascade and the specific components measured by each.

Numerous laboratory tests evaluate specific components of the coagulation cascade. The standard skin BT is one way to measure for platelet function; however, BT lacks specificity because results may be prolonged as a result of factors other than platelet dysfunction, including anemia, low platelet count, or patient movement; this technique may also lack precision based on use of an inconsistent measurement technique (e.g., area of skin incision, depth of incision, blood pressure cuff pressure). Although very few studies have reported a consistent correlation between an abnormal BT and an increased risk for hemorrhage in part related to its imprecision, there are a few published. Moreover, a normal BT does not predict absence of bleeding risk. BT is not recommended as a preoperative screening test. It plays a limited role, if any, in evaluating patients for hemostatic defects. More recent tests for analyzing platelet function include the VerifyNow and PFA-100. VerifyNow (Accumetrics, San Diego, CA) is a point-of-care instrument designed specifically to measure the degree of platelet activity and/or inhibition. In whole blood, it measures the ability of a potent thrombin receptor agonist peptide to activate platelets, thus facilitating platelet aggregation with fibrinogen-coated beads. When normal platelets aggregate, more light is transmitted as the platelets coalesce at the bottom of the test chamber. Platelets, which are inhibited by antiplatelet agents, do not aggregate as effectively, and therefore, light transmission is reduced. Much of the data using VerifyNow has focused on the assessment of antiplatelet effects of ADP P2Y12 receptor antagonists such as clopidogrel and prasugrel. It also may be used to assess inhibition of platelet aggregation in the setting of GP IIb/IIIa receptor antagonists (e.g., abciximab and eptifibatide). PFA-100 (Dade Behring, Miami, FL) is a test that assesses platelet adhesion and aggregation as related to activation of one of two agonists. It has been used to identify drug-induced platelet abnormalities, Bernard-Soulier syndrome, vWD, and other acquired and congenital platelet defects. The test is conducted as a modified in vitro BT. In this test, whole blood is drawn through a chamber by vacuum past a 150-μm aperture within a collagen membrane coated

with either epinephrine or ADP. Platelet adhesion and formation of aggregates will ultimately seal the aperture, and the time required for complete aperture closure or the “closure time” is recorded by the PFA-100. This test may be useful in detecting hereditary or pharmacologicinduced platelet dysfunction or vWD before surgery. Koscielny studied over 5,500 patients using a standard bleeding history in addition to laboratory screening tests, including PFA-100. Of the patients having what was determined to be impaired clinical hemostasis, the PFA-100 was more sensitive than the other screening tests (BT, aPTT, PT, and vWF).

Routine assessment or monitoring (i.e., pharmacologic anticoagulation) of the coagulation cascade is usually performed with both prothrombin time (PT) and aPTT. The PT is measured by adding TF to a plasma specimen and measuring the time until clot formation. This test will detect abnormalities in factors I (fibrinogen), II, V, VII, or X. A normal PT can be observed in the setting of abnormally low fibrinogen level because the PT is only prolonged if the fibrinogen level is below 100 mg per dL. With respect to warfarin monitoring, in order to standardize test results performed with different types of thromboplastin activating agents, the international sensitivity index (ISI) rates the sensitivity of the reagent when compared to a standard that has an ISI value of one. The international normalized ratio (INR) is calculated by placing the patient to control result to the ISI power as follows: PT INR = (patient test result/mean of normal reference population)^{ISI}. The aPTT result is determined as the time to clot when partial thromboplastin (no TF) and a negatively charged activating substance (e.g., celite or kaolin) are added to a test tube of citrated plasma then recalcified. The time measured until clot forms and assesses deficiencies in factors I, II, V, VIII, IX, X, XI, and XII. The activated clotting time (ACT) measures the time to clot

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formation when whole blood is activated by diatomaceous earth or other activators (e.g., celite). This test is used most often to measure the response to large heparin doses (concentrations greater than 1 U per mL and up to 10 U per mL) during percutaneous cardiology interventions, renal dialysis, or cardiopulmonary bypass (CPB). Although the relationship between ACT and heparin level is fairly linear within a given patient, there are substantial between patient differences in this linear heparin dose-response relationship. Unfortunately, the ACT has several limitations: It may be insensitive to specific factor deficiencies; it lacks specificity for inhibition of coagulation protein function as it is affected by quantitative and qualitative platelet abnormalities; and similar to aPTT values, ACT values can be prolonged as related to lupus anticoagulant antibodies and ACT values can be prolonged independent of heparin levels by either hypothermia or hemodilution that are commonly observed with extracorporeal circulation during cardiac surgery. The thrombin time bypasses most of the coagulation cascade to measure the conversion of fibrinogen to fibrin, a useful test to determine both inadequate amounts of fibrinogen as well as inadequate fibrinogen molecules. The thrombin time is also much more sensitive to very low concentrations of heparin than the aPTT. The thrombin time may be used to exclude the presence of residual direct thrombin inhibitors such as bivalirudin as well as small amounts of circulating heparin. A modified (i.e., patient plasma diluted eightfold) version of the thrombin time may be helpful to assess the effects of some of the new oral anti-IIa inhibitors (e.g., dabigatran).

The thromboelastogram (TEG) or ROTEM assesses the viscoelastic properties of blood by measuring the speed of clot formation and clot firmness (i.e., maximum amplitude vs. maximal clot firmness). These tests allow evaluation of a clot from early formation of fibrin strands to fibrinolysis. The TEG tracings are made up of several parameters: reaction time (R value), coagulation time (K value), maximum amplitude (MA value), an α angle, and the amplitude 60 degrees after the MA or maximum clot firmness (MCF) (A60) or fibrinolysis indices (MA/A60 ratio). A deviation from a prototypical tracing represents one or more abnormalities in the patient's coagulation profile, and these abnormalities have been shown to be related to bleeding or thrombotic complications (e.g., wide MA). Although abnormal TEG or ROTEM tracings can provide useful information, many of the parameters are not necessarily specific for any defined hemostatic system abnormality. The MA or MCF, for example, can be affected by thrombocytopenia or qualitative platelet abnormalities, fibrinogen deficiencies, or degree of anemia. More recent modifications of the TEG and ROTEM devices that incorporate the use of various agonists (e.g., kaolin vs. TF) or inhibitors (i.e., of platelets with cytochalasin D or fibrinolysis with aprotinin) may enhance the systematic analysis of intraoperative coagulation defects and facilitate a more directed approach to therapy (see Chapter 14, section A.22

and Chapter 57, section C.25). An example of this approach involves the use of the fib-tem result to guide the administration of fibrinogen concentrates in patients with excessive bleeding after cardiac surgery as was performed by Rahe-Meyer et al. Laboratory evaluation of the coagulation cascade can be defined as shown in Table 31.3.

TABLE 31.3 Specific Factors Assessed by Different Coagulation Tests

LABORATORY TESTS	COMPONENTS MEASURED
Bleeding time	vWF, platelet count/function, vascular integrity
Prothrombin time	I, II, V, VII, and X
Activated partial thromboplastin time	I, II, V, VII, IX, X, XI, and XII
Thrombin time	I, II
Platelet Function Analyzer 100 (PFA-100)	vWF, platelet count/function, vascular integrity

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:408-442.

Despotis GJ, Levine V, Saleem R, et al. Use of point-of-care test in identification of patients who can benefit from

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desmopressin during cardiac surgery: a randomised controlled trial. *Lancet*.1999;354(9173):106-110.

Ferris VA, Saha SP, Oestreich JH, et al. 2012 Update to the Society of Thoracic surgeons guideline on use of antiplatelet drugs in patients having cardiac and noncardiac operations. *Ann Thorac Surg*. 2012;94(5):1761-1781.

Fischer GW, Shore-Lesserson L. Hematologic diseases. In: Fleisher L, ed. *Anesthesia and Uncommon Diseases*. 5th ed. Philadelphia, PA: Elsevier Science; 2005:359-376.

Gewirtz AS, Miller ML, Keys TF. The clinical usefulness of the preoperative bleeding time. *Arch Pathol Lab Med*. 1996;120(4):353-356.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Koscielny J, Kiesewetter H, Von Tempelhoff GF. More on: platelet function analyzer (PFA)-100 closure time in the evaluation of platelet disorders and platelet function. *J Thromb Haemost*. 2006;4(6):1426-1434.

Koscielny J, Ziemer S, Radtke H, et al. Preoperative identification of patients with impaired (primary) haemostasis. A practical concept [in German]. *Hamostaseologie*. 2007;27(3):177-184.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

Rahe-Meyer N, Solomon C, Hanke A, et al. Effects of fibrinogen concentrate as first-line therapy during major aortic replacement surgery: a randomized, placebo-controlled trial. *Anesthesiology*. 2013;118(1):40-50.

Whiting D, DiNardo JA. TEG and ROTEM: technology and clinical applications. *Am J Hematol*. 2014;89(2):228-232.

A.10. Would there be any differences in preoperative factor replacement therapy between a patient with hemophilia A and hemophilia B? If so, describe the difference.

Patients with hemophilia A typically need transfusion of factor VIII before major surgery to normalize factor VIII levels to approximately 100% of normal (i.e., based on use of pooled plasma specimens from a normal population) that is synonymous with the 1 U per mL convention. The half-life of administered factor VIII is approximately 12 hours but can vary based on the formulation. Further supplementation or redosing is typically repeated approximately every 12 hours or longer depending on the severity of the bleeding episode and measured factor levels. The patient with hemophilia B typically needs high initial doses of factor IX due to the extensive distribution of factor IX to the intravascular and extravascular compartments. However, the longer half-life of factor IX (18 to 30 hours) requires less frequent dosing.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:408-442.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Lee CA, Owens D, Bray G, et al. Pharmacokinetics of recombinant factor VIII (recombinate) using one-stage clotting and chromogenic factor VIII assay. *Thromb Haemost*. 1999;82(6):1644-1647.

Löfqvist T, Nilsson IM, Petersson C. Orthopaedic surgery in hemophilia. 20 years' experience in Sweden. *Clin Orthop Relat Res*. 1996;332:232-241.

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Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

B. Preoperative Evaluation and Preparation

B.1. What steps would you take to normalize this patient's coagulation status before surgery?

Orthopedic surgical procedures require maintenance of normal levels due to a raw bone surface in order to minimize bleeding into and/or around a prosthetic joint, which can lead to infection risk or destruction of the surrounding tissue or hematoma formation. In contrast, an extremity or operative site can be secured with plaster, or if good surgical apposition of tissues can be achieved, maintenance of normal factor levels at 100% activity may not be required. Factor VIII levels of 30% of normal will usually provide adequate hemostasis; nevertheless, most clinicians will target normal factor VIII levels (˜100%) in part because factor levels typically decrease due to redistribution as well as normal decay.

For major orthopedic procedures, factor VIII levels should be corrected to 100% of normal approximately 1 hour before the procedure. A repeat dose may be needed based on the duration of the procedure, amount of blood loss, dose initially used, and factor level quantification.

Rodriguez-Merchan EC. Aspects of current management: orthopaedic surgery in haemophilia. *Haemophilia* 2012;18(1):8-16.

B.2. What is meant by 1 unit of factor VIII clotting activity, and how much does 1 unit of factor VIII clotting activity per kilogram of body weight increase factor VIII concentrations?

One unit of factor VIII clotting activity is defined as the amount of factor present in 1 mL of fresh normal, pooled plasma; however, normal factor levels typically range between 0.8 and 1.2 U per mL because there is substantial variability in factor levels in normal patients. On average, an individual with a plasma volume of 3,000 mL would have 3,000 international units of each clotting factor in their circulation. If an individual has less than 1% of normal factor VIII activity, it would take 3,000 international units of factor VIII to raise the plasma levels to normal, which is around 100%, assuming the source of the factor VIII does not result in dilution of the patient plasma volume compartment beyond 3,000 mL (e.g., 3,000 U administered via a factor concentrate requiring reconstitution using only 50 to 100 mL) and the patient does not have a neutralizing antibody. In other words, 100% factor activity is equivalent to a concentration of 1 international unit per mL of the factor of interest. Dosing a single unit of factor VIII clotting activity per kilogram of body weight will increase plasma factor VIII levels approximately 2%. Therefore, to prescribe the factor VIII activity necessary to correct a 70-kg hemophilia patient with 5% factor VIII activity to 95% of normal, one can calculate using either of the following approaches:

Approach 1

Weight (kg) × (desired percent increase) × 0.5 = Dose of factor VIII (international units) 70 kg × (95% - 5%) × 0.5 = 3,150 IU of factor VIII

Approach 2

(Plasma Volume [PV]) × (desired increase in factor level [U per mL]) = Dose of factor VIII (international units)

PV calculation

PV = kg weight × (65 (female) or 75 (male) mL per kg) × (1 - Hematocrit [Hct])

For example, PV = 70 kg × 75 mL per kg × (1 - 0.4) = 3,150 mL

3,150 mL × (0.95 - 0.05 U per mL) = 2,835 U

Henrard S, Speybroeck N, Hermans C. Body weight and fat mass index as strong predictors of factor VIII in vivo recovery in adults with hemophilia A. *J Thromb Haemost*. 2011;9(9):1784-1790.

Longo DL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:400-407.

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B.3. Would you administer factor VIII using a bolus or infusion technique?

Based on the stability of factor VIII concentrates at room temperature after reconstitution, infusions can be used. By titrating the infusion, the desired factor VIII level can be maintained, eliminating both the overshoot and the subtherapeutic levels seen with the bolus technique. A continuous infusion is typically initiated to maintain factor levels after administration of an initial loading dose of factor VIII.

Batorova A, Martinowitz U. Intermittent injections vs. continuous infusion of factor VIII in haemophilia patients undergoing major surgery. *Br J Haematol*. 2000;110(3):715-720.

Longo DL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: McGraw-Hill; 2012:2042-2059.

B.4. Can a hemophiliac patient fail to mount an appropriate coagulation response following factor VIII infusion?

A substantial percentage (i.e., approximately 30%) of hemophiliacs can develop a neutralizing antibody (i.e., inhibitor) against factor VIII and will not achieve the anticipated response following factor VIII infusion. Inhibitor titers can vary between patients. The risk of developing an inhibitor depends on the genetic mutation leading to the factor defect as well as other factors such as related to the source of factor VIII (i.e., subtle structural differences in recombinant products). Inhibitors are more common in factor VIII deficiency relative to factor IX deficiency. Development of neutralizing inhibitors is important to recognize because they can lead to refractoriness of response even when patients receive factor VIII concentrates, which if undiagnosed can lead to excessive and perhaps life-threatening bleeding unresponsive to conventional therapy. It is also important to characterize the titer of the inhibitor (i.e., typically described in Bethesda units or titer) to facilitate proper management. Specifically, patients with high Bethesda titer inhibitors may require alternative acute management interventions (e.g., rFVIIa, intravenous immunoglobulin [IVIg]) or when time permits, more sustainable effects with other interventions (e.g., plasma exchange or rituximab).

Individuals with congenital factor deficiencies may develop these alloantibody inhibitors targeting specific epitopes of the hemostatic factor. The mechanisms leading to functional factor inhibition by these inhibitors include steric hindrance of appropriate functional binding sites, hydrolysis of the factor, as well as more rapid clearance by the reticuloendothelial system. The antibodies may be directed against one of many different domains, some of which are pathologic and others are not. Pathogenicity is generally determined by which of the domains is targeted by the antibody. In addition to the development of alloantibody inhibitors to exogenous factor VIII, inhibitors may develop in patients with previously normal levels of appropriately functioning factor VIII, leading to an acquired hemophilia.

Bayry JS, Lacroix-Desmazes A, Pashov D, et al. Autoantibodies to factor VIII with catalytic activity. *Autoimmun Rev*. 2003;2(1):30-35.

Bolton-Maggs PHB, Pasi KJ. Haemophilias A and B. *Lancet*. 2003;361(9371):1801-1809.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

B.5. If a patient with hemophilia does not respond to a bolus injection of factor VIII, can an infusion technique be effective?

Some patients who do not respond well to bolus injections may have low titers of inhibitors. A continuous infusion may prove effective in this situation to stop hemorrhage because appropriate levels of the missing factor can be achieved relatively easily by an infusion method. Bleeding patients with high titers and without measurable factor level during the infusion may respond to an infusion technique, most likely based on the kinetics of inhibitors, that is, complete inhibition of the factor may require 1 to 2 hours. With a continuous infusion, there will always be some factor that is circulating,

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unneutralized, and hemostatically active. Depending on the degree of the inhibitor, efforts at immune tolerance may be effective. An immune tolerance regimen consists of continuous infusions in conjunction with

immunosuppression over an extended period of time to promote development of immune tolerance to the factor and thereby eradicate the inhibitor.

Bolton-Maggs PHB, Pasi KJ. Haemophilias A and B. *Lancet*. 2003;361(9371):1801-1809.

Gordon EM, Mungo R, Goldsmith JC. Lingual hemorrhage in a patient with hemophilia A complicated by a high titer inhibitor. Management by continuous infusion of monoclonal antibody-purified factor VIII. *Am J Pediatr Hematol Oncol*. 1993;15:107-110.

Schulman S, Martinowitz U. Continuous infusion instead of bolus injections of factor concentrate? *Haemophilia*. 1996;2:189-191.

B.6. How much factor VIII activity is present in fresh frozen plasma (FFP)? What are the risks associated with administration of FFP?

FFP is prepared from a single donor and contains all plasma proteins, including factor VIII. Typical factor VIII activity is between 0.5 and 0.9 units of clotting activity per milliliter of FFP because factor VIII activity decays to some extent. Following whole blood donation and plasma separation via centrifugation, approximately 200 mL of FFP is produced from one unit of whole blood.

The risks associated with the transfusion of FFP are similar to those of any other single donor blood product. These include associated potential for allergic reactions to blood proteins and potential exposure to infectious agents such as the lipid-enveloped viruses that cause hepatitis B and C as well as HIV. The incidence of transfusion-related infections has decreased over the last several decades as several screening procedures (e.g., donor history questionnaires, serologic and nucleic acid amplification technology [NAT]/polymerase chain reaction [PCR]-based testing) have been developed and/or implemented. Currently, the risk of transmitting hepatitis B infection following transfusion of FFP slightly exceeds that of HIV and hepatitis C. The decrease in transfusion-related hepatitis C is in part related to the implementation of NAT to reduce or minimize the window period. Hepatitis B currently occurs at a frequency of about 1:300,000, and hepatitis C occurs at about 1:1,700,000. HIV infection currently occurs at about 1:1,900,000 donor exposures. In contrast to FFP, nonrecombinant factor concentrates undergo several interventions to reduce infectious risk of pooled products. Techniques commonly used for factor concentrate preparation can include donor retesting after 12 months, heat (pasteurization), nanofiltration, and solvent detergent treatments, which can minimize the risk of viral pathogen transmission. There are other risks associated with transfusion not related to transmission of infectious organisms. These include transfusion-related acute lung injury (TRALI), which occurs with an incidence of 1 in 3,000-5,000 units transfused and is more commonly seen after transfusion of FFP than other blood products as related to higher content of plasma. The incidence of TRALI after FFP transfusion has decreased with the deferral of female plasma donors. Female donors have been excluded from the donor pool because of the higher likelihood of antibodies in their plasma (anti-human leukocyte and anti-neutrophil antigens) which can activate recipient neutrophils along the pulmonary endothelium resulting in degranulation and the rapid development of a noncardiogenic pulmonary edema which results in the typical clinical picture of acute respiratory distress of TRALI. Other aspects of transfusion risk include immune modulation after transfusion, which may increase the risk of infection and other postoperative complications.

American Society of Anesthesiologists. Practice guidelines for perioperative blood transfusions and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusions and Adjuvant Therapies. *Anesthesiology*. 2006;105:198-208.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:423-425.

Chapman CE, Stainsby D, Jones H, et al; for Serious Hazards of Transfusion Steering Group. Ten years of hemovigilance reports of transfusion-related acute lung injury in the United Kingdom and the impact of preferential use of male donor plasma. *Transfusion*. 2009;49(3):440-452.

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Goodnough LT. Risk of blood transfusion. *Anesthesiol Clin North America*. 2005;23:241-252.

Kaufman RM, Djulbegovic B, Gernsheimer T, et al. Platelet transfusion: a clinical practice guideline from the AABB. *Ann Intern Med*. 2015;162(3):205-213.

Theusinger OM, Baulig W, Seifert B, et al. Relative concentrations of haemostatic factors and cytokines in solvent/detergent-treated and fresh-frozen plasma. *Br J Anaesth*. 2011;106(4):505-511.

Zou S, Stramer SL, Dodd RY. Donor testing and risk: current prevalence, incidence, and residual risk of transfusion-transmissible agents in US allogeneic donations. *Transfus Med Rev*. 2012;26(2):119-128.

B.7. What are the indications for the administration of FFP?

The National Institutes of Health multidisciplinary consensus development panel determined that FFP was the most overused blood product for transfusion. Many clinicians have used FFP as a volume expander despite previous recommendations that state the indications for its use should be limited to documented evidence of isolated factor deficiency (if factor concentrates are not available), reversal of vitamin K antagonists (prothrombin complex concentrates may be more effective), and/or treatment of antithrombin (AT) deficiency (if AT concentrate is unavailable), hereditary angioedema (if C1-esterase inhibitor is unavailable), or thrombotic thrombocytopenia purpura, and massive blood transfusion.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:422-424.

Puetz J. Fresh frozen plasma: the most commonly prescribed hemostatic agent. *J Thromb Haemost*. 2013;11(10):1794-1799.

B.8. How is cryoprecipitate prepared? What are the components in cryoprecipitate? How much factor VIII activity is present in cryoprecipitate? What are the indications for cryoprecipitate?

Cryoprecipitate is the fraction of plasma that precipitates when FFP is thawed. In addition to factor VIII, this blood component also contains significant levels of factor VIII: vWF, factor XIII, and fibrinogen. The American Association of Blood Banks (AABB) Standards state that 1 unit of cryoprecipitate must contain at least 80 international units of factor VIII as well at least 150 mg of fibrinogen.

Cryoprecipitate is indicated for patients with hemophilia A, vWD, hereditary or acquired hypofibrinogenemia (when concentrates are unavailable), hereditary factor XIII deficiency (if concentrates are unavailable), uremic platelet dysfunction along with DDAVP, as well as thrombolysis-related bleeding. Small amounts of red cell fragments may be present in cryoprecipitate; therefore, it may sensitize Rh-negative individuals to Rh antigens if any of the donors are Rh-positive.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:421-422.

Callum JL, Karkouti K, Lin Y. Cryoprecipitate: the current state of knowledge. *Transfus Med Rev*. 2009;23(3):177-188.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

B.9. Describe the advantages and disadvantages of the products that are

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available for transfusion of factor VIII activity.

The advantages and disadvantages of factor VIII products are shown in Table 31.4. When cost is not an issue, recombinant or monoclonal purified factor VIII is generally considered preferred over FFP, cryoprecipitate, or prothrombin complex concentrates based on reduced risk of infectious disease transmission.

Franchini M. Plasma-derived versus recombinant factor VIII concentrates for the treatment of haemophilia A: recombinant is better. *Blood Transfus*. 2010;8(4):292-296.

Schulman S, Varon D, Keller N, et al. Monoclonal purified F VIII for continuous infusion: stability, microbiological safety, and clinical experience. *Thromb Haemost*. 1994;72:403-407.

B.10. What is the role of desmopressin D-arginine vasopressin (DDAVP) for hemostatic management in this patient?

This synthetic analog of the antidiuretic hormone is U.S. Food and Drug Administration (FDA)-approved to be used to prepare patients with mild and moderate hemophilia for minor surgery. Intravenous DDAVP will rapidly release preformed factor VIII complex, which leads to a twofold to threefold increase in circulating factor VIII within 30 to 60 minutes of administration. In addition, factor VIII and vWF are released from the endothelial cells. In a patient with mild or moderate hemophilia A or vWD, this influx may provide adequate hemostasis

for minor elective surgical procedures. The halftime of this released factor is approximately 12 hours, and repeated administration of DDAVP will have diminishing returns as the storage reservoir is depleted in the endothelial cells. DDAVP is also approved to manage some patients with type 1 vWD. DDAVP may also be useful for patients with hereditary or acquired platelet abnormalities (e.g., uremic-induced or CPB-induced platelet dysfunction).

TABLE 31.4 The Advantages and Disadvantages of Factor VIII Products

COMPONENT	ADVANTAGE	DISADVANTAGE
Cryoprecipitate	Readily available, long shelf life in cold conditions, low to moderate risk for hepatitis and AIDS; contains vWF, FXIII	Allergic reaction, hyperfibrinogenemia if large volumes are used, multiple donor exposures
Factor VIII concentrates (various purities are available)	Easily stored and reconstituted, long life, known potency, rapid normalization of factor levels including anticoagulants (e.g., Protein C/S)	Large (e.g., 10-20,000) donor exposure with risk of infectious disease, although product safety is enhanced via use of several viral inactivation steps (e.g., donor retesting, nanofiltration, pasteurization)
Monoclonal purified factor VIII	Stability, biologic safety, reduced transfusion risks	Cost
Recombinant factor VIII	Easily stored, reconstituted, long shelf life	Cost

FXIII, factor XIII; vWF, von Willebrand factor.

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Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:433-435.

Despotis GJ, Levine V, Saleem R, et al. Use of point-of-care test in identification of patients who can benefit from desmopressin during cardiac surgery: a randomised controlled trial. *Lancet*. 1999;354(9173):106-110.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Mannucci PM. Desmopressin (DDAVP) in the treatment of bleeding disorders: the first twenty years. *Hemophilia*. 2000;6(suppl 1):60-67.

B.11. What is the role of antifibrinolytic therapy in the perioperative period for the patient with hemophilia? What are examples of antifibrinolytics used in treatment of hemophilia?

Antifibrinolytics have been used successfully in patients with hemophilia to prevent or manage bleeding, following minor bleeding (e.g., menorrhagia and epistaxis) and in preparation for minor surgical procedures (e.g., dental extractions). Their use in major surgical procedures for patients with hemophilia has not been well documented. Tranexamic acid (TXA) as well as ε-aminocaproic acid (EACA) are both lysine analogue antifibrinolytic agents that have been used for treatment of bleeding. Use of these agents to minimize bleeding and transfusion has been extensively studied; these agents have been shown to be effective to a variable degree in several surgical populations such as liver transplantation (i.e., during anhepatic stage), with trauma, and high-risk cardiac and orthopedic procedures. DDAVP does also cause the release of plasminogen activator in vivo (which can cause fibrinolysis), but it is usually unnecessary to inhibit fibrinolysis when DDAVP is used clinically.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:408-442.

Mannucci PM. Desmopressin (DDAVP) in the treatment of bleeding disorders: the first twenty years. *Haemophilia*. 2000;6(suppl 1):60-67.

B.12. Is there a role for recombinant activated factor VII (rFVIIa) in the treatment of hemophilia?

Hemophilia A represents the majority of patients afflicted with hemophilia. Approximately 30% of patients with hemophilia A have inhibitory antibodies (“inhibitors”) to factor VIII.

Fewer patients afflicted with hemophilia B develop inhibitory antibodies (1% to 3%). Risk factors for the development of “inhibitors” include race, severity of the disease (less than 1% factor VIII levels), having a hemophiliac brother with inhibitors, and certain mutations involving the factor VIII gene and exposure to factor VIII either from animal sources or recombinant techniques. In patients with inhibitors, alternative treatment is occasionally necessary to address surgical and nonsurgical hemorrhagic crises. FDA has approved the use of rFVIIa (NovoSeven, Novo Nordisk, Bagsvaerd, Denmark) for actively bleeding patients with congenital hemophilia with inhibitors, acquired hemophilia, congenital factor VII deficiency, and Glanzmann thrombasthenia (rare platelet receptor defect).

Hedner U. Treatment of patients with factor VIII and factor IX inhibitors with special focus on the use of recombinant factor VIIa. *Thromb Haemost*. 1999;82:531-539.

Ingerslev J. Efficacy and safety of recombinant factor VIIa in the prophylaxis of bleeding in various surgical procedures in hemophilic patients with factor VIII and factor IX inhibitors. *Semin Thromb Hemost*. 2000;26:425-432.

Negrier C, Hay CR. The treatment of bleeding in hemophilic patients with inhibitors with recombinant factor VIIa. *Semin Thromb Hemost*. 2000;26:407-412.

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B.13. What is the mechanism of action and dosing of rFVIIa?

Factor VIIa binds to TF exposed at the site of injury and leads to generation of enough local thrombin to activate factors V, VIII, and XI as well as platelets via an alternate mechanism other than the FVIIIa/FIXa complex. In high doses, rFVIIa binds to thrombin-activated platelets and activates factor X to factor Xa independent of factor VIII or IX. This mechanism of activating factor X and generating thrombin bypasses the need for factor VIII and factor IX. This alternative pathway for providing hemostasis makes rFVIIa a potent treatment for patients afflicted by hemophilia with inhibitors. The prohemostatic effect of rFVIIa is generally limited to when there are one or a few sites of local injury (e.g., spontaneous or traumatic CNS bleeding) because the expression of TF is limited to these localized sites. However, the risk of thrombosis is increased when there is a systemic state of TF activation that can occur with many clinical conditions that result in DIC (e.g., ischemic or gangrenous bowel, extremities, reduced tissue perfusion, hematologic malignancies involving release of TF from leukocytes, placental abruption). For on-label use, the typical doing schedule for hemostatic prophylaxis in patients undergoing elective surgery is 90 to 120 μg per kg, with repeated doses every 2 to 3 hours. This dosing regimen has also been effective most of the time in treating mild to moderate bleeding episodes in patients with hemophilia and inhibitors.

Abshire T, Kenet G. Recombinant factor VIIa review of efficacy, dosing regimens and safety in patients with congenital and acquired factor VIII or IX inhibitors. *J Thromb Haemost*. 2004;2:899-909.

Abshire T, Kenet G. Safety update on the use of recombinant VIIa and the treatment of congenital and acquired deficiency of factor VIII or IX with inhibitors. *Haemophilia*. 2008;14:898-902.

Hedner U. Mechanism of action, development and clinical experience of recombinant FVIIa. *J Biotechnol*. 2006;124:747-757.

Rajpurkar M, Chitlur M, Recht M, et al. Use of recombinant activated factor VII in patients with Glanzmann's thrombasthenia: a review of the literature. *Haemophilia*. 2014;20(4):464-471.

C. Intraoperative Management

C.1. Is it safe to administer an intramuscular injection to this patient before surgery?

Intramuscular injections can be safely administered to any patient with a factor VIII activity greater than 30%. Therefore, if appropriate factor VIII correction has occurred before surgery, an intramuscular injection would be considered safe. It is unlikely, though, that an intramuscular injection would be necessary for this patient. If a sedative hypnotic or anticholinergic drug is indicated before the induction of anesthesia, it may be more appropriate to use an intravenous route, if available. Intravenous administration also enables immediate bioavailability with attainment of higher peak levels.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

C.2. Would an axillary block be appropriate for this patient?

Regional anesthesia has long been considered contraindicated in patients with hemophilia because the concern of hematoma formation at the regional site. With proper management of the coagulation status, regional techniques have been successfully performed in patients with hemophilia. As with any patient, the benefit of regional technique must be weighed against the potential risks associated with the technique. Certainly, in a patient with a full stomach, a regional technique may be more appropriate because of the relative risk of aspiration. For a completely elective procedure in the patient with hemophilia, a more prudent course might be general anesthesia. If a regional anesthetic technique were being considered, it would be prudent to verify appropriate levels of factor activity at the time of the intervention as well as prior to removal of an epidural catheter, especially in light of the potential for the presence of neutralizing antibodies.

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Sampson JF, Hamstra R, Aldrete JA. Management of hemophiliac patients undergoing surgical procedures. *Anesth Analg*. 1979;58:133-135.

C.3. If general anesthesia is used as a technique, would it be safe to intubate the patient's trachea?

Airway management of the patient with hemophilia presents a unique challenge for the anesthesiologist because of the risk of hemorrhage in the tongue or neck, which could compromise (i.e., complete or near complete occlusion) the upper airway of the patient. Therefore, manipulation of the airway during elective intubation should not be performed until appropriate replacement factors have been administered. Care should be used when applying pressure during mask ventilation to avoid trauma to the lips, tongue, or face; elective laryngoscopy should be attempted only following appropriate factor correction. Depending on the procedure and operative needs, a smaller than predicted well-lubricated endotracheal tube should be considered for intubation. Nasal intubation, with its propensity for epistaxis, should be avoided if possible.

Bogdan CJ, Strauss M, Ratnoff OD. Airway obstruction in hemophilia (factor VIII deficiency): a 28-year institutional review. *Laryngoscope*. 1994;104:789-794.

C.4. Would you use any special precautions for this patient who is positive for HIV?

Standard precautions should be used for all patients regardless of their HIV status. Strict attention to aseptic technique throughout the surgical procedure should be emphasized (postoperative infections may be more common in HIV-positive patients undergoing orthopedic procedures such as these due to the potentially immunocompromised state in these patients.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Thomason HC III, Wilson FC, Lachiewicz PF, et al. Knee arthroplasty in hemophiliac arthropathy. *Clin Ortho*. 1999;360:169-173.

C.5. What special considerations should be taken in choosing anesthetic drugs for this patient?

Coexisting liver disease is not infrequent complication (although the incidence of virusinduced hepatopathy has decreased dramatically since improvement in donor screening and allogeneic blood testing) in the patient with hemophilia because of transfusion-associated hepatitis as a consequence of a history of multiple previous blood or factor transfusions. It is thus reasonable to use caution with drugs that are metabolized by the liver in the setting of substantial liver dysfunction (i.e., reduced protein synthetic function).

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

C.6. During an operative procedure, if the surgeon indicates that significant blood loss is occurring, would you transfuse this patient with packed red blood cells (RBCs) or whole blood?

As general transfusion practice, blood banks fractionate donated blood into component parts, leading to generation of RBCs, platelets, FFP, or cryoprecipitate blood components.

Following blood loss and subsequent to substantial volume replacement with crystalloids and/or colloids, RBCs may be required when the oxygen-carrying capacity and oxygen delivery reach critically low levels. The trigger for RBC transfusion can be quite variable between patients in various clinical scenarios. Important factors that need to be considered include

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the following: hematocrit values, rate of blood loss, patient age, and coexisting comorbidities as well as monitoring of other indices that allow assessment of a critical imbalance in oxygen delivery/consumption systemically or in critical organ systems (i.e., as reflected by CNS or myocardial ischemia). In a patient with hemophilia, transfusion of packed RBCs will further dilute already depressed circulating factor VIII levels; therefore, transfusion of whole blood in such a patient would be appropriate, if it can be obtained. With this technique, both oxygen-carrying capacity and all components of coagulation would be replenished. Given the general unavailability of whole blood, additional factor repletion is typically required depending on the amount, rate, and expected course of the bleeding. This may take the form of whole blood fractions (cryoprecipitate or FFP), additional recombinant factor replacements, or pooled factor concentrates.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

C.7. During the transfusion of the first unit of whole blood, the patient's temperature rose from 36.8°C to 37.9°C (98.24°F to 100.22°F). What immediate steps should be taken by the anesthesiologist at this time?

Ruling out an acute hemolytic transfusion reaction should always be considered when a patient becomes febrile during a blood transfusion because a febrile response (i.e., as related to release of interleukin 6 [IL6]) has a 50% sensitivity for hemolysis in the setting of ABO incompatible transfusion. The anesthesiologist should immediately discontinue the transfusion and drain any remaining allogeneic blood from the intravenous blood administration set, and blood should be drawn from the patient and sent to the blood bank with the unit of blood in question to allow repeat crossmatching. An additional tube of blood should be collected and sent for analysis of plasma free hemoglobin, haptoglobin, bilirubin, and lactate dehydrogenase (LDH) as well as a direct Coombs test. Urine may also be assessed for hematuria versus urine free hemoglobin. In the presence of an acute hemolytic blood transfusion reaction, profound hypotension requiring the use of vasopressors is likely related to release of a number of vasoactive mediators (e.g., serotonin, bradykinin, cytokines, histamine). Fluid and diuretic therapy as well as alkalization of the urine should be considered to reduce renal injury and maintain function. A febrile reaction that is not due to an acute hemolytic transfusion reaction frequently (e.g., 1% to 2%) occurs with blood transfusion; these are usually self-limited and is related to the release of cytokines by apoptotic leukocytes during red cell processing and storage. Simultaneously to the transfusion reaction evaluation, further investigations into the temperature increase is warranted because there are many possible causes of fever and transfusion reaction evaluation may take a few hours; however, a negative direct antiglobulin test (DAT) makes transfusion-related immune-mediated intravascular hemolysis unlikely.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:408-442.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

C.8. Does giving blood intraoperatively increase the potential for the development of factor VIII inhibitors?

Although approximately 30% of all patients with hemophilia A will develop a circulating inhibitor of factor VIII, no evidence has been demonstrated that development of such an inhibitor is related to the number of transfusions a patient receives. As a result, the administration of blood products in this setting should not be withheld for fear of inducing inhibitor development.

Rodriguez-Merchan EC, Lee CA, eds. *Inhibitors in Patients with Haemophilia*. Oxford, United Kingdom: Wiley-Blackwell; 2002:17-19.

C.9. Can factor VIII be safely administered to patients who have developed circulating inhibitors?

Occasionally, patients with the most severe phenotype of hemophilia (factor levels less than 1%) develop immunoglobulin antibodies (IgG) to the deficient factor. The inhibitors may be of low titer (generally thought of as less than 5 Bethesda units) or of extremely higher titer. The “Bethesda unit” of inhibition is defined as the amount of inhibitory activity present in 1

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mL of plasma that decreases the factor VIII level in 1 mL of normal plasma by 50% (i.e., from 1 to 0.5 units). The more dilutions needed to produce 50% activity, the higher the titer of antibody and the greater the number of Bethesda units. It is almost impossible to overpower a high-titer inhibitor with large doses of factor VIII, but when life-threatening hemorrhage occurs, massive doses of factor VIII concentrates or plasmapheresis with concomitant administration of factor VIII may be of temporary benefit. However, this approach requires a substantial amount of time since four to five plasma exchange procedures are typically required to reduce IgG levels by 90%. Replacement with large amounts of factor VIII concentrate may provide temporary hemostasis but may stimulate an increase in the antibody titer. Porcine factor VIII, when available, may provide hemostasis because of its distinct antigenicity, even in the presence of a circulating inhibitor. Immunosuppressive therapy is of no value in the acute setting.

Alternative approaches to therapy of the hemophiliac patient with inhibitors involve the use of other agents, such as activated prothrombin complex concentrated (aPCCs) such as FEIBA (factor eight inhibitor bypassing activity) which contain activated vitamin K-dependent coagulation factors as well as use of recombinant factor VIIa. These activated factors enter the coagulation cascade beyond the level of factor VIII and therefore bypass the FVIII mechanism for hemostatic system activation and negate the effects of the inhibitor. FEIBA, prothrombin complex concentrate that is used in the United States to treat hemophilia patients with inhibitors, has been associated with thrombosis in several case reports; the propensity for thrombosis with this agent may be related to the fact that it contains four activated factors as well as other by-products that may promote hemostatic system activation. Thrombosis is a possible complication when using aPCC.

Porcine factor VIII is sometimes effective in patients with hemophilia with inhibitors. The porcine factor VIII provides adequate factor VIII activity in patients with less than 50 Bethesda units of inhibitor. The usual starting dose is 100 to 150 porcine units per kg.

Bui JD, Despotis GD, Trulock EP, et al. Fatal thrombosis after administration of activated prothrombin complex concentrates in a patient supported by extracorporeal membrane oxygenation who had received activated recombinant factor VII. *J Thorac Cardiovasc Surg*. 2002;124(4):852-854.

DiMichele D. Hemophilia. *Pediatr Clin North Am*. 1996;43:709-736.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

C.10. The surgeon has requested the use of a tourniquet to minimize surgical bleeding. What are the physiologic and hemodynamic responses to tourniquet use?

Although the tourniquet may optimize surgical conditions, the physiologic and hemodynamic consequences can be significant. Anaerobic metabolism distal to the tourniquet begins approximately 8 minutes after inflation; a decrease in nicotinamide adenine dinucleotide and creatine phosphate stores in muscle will occur over the next 30 to 60 minutes. As a result, the anaerobic conditions will lead to cellular acidosis which will in turn cause the release of myoglobin, intracellular enzymes, and potassium. In addition, the limb looses heat and may approach room temperature.

Hemodynamic disturbances are seen when the tourniquet is inflated and deflated. Exsanguination of the limb and tourniquet inflation acutely expands central venous blood volume, which may have significant hemodynamic consequences in a patient with limited cardiac reserve (i.e., as related to reduced myocardial function). Tourniquet deflation and reperfusion of the limb can be associated with profound decreases in central venous and arterial blood pressure, as a result in a decrease in vascular resistance which is related to vasodilation that occurs with the circulation of metabolites produced during the ischemic period. Prolonged

inflation (greater than 45 to 60 minutes) can result in systemic hypertension for reasons that are likely due to the presence of a critical level of ischemia in the muscle or nerve or as related to pain.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

C.11. Is it appropriate to suction the endotracheal tube and oropharynx

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of this patient before extubation?

Removal of secretions that might be aspirated is essential before the extubation of any patient; nevertheless, suctioning of the oropharynx of hemophiliac patient can irritate mucosa by the suction catheter and result in the formation of an oral hematoma. In a patient with hemophilia, gentle oral suctioning with reduced suction pressures under direct vision is appropriate to eliminate all secretions.

Hyderally H, Stark DC. Hemophilia: anesthetic implications. *Mt. Sinai J Med*. 1977;44:397-399.

D. Postoperative Management

D.1. What special consideration should be given to postoperative pain management for this patient?

It is important to avoid any postoperative pain supplements that may predispose hemophiliac patients to a bleeding diathesis. Analgesics containing aspirin or nonsteroidal anti-inflammatory drugs should certainly be avoided based on their antiplatelet effects. Antihistamines and antitussives may also inhibit platelet aggregation. Opioid analgesics or acetaminophen-based products should be appropriately titrated for postoperative pain management. If regional blockade with a catheter technique was used for anesthesia, postoperative analgesics should be administered through this route; because the patient has undergone the risk of placement, they should also receive the benefit. Care must be taken to ensure appropriate timing for removal of the catheter, preferably after confirmation of normal factor VIII levels.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1868-1880.

D.2. What steps should be taken to enhance the coagulation status of this patient in the postoperative period while at home?

It is important that factor VIII levels are supplemented for at least 2 to 4 weeks following surgery. If factor VIII levels are allowed to fall to the levels normally seen in these patients, this can result in postoperative hemorrhage. Postoperatively, many clinicians recommend maintaining levels at 80% of normal for the first 4 postoperative days, whereas others have opined that levels of at least 40% of normal are adequate. The consensus is that factor VIII levels on postoperative days 5 to 8 should be maintained at least at 30% to 40% of normal, whereas levels of 10% to 20% of normal should be maintained for the following 2 to 4 weeks.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407-436.

Löfqvist T, Nilsson IM, Petersson C. Orthopaedic surgery in hemophilia. 20 years' experience in Sweden. *Clin Orthop Relat Res*. 1996;332:232-241.

D.3. Can this patient be treated with factor VIII supplements using home infusion?

Administration of factor VIII concentrate by continuous infusion may be administered to patients with hemophilia at medical centers in the postoperative inpatient period. With transition of many surgical procedures to the outpatient arena, home infusion of factor VIII can provide the same level of hemostatic integrity. Home infusion of purified factor VIII concentrate has been shown to be safe, efficacious, and convenient for postoperative patients and should be considered for patients with hemophilia.

Lee CA, Berntop EE, Hoots WK. *Textbook of Hemophilia* . New York: Wiley; 2010:48-51.

Varon D, Schulman S, Bashari D, et al. Home therapy with continuous infusion of factor VIII after minor surgery or serious hemorrhage. *Hemophilia*. 1996;2:207-210.

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Chapter 32
Sickle Cell Disease

Chris R. Edmonds

Vinod Malhotra

A 30-year-old African-American woman with avascular necrosis of her right hip was admitted for a total hip arthroplasty. Her hematocrit was 22%, blood pressure was 130/90 mm Hg, and pulse was 107 beats per minute. She has a past medical history of recurrent joint pain, bone pain, jaundice, and abdominal pain requiring multiple hospitalizations for analgesia. Her past surgical history was remarkable for a cholecystectomy, and her postoperative course was remarkable for a prolonged hospitalization for respiratory complications.

A. Medical Disease and Differential Diagnosis

1. What was the most likely underlying medical problem in this patient? How would you confirm the diagnosis of sickle cell anemia (SCA)?
2. What is sickle cell disease (SCD)?
3. What is sickle cell trait (SCT)?
4. What are some of the other hemoglobinopathies and what are their clinical features?
5. What are the clinical features of SCD?
6. Describe the different types of sickle cell crises.
7. Discuss the pathophysiologic effects of SCD.
8. What is acute chest syndrome?

B. Preoperative Evaluation and Preparation

1. What preoperative evaluation would you perform on this patient before anesthesia?
2. How would you prepare this patient for general anesthesia and regional anesthesia?
3. Discuss the indications for preoperative exchange transfusion in this patient.
4. What are the indications for blood transfusion in SCD?

C. Intraoperative Management

1. Discuss the anesthetic management for this patient. Discuss both regional and general anesthesia considerations.
2. Discuss how the comorbidities associated with SCD can affect your anesthetic management.
3. What precautions should one take to prevent sickling in this patient?

D. Postoperative Management

1. Discuss the postoperative management of this patient.
2. What complications might occur in this patient in the immediate postoperative period?
3. What is the treatment of sickle cell crisis?
4. What is the role of hyperbaric oxygen therapy in treatment of sickle cell crisis?

A. Medical Disease and Differential Diagnosis

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A.1. What was the most likely underlying medical problem in this patient? How would you confirm the diagnosis of sickle cell anemia (SCA)?

For a young African-American patient presenting with a history of joint pain, bone pain, abdominal pain, and anemia, the most likely diagnosis is SCD. Other diagnoses to consider include other hemoglobinopathies, dermatomyositis, glucose-6-phosphate dehydrogenase (G6PD) deficiency, and porphyria. Nevertheless, given the constellation of symptoms and the laboratory findings, SCD is the most likely diagnosis. A hemoglobin (Hgb) electrophoresis will confirm the diagnosis and provide the percentage of abnormal hemoglobin S (HgbS).

Firth PG. Anaesthesia for peculiar cells—a century of sickle cell disease. *Br J Anaesth*. 2005;95:287-299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321-336.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1122-1123.

Wilson M, Forsyth P, Whiteside J. Haemoglobinopathy and sickle cell disease. *Br J Anaesth Contin Educ Anaesth Crit Care Pain Med*. 2010;10(1):24-28.

A.2. What is sickle cell disease (SCD)?

SCD is a hereditary hemoglobinopathy resulting from inheritance of a *β-globin* gene mutation located on chromosome 11. This mutation leads to a single-point mutation where adenine is replaced with thymine. The mutant *β*-allele codes for production and assembly of a variant Hgb (*β*-S). The molecular basis of SCD has been demonstrated to be the substitution of valine for glutamic acid in the sixth position from the *N*-terminus of the *β*-chains of Hgb. This substitution replaces a hydrophilic negative-charged amino acid (glutamic acid) with a hydrophobic nonpolar amino acid (valine). This greatly destabilizes the structure of Hgb and exposes highly reactive hydroxyl groups on the protein surface. The mutation in *β*-S Hgb accelerates the denaturation of the Hgb molecule and significantly decreases its solubility. Decreased oxygen tension causes conformational changes in the Hgb molecule, allowing hydrophobic bonds to form between the BS-6 valine of one chain and the BS-85 phenylalanine and the BS-88 leucine of a second chain. This bond forms insoluble tetramers that bond with other tetramers to form long helical strands that subsequently polymerize, causing deformation of the red blood cell membrane into a sickle shape. The result is a red blood cell that is less able to transverse the capillaries of the microcirculation, disposing the end organ to hypoxia and ischemic damage when sickle cells are present in sufficient quantity. In the United States, the estimated prevalence of Hgb SS disease is 1:625 (0.2%) in people of African descent. Patients with SCA have early mortality, with the median age of death in the late 40s to early 50s.

Coté CJ, Lehrman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:178-197.

Firth PG. Anaesthesia for peculiar cells—a century of sickle cell disease. *Br J Anaesth*. 2005;95:287-299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321-336.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1122-1123.

Wilson M, Forsyth P, Whiteside J. Haemoglobinopathy and sickle cell disease. *Br J Anaesth Contin Educ Anaesth Crit Care Pain Med*. 2010;10(1):24-28.

A.3. What is sickle cell trait (SCT)?

SCT is the heterozygous or carrier state of SCD. Large-scale screening for SCD in American military recruits revealed an incidence of SCT (HbAS) of 8% to 10% in African Americans and 0.05% to 0.08% in others. HbAS cells begin to sickle only when oxygen saturation of Hgb is less than 20%. No difference has been found between normal persons (HbAA) and those with HbAS regarding survival rates or incidence of severe disease, with one exception: Patients with

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HbAS have a 50% increased risk for pulmonary infarctions. Studies have suggested that SCT provides a survival advantage over hematologic normal individuals when infected by the malarial parasite *Plasmodium falciparum*.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321-336.

Gong L, Parikh S, Rosenthal PJ, et al. Biochemical and immunological mechanisms by which sickle cell trait protects against malaria. *Malar J*. 2013;12:317.

A.4. What are some of the other hemoglobinopathies and what are their clinical features?

The most common hemoglobinopathies include the thalassemias, Hgb C disease, and SCA. Thalassemia arises from alterations in one or more of the four genes that code for the *α*-chain. The mildest form of thalassemia (loss of one *α*-gene) presents as a mild form of anemia, whereas the most severe form (loss of all four genes) is incompatible with life. Hgb C results from a mutation in the *β-globin* gene. Hgb C disease is a relatively benign disease producing a mild hemolytic anemia and splenomegaly. However, when it is paired with a *β*-S mutation, the disease is more severe. Other rare hemoglobinopathies will not be discussed further.

Each Hgb gene mutation of the heterozygous form causes little or no clinical consequence, but when both genes of a heterozygote are abnormal, a disease state is evident. Heterozygous combinations such as HbS and HbC (HbSC disease), and *β*-thalassemia mutation (HbS-*β*-thalassemia) usually cause a milder clinical course than that of SCD.

Coté CJ, Lehrman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:178-197.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321-336.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1122-1123.

Wilson M, Forsyth P, Whiteside J. Haemoglobinopathy and sickle cell disease. *Br J Anaesth Contin Educ Anaesth Crit Care Pain Med*. 2010;10(1):24-28.

A.5. What are the clinical features of SCD?

The clinical features of SCD are manifested through indolent end-organ damage with intermittent acute episodes of severe pain and pulmonary complications. Although SCD is a disease of Hgb, it ultimately affects all organ systems. It is usually the acute problems that bring these individuals to the attention of a physician. The clinical manifestations by organ systems are presented in Table 32.1.

The progression and severity of SCD is variable. Many of the patients have an indolent course, whereas a smaller subset suffer from an early end-organ failure and an early death. Pulmonary, neurologic, and renal disease are the leading causes of morbidity and mortality.

Ataga KI, Derebail VK, Archer DR. The glomerulopathy of sickle cell disease. *Am J Hematol*. 2014;89(9):907-914.

Coté CJ, Lehrman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:178-197.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1122-1123.

A.6. Describe the different types of sickle cell crises.

Sickle cell crisis refers to the acute clinical picture generally caused by sickling of red blood cells in the *microcirculation*.

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Four main clinical types of crises have been described as follows in Table 32.2.

The most common crises in SCD is vaso-occlusive crisis, which is characterized with intermittent, recurrent acute episodes of severe pain. It is generally felt that the central cause of pain is ongoing acute ischemia, vaso-occlusion, and infarction. The precise pathophysiology and nociceptive pathways have not been elucidated. Patients in vaso-occlusive crisis present with fever, anemia, spine pain, limb pain, and abdominal pain. They are tachypneic and may have an enlarged liver and spleen in addition to abdominal tenderness. Serjent et al. reported that in 118 patients having 183 painful crises, the location was noted to be in the lumbar spine (49%), abdomen (32%), femoral shaft (30%), and the knee (21%). There is usually no identifying triggering agent for most vaso-occlusive crises. The average rate of painful crises per patient year is 0.8%. There is a subset of patients (5.2%) who average 8 to 10 crises a year, which accounts for 33% of all hospitalizations. Mortality positively correlates with increased pain rate in adults.

Coté CJ, Lehrman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:178-197.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321-336.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1122-1123.

Serjeant GR, Ceulaer CD, Lethbridge R, et al. The painful crisis of homozygous sickle cell disease: clinical features. *Br J Haematol*. 1994;87(3):586-591.

TABLE 32.1 Clinical Manifestations of Sickle Cell Disease

SYSTEM	SYMPTOMS
Central nervous system/neurologic	• Stroke (cerebrovascular accident) in children as well as adults (50%-70% recurrence within 3 years) • Proliferative retinopathy/blindness • Painful crisis • Chronic pain • Peripheral neuropathy • Poor school performance
Cardiovascular	• Conduction abnormalities secondary to iron overload • Hypertension • Cor pulmonale • Left and right ventricular dysfunction • Chronic ulcers
Pulmonary	• Infarction, pulmonary fibrosis • Infection • Restrictive/obstructive lung disease • Acute chest syndrome • Pulmonary hypertension (30%-40%) • Airway hyperactivity
Genitourinary	• Hyposthenuria, hematuria, proteinuria • Chronic renal insufficiency (5%-20%) • Renal failure

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	• Priapism (10%-40% of men)
Gastrointestinal	• Cholelithiasis (70%) • Acute hepatic syndrome • Elevated liver function tests, hyperbilirubinemia • Hepatopathy • Cirrhosis (16%-29%) • Dyspepsia secondary to mucosal ischemia • Sickle girdle syndrome (mesenteric ischemia)
Musculoskeletal	• Osteomyelitis (*Staphylococcus/Salmonella*) • Dactylitis • Avascular necrosis • Infarction
Heme/immunologic	• Chronic anemia • Autosplenism • Susceptibility to infections with encapsulated organisms • Erythrocyte alloimmunization from blood transfusions • Sequestration crisis • Hemolytic crisis • Aplastic crisis • Immune dysfunction • Hypercoagulability • Chronic inflammation

A.7. Discuss the pathophysiologic effects of SCD.

The pathophysiologic effects of SCD are not limited to the structure or deformation of the erythrocyte. The interaction and balance between the Hgb molecule, cytoplasm, and cell wall and the vascular endothelium is drastically altered to create chronic systemic biochemical alterations that produce the clinical features of SCD. As in vaso-occlusive crisis, there is a triggering insult, such as infection, surgical stress, or ischemia-reperfusion injury, that catalyzes a complex interaction among sickled cells, endothelial regulation of flow, inflammatory cytokines, platelet aggregation factors, and vasoconstriction, leading eventually to ischemia, infarction,

and cell death. This cascade leads to a vicious cycle that eventually causes end-organ damage and dysfunction. End-organ damage that occurs in sickle cell states is attributable to three pathways. In the erythrocyte cytoplasm, the loss of Hgb structural stability leads to increased oxidation of heme with subsequent denaturation, deterioration, and polymerization. Iron oxidation produces superoxides (O^-_2) and hydrogen peroxides ($H_2O_2^-$), which increases the formation of highly reactive hydroxyl radicals (-OH). In the cell membrane, free iron and ironcontaining compounds accumulate, leading to clustering of membrane surface membranes, abnormal cation permeability, and cellular dehydration. This complex series of events within the erythrocyte increases adherence to the vascular endothelium, exposing it to shear and oxidative stress. The interaction between the abnormal erythrocytes and the vascular endothelium produces chronic inflammation, upregulation of endothelial cell adhesion molecules, and altered expression of endothelial nitric oxide synthetase. Systemically, there is an increase in leukocyte counts, activation of the coagulation pathways, increase in inflammatory compounds, and increase in circulating endothelial cells in the plasma. The complex pathologic interaction between sickling of cells in blood vessels and the vascular endothelium leads to infarcts, tissue destruction, and consequent end-organ failure. The pathogenesis is shown in Figure 32.1.

TABLE 32.2 Types of Sickle Cell Crises

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TYPE	PATHOPHYSIOLOGY	TREATMENT
Vaso-occlusive	Pain secondary to obstruction of flow in the microvascular beds leading to localized ischemia	• Hydration • Analgesia • Incentive spirometry
Splenic sequestration	Acute painful enlargement of the spleen Acute hypovolemia	• Restore circulatory volume, possible splenectomy
Aplastic	Sudden cessation of bone marrow activity Acute worsening of anemia usually associated with viral infection (parvovirus B19) Recovery in 7-10 days	• Supportive therapy • Blood transfusion
Hemolytic crisis	Acute accentuated decrease in hemoglobin level Secondary to red cell destruction Usually associated with coexisting G6PD deficiency	• Supportive therapy • Blood transfusion

G6PD, glucose-6-phosphate dehydrogenase.

Bunn HF. Pathogenesis and treatment of sickle cell disease. *N Eng J Med*. 1997;337:762-769.

Conran N, Franco-Penteado CF, Costa FF. Newer aspects of the pathophysiology of sickle cell disease vaso-occlusion. *Hemoglobin*. 2009;33(1):1-16.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321-336.

Strijbos MH, Landburg PP. Circulating endothelial cells: a potential parameter of organ damage in sickle cell anemia. *Blood Cell Mol Dis*. 2009;43:63-67.

A.8. What is acute chest syndrome?

Acute chest syndrome is a term used to describe an acute pulmonary complication of SCD. It is defined by the finding of a new pulmonary infiltrate involving at least one complete lung segment on chest radiograph that is not due to atelectasis. It presents with a constellation of pulmonary symptoms and signs in a patient with SCD. These include fever (temperature 38.5°C [101.3°F]), wheezing, coughing, tachypnea, chest pain, and hypoxemia (less than 92% on room air). Pleural effusions (55%) are commonly seen on chest radiographs. Acute chest syndrome frequently follows vaso-occlusive crises; therefore, vaso-occlusive pulmonary infarction may be a precipitating factor. Other causes include infection (viral, chlamydia, mycoplasma, and

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bacterial) and pulmonary fat embolism resulting from bone marrow necrosis. Acute chest syndrome is a common postoperative complication in patients with SCD who have a history of pulmonary disease following general anesthesia. It is one of the most common causes of death in adults with SCD. Acute chest syndrome can be prevented by judicious hydration, incentive spirometry, effective analgesia, and avoidance of even mild hypothermia during the crises. Acute chest syndrome should be treated with bronchodilators, antibiotics, and exchange transfusion, when necessary. Exchange transfusion is recommended if the patient is clinically deteriorating.

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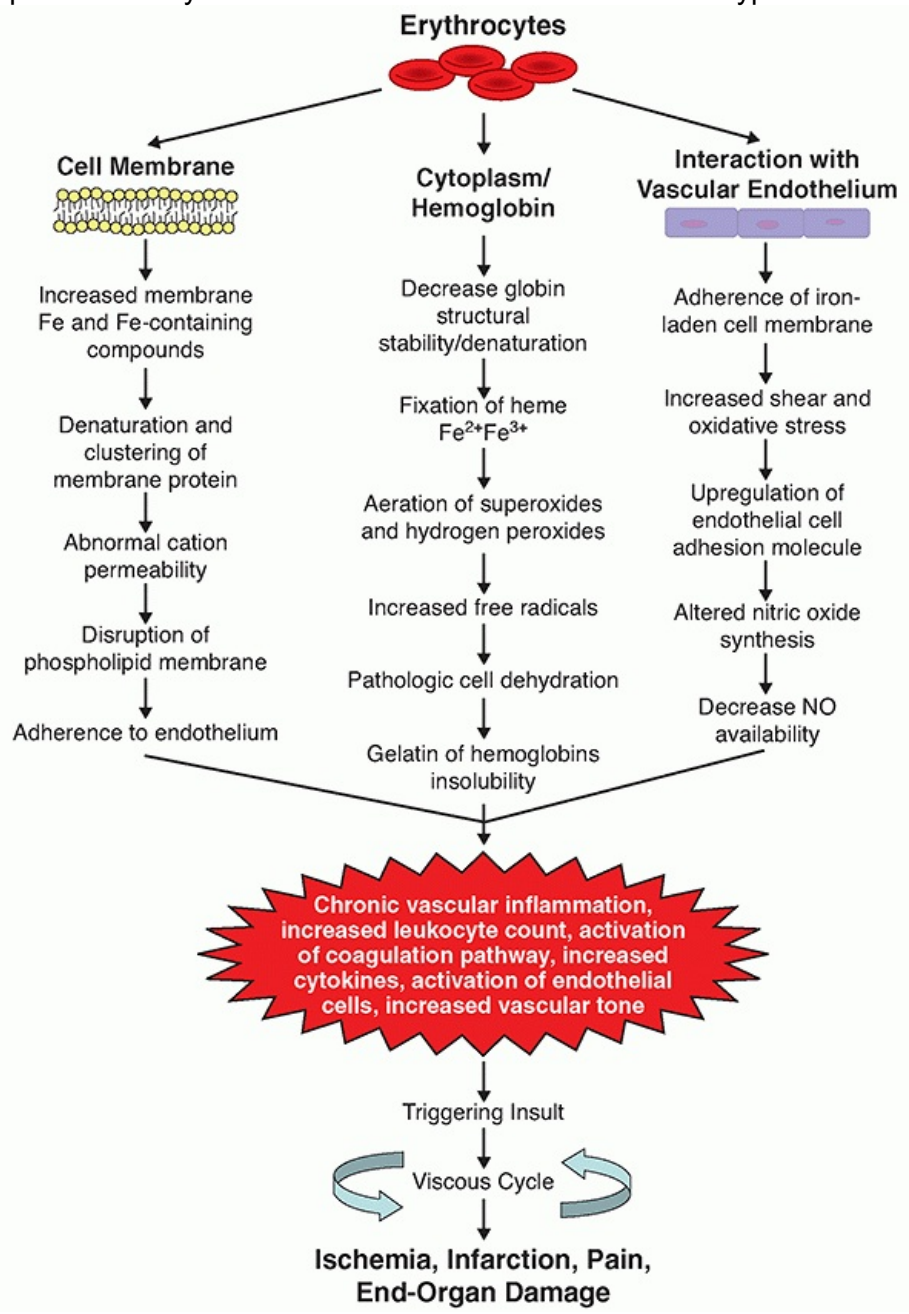


FIGURE 32.1 Pathogenesis of sickle cell damage.

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Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1122-1123.

Stuart MJ, Setty BN. Sickle cell acute chest syndrome: pathogenesis and rationale for treatment. *Blood*. 1999;94:1555-1560.

Vichinsky EP, Neumayr LD. Causes and outcomes of the acute chest syndrome in sickle cell disease. *NewEngl J Med*. 2000;342:1855-1865.

B. Preoperative Evaluation and Preparation

B.1. What preoperative evaluation would you perform on this patient

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before anesthesia?

The aim of the preoperative assessment in a patient with SCD is to determine the preoperative risk of this multisystemic disease and how the end-organ damage will affect the anesthetic management (see Table 32.1). A careful history should be obtained and physical examination done, and the cardiopulmonary status should be thoroughly investigated, in view of the increased incidence of cardiac and pulmonary morbidity in these patients. A history of frequent hospitalizations in the year before surgery significantly increases the likelihood of a vaso-occlusive crisis in the perioperative period. Immunization status for Pneumovax and *Haemophilus influenzae* vaccine should be checked. Other characteristics that increase the perioperative risk are age, pregnancy, smoking, and infection. If possible, cessation of smoking prior to elective surgery should be strongly encouraged because smoking increases the risk of acute chest syndrome and pain in the preoperative period. One should correct hypovolemia and treat infection appropriately preoperatively. Laboratory investigation should include a complete blood count, blood urea nitrogen, serum creatinine, urinalysis, electrocardiogram, chest radiograph, pulse oximetry, and liver function tests. In addition, the following tests may be helpful:

- Arterial blood gas, if indicated
- Sickle cell preparation (if diagnosis is unclear)
- Hgb electrophoresis to determine HbS, quantitatively
- Reticulocyte count
- Type and cross (alloimmunization may make this difficult)
- Pulmonary function test (if severe pathology, paroxysmal dyspnea, or history of acute chest syndrome)
- Echocardiogram in patients with history of pulmonary hypertension or cardiomegaly
- Neurologic imaging (if there are psychological or behavioral changes)

Cohen RT, DeBaun MR, Blinder MA, et al. Smoking is associated with an increased risk of acute syndrome and pain among adults with sickle cell disease. *Blood*. 2010;115(18):3852-3854.

Coté CJ, Lehrman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:178-197.

Knight-Madden JM, Barton-Gooden A, Weaver SR, et al. Mortality, asthma, smoking and acute chest syndrome in young adults with sickle cell disease. *Lung*. 2013;191(1):95-100.

B.2. How would you prepare this patient for general anesthesia and regional anesthesia?

- Informed consent should be obtained to explain the options, risk, and benefits of the different types of anesthetics used.

- Preoperative hydration should be initiated to treat baseline volume deficit.
- Euvolemia should be maintained preoperatively (remembering that the patient is on nothing-by-mouth status and may have a urine concentration defect requiring volume replacement).
- Any infections should be treated preoperatively, if possible.
- End-organ dysfunction should be identified and treated appropriately.
- Type and crossmatching may be difficult in these patients because of alloimmunization.
- Consider transfusion of red blood cells to maintain oxygen-carrying capacity. Transfusion guidelines should be based on comorbidities, surgical risk, and degree of anemia. Transfusions should be individualized and based on the patient's risk/benefit. Efforts should be made for leukocyte reduction techniques, as with buffy coat-poor red cells, to reduce the incidence of leukocyte antigen alloimmunization. The goals of transfusion are to achieve an Hgb concentration of greater than 8 g per dL and to ensure that Hgb A represents more than 40% of the total Hgb present. Past practices of reducing HgbS levels to less than 30% do not seem to improve outcome and increase transfusion-related complications.

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Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321-336.

B.3. Discuss the indications for preoperative exchange transfusion in this patient.

Controversy exists whether these patients benefit from preoperative exchange transfusion. For high-risk surgical procedures such as cardiopulmonary bypass, an exchange transfusion may be recommended. Nevertheless, a series of reports of cardiopulmonary bypass cases in which exchange tranfusions were not performed or only a partial exchange tranfusion was performed have had sucessful outcomes. If an exchange transfusion is required, the exchange transfusion should be performed with buffy coat-free packed red blood cells to reduce the HbS fraction to less than 40%. Nevertheless, growing evidence indicates that most surgical procedures can be safely performed in patients with SCD without aggressively transfusing. For example, for certain surgical procedures, it has been shown that a packed red blood cell transfusion done simply to increase the Hgb level to 10 g per dL is as effective in decreasing perioperative morbidity as is exchange transfusions to reduce the HbS(S) levels to less than 40%. Exchange transfusion is a therapy often used in patients with SCD complicated by acute chest syndrome. It is beneficial to keep the hematocrit lower than 35% with an exchange transfusion because an increased hematocrit will increase blood viscosity and stasis in the circulation.

Adhikari RK, Maddi MM, Zacharias S. Preoperative exchange transfusion for sickle cell disease patients undergoing open heart surgery: an exception to the rule. *J Cardiac Surg*. 2010;25(6):691-693.

Coté CJ, Lehrman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:178-197.

Maddali MM, Rajakumar MC, Fahr J, et al. Cardiopulmonary bypass without preoperative exchange transfusion in sicklers. *Asian Cardiovasc Thorac Ann*. 2006;14:51-56.

Vichinsky EP, Haberkern CM, Neumayr L, et al. A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. *N Engl J Med*. 1995;333:206-213.

B.4. What are the indications for blood transfusion in SCD?

Blood transfusions should be guided by the clinical picture and the potential for blood loss. Prophylactic transfusion remains controversial and is of questionable benefit in mild-tomoderate risk cases. Some of the clinical indications for blood transfusion in SCD include the following:

Acute conditions

- Vaso-occlusive crises with organ infarction and dysfunction
- Sequestration syndrome
- Acute hemolysis with exacerbation of anemia
- Aplastic crisis
- Acute chest syndrome
- Acute multiorgan failure

- Severe unresponsive priapism
- Protracted painful crisis
- High-risk surgery (e.g., cardiovascular, thoracic)

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Chronic conditions

- Intractable leg ulcers
- Complicated pregnancy
- Stroke
- Recurrent painful syndrome
- Recurrent acute chest syndrome

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Wilson M, Forsyth P, Whiteside J. Haemoglobinopathy and sickle cell disease. *Br J Anaesth Contin Educ Anaesth Crit Care Pain Med*. 2010;10(1):24-28.

Wun T, Hassell K. Best practice for transfusion for patients with sickle cell disease. *Hematol Rev*. 2009;1(2):e22.

C. Intraoperative Management

C.1. Discuss the anesthetic management for this patient. Discuss both regional and general anesthesia considerations.

The definitive anesthetic technique has not been established secondary to the wide clinical spectrum of SCD and the different severities in the surgical procedures. Koshy et al. retrospectively reviewed 1,079 anesthetics and noted an apparent association between postoperative complications and the use of regional anesthesia. Nevertheless, this study did not control for obstetric procedures and the tendency that clinicians often use regional anesthesia for sicker patients. Other studies did not find an adverse effect of regional anesthesia. Theoretically, regional anesthesia, especially when used with epinephrine, may produce a compensatory vasoconstriction in the nonblocked area, but this has not been supported in the literature. Yaster et al. found that epidural analgesia markedly improved oxygenation in children in vasoocclusive crises, either through superior pain control or opioid sparing effects. Therefore, almost any anesthetic technique can be used, provided the following principles are considered:

- Good intravenous access for maintenance of intravascular volume
- Adequate oxygenation
- Denitrogenation before induction of general anesthesia
- Endotracheal intubation for general anesthesia to ensure a controlled airway and adequate ventilation
- Maintenance of adequate oxygen-carrying capacity through judicious use of red cell transfusions
- Maintenance of normothermia
- Opioids for analgesia carefully titrated for perioperative and postoperative analgesia
- Avoidance of tourniquet use
- Considering regional analgesia for both intraoperative and postoperative courses
- Avoidance of hypotension and venous stasis to prevent sickling of red blood cells
- Considering invasive monitoring (arterial line, central venous pressure line) for beat-to-beat blood pressure monitoring, volume monitoring, and frequent laboratory test
- Avoidance of hypoventilation of lungs to prevent acidosis
- Possible increased inspired oxygen concentration to ensure maintenance of normal to increased PaO_2

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Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321-336.

Koshy M, Weiner SJ, Miller ST, et al. Surgery and anesthesia in sickle cell disease. Cooperative study of sickle cell diseases. *Blood*. 1995;86:3676-3684.

Yaster M, Tobin JR, Billett C, et al. Epidural analgesia in the management of severe vaso-occlusive sickle cell crises. *Pediatrics*. 1994;93:310-315.

C.2. Discuss how the comorbidities associated with SCD can affect your anesthetic management.

Sickle cell anemia is a disease that can affect every end organ. Therefore, evaluating the patient for end-organ dysfunction is paramount. This patient is anemic, tachycardic, and hypertensive. She may have dyspepsia, a hyperreactive airway, chronic renal insufficiency, liver disease, and might be debilitated with cardiopulmonary complications. Patients with SCD often present with cardiomegaly, pulmonary hypertension, and heart failure. For this surgery, she will probably require transfusions and may be difficult to crossmatch. In the postoperative period, pulmonary infarcts and infection are common, which can lead to acute chest syndrome. These problems, in addition to the potential for sickling crisis or sequestration syndrome, pose a greater risk than normal for perioperative morbidity and mortality. The patients at greater risk include those with a homozygous state SCD, sickle C disease (HbSC), and sickle thalassemia. In contrast, patients with SCT do not present an increased risk for intraoperative morbidity. As a perioperative specialist, one can have a profound effect on outcome in these patients by attention to detail, with a multisystem approach to address all end-organ dysfunction to reduce morbidity by maintaining oxygen delivery and preventing ongoing sickling.

Coté CJ, Lehrman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:178-197.

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Koshy M, Weiner SJ, Miller ST, et al. Surgery and anesthesia in sickle cell disease. Cooperative study of sickle cell diseases. *Blood*. 1995;86:3676-3684.

C.3. What precautions should one take to prevent sickling in this patient?

Sickling of red blood cells is triggered by a variety of factors. One should avoid or correct factors that can precipitate sickling. Special precautions include the following:

- Avoid hypoxia by preoxygenating the patient and employing higher than usual concentrations of inspired oxygen.
- Prevent acidosis by maintaining adequate oxygenation, normovolemia, and cardiac output.
- Prevent respiratory acidosis by avoiding hypoventilation.
- Prevent stasis. This requires proper hydration and good regional blood flow. Blood viscosity should be maintained at a low level by limiting a rise in hematocrit to 35% and avoiding over transfusion.
- Avoid hypovolemia.
- Avoid hypothermia by using body warming and intravenous fluid warming devices perioperatively.
- Replace blood loss to prevent anemia.

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- The use of tourniquets is controversial. Some advise against the use of tourniquets, although they have been used without ill effects by others. If a tourniquet is to be used, it should only be used when absolutely necessary and for a short period as possible. Special attention should be paid to maintain adequate oxygenation and to prevent respiratory or metabolic acidosis at the time of tourniquet release.

Coté CJ, Lehrman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:178-197.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321-336.

Oginni LM, Rufai MB. How safe is tourniquet use in sickle-cell disease? *Afr J Med Med Sci*. 1996;25:3-6.

D. Postoperative Management

D.1. Discuss the postoperative management of this patient.

The postoperative period is a crucial time with SCD. Surgical pain, hypoventilation, a high incidence of pulmonary infarction, and an expected decrease in PaO_2 will predispose these

patients to the formation of sickle cells, leading to the possibility of developing vaso-occlusive crisis or acute chest syndrome. The mainstay of postoperative management is supportive and preventive care. Supplemental oxygen, maintenance of intravascular fluid volume, maintenance of normothermia, and adequate analgesia are important considerations. There is evidence that suggests that patients with SCD have an altered pain response and both intravenous patient-controlled analgesia and epidural patient-controlled analgesia have been shown to improve postoperative pain control. However, regional analgesia has been shown to decrease pain scores while improving oxygenation. Supportive and preventive care should be continued in the extended postoperative period. The basic outline of routine postoperative care includes the following:

- Early mobilization
- Maintenance of normothermia
- Supplemental oxygenation
- Early effective analgesia or adjunctive analgesics—nonsteroidal anti-inflammatory drugs, acetaminophen
- Maintain euvolemia
- Incentive spirometry
- Pulse oximetry
- Pulmonary monitoring
- Psychological support
- Considering extended postoperative cardiovascular monitoring
- Considering regional analgesia for postoperative pain management

Coté CJ, Lehrman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:178-197.

Dampier CD, Smith WR, Kim HY, et al; and Investigators of the Sickle Cell Disease Clinical Research Network. Opioid patient controlled analgesia use during the initial experience with the IMPROVE PCA trial: a phase III analgesic trial for hospitalized sickle cell patients with painful episodes. *Am J Hematol*. 2011;86(12):E70-E73.

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Miller ST, Kim HY, Weiner D, et al; and Investigators of the Sickle Cell Disease Clinical Research Network. Inpatient

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O'Leary JD, Crawford MW, Odame I, et al. Thermal pain and sensory processing in children with sickle cell disease. *Clin J Pain*. 2014;30(3):244-250.

Yaster M, Tobin JR, Billett C, et al. Epidural analgesia in the management of severe vaso-occlusive sickle cell crises. *Pediatrics*. 1994;93:310-315.

D.2. What complications might occur in this patient in the immediate postoperative period?

The postoperative complications most likely to occur in the patient with SCD include deep vein thrombosis, vaso-occlusive crisis, pulmonary infarction, acute chest syndrome, and infection. Hypoxemic episodes are always a threat in the postoperative period secondary to pain, splinting, or oversedation and can precipitate a sickling crisis. The incidence of postoperative respiratory infection is high and is a leading cause of morbidity and mortality. Acute chest syndrome is one of the most common causes of death in adult patients and is a potentially lethal postoperative complication in patients with SCD who undergo major or high-risk surgery. Sequestration syndrome with shock is another potentially lethal complication, especially in the obstetric patient immediately postpartum. Patients with cardiomegaly and pulmonary hypertension are susceptible to heart failure. Renal and hepatic dysfunction may result in prolongation of the effects of certain medications. Orthopedic patients with SCD are at risk for deep vein thrombosis, acute thrombosis, and pulmonary embolism. Antithrombotic therapy has to be geared toward decreasing this common complication.

Coté CJ, Lehrman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:178-197.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321-336.

Hyder O, Yaster M, Bateman BT, et al. Surgical procedures and outcomes among children with sickle cell disease. *Anesth Analg*. 2013;117(5):1192-1196.

D.3. What is the treatment of sickle cell crisis?

The treatment of sickle cell crisis is to break the vicious cycle of sickling, ischemia, infarction, pain, and end-organ failure. An aggressive multimodal approach can reduce the clinical symptoms of the crises. The principles of treatment of painful sickle cell crisis include the following:

- Rest
- Hydration
- Oxygen therapy
- Treatment of infection
- Analgesics (consider patient-controlled analgesia)
- Considering regional analgesia
- Transfusion to reduce the Hgb SS disease concentration
- Incentive spirometry
- Maintenance of normothermia

Coté CJ, Lehrman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:178-197.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321-336.

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D.4. What is the role of hyperbaric oxygen therapy in treatment of sickle cell crisis?

Hyperbaric oxygen has been used empirically in some institutions for treatment of acute sickle cell crisis, although it is not widely available. Although some published reports claim instant improvement of symptoms, others have failed to show beneficial effects. There is better evidence that therapy is useful in management of ischemic disorders of the anterior segment of the eye or in chronic leg ulcers. Studies have shown no apparent effects of hyperbaric oxygen on sickle cell morphology in vitro. It appears, then, that its reported benefit in vivo may be due to a decrease in the rate of sickling or improved tissue oxygenation by direct diffusion. Although case series have supported its use, there is not enough evidence to recommend its routine use over conventional therapy.

Butler FK Jr, Hagan C, Murphy-Lavoie H. Hyperbaric oxygen therapy and the eye. *Undersea Hyperb Med*. 2008;35:333-387.

Mychaskiw G II, Woodyard SA, Brunson CD, et al. In vitro effects of hyperbaric oxygen on sickle cell morphology. *J Clin Anesth*. 2001;13:255-258.

Stirnemann J, Letellier E, Aras N, et al. Hyperbaric oxygen therapy for vaso-occlusive crises in nine patients with sickle cell disease. *Diving Hyperb Med*. 2012;42(2):82-84.

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Chapter 33
Airway Trauma

Richard P. Dutton

LaRita Yvette Fouchè-Weber

A 46-year-old man was thrown from his motorcycle at a high rate of speed and impaled in the base of the neck by a tree branch. At presentation to the trauma center, he is awake and alert with a heart rate (HR) of 122 beats per minute, blood pressure (BP) of 143/85 mm Hg, respiratory rate of 20 breaths per minute, and oxygen saturation of 98% on 100% nonrebreathing mask. There is a 5-cm wide piece of wood protruding from his anterior lower neck at the sternal notch, without visible bleeding. The patient is neurologically intact but admits to consuming six beers in the hours before injury. His medical history is unremarkable.

A. Medical Disease and Differential Diagnosis

1. What variables mitigate injury from motorcycle collisions?
2. What other significant trauma may be present?
3. How is the initial assessment of a trauma patient organized?
4. How would you evaluate airway and breathing?
5. How would you evaluate the circulation?
6. How would you evaluate mental status and neurologic condition?
7. What diagnostic tests are indicated for this patient based on the mechanism of injury?
8. What are the zones of the neck, and what is their clinical significance?
9. What immediate treatment is necessary before diagnostic studies?
10. When and where should the impaling object be removed?

B. Preoperative Evaluation and Preparation

1. What laboratory tests would you want?
2. What x-ray studies are most important to the anesthesiologist?
3. Is an electrocardiogram (ECG) necessary?
4. Should this patient be intubated before going for computed tomographic (CT) scanning?
5. When and where should this patient's airway be managed?
6. Are any prophylactic medications indicated?

C. Intraoperative Management

1. What monitors would you use? Is invasive monitoring necessary before definitive airway control?
2. What is the surgical approach to a zone I neck injury?
3. Is the patient likely to require tube thoracostomy? Should this be placed before managing the airway?
4. What are the options for managing this patient's airway?
5. What are the risks of rapid sequence induction in this patient?
6. What anesthetic agents would you use for a rapid sequence induction?
7. How can you minimize the risk of exacerbating cervical spine trauma?

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8. How can you minimize the risks of aspiration?
9. How would you anesthetize the airway for an awake intubation?
10. What are the risks of awake fiberoptic intubation?
11. If the patient cannot be ventilated, what options are available?
12. Would a laryngeal mask airway (LMA) or other pharyngeal airway be of assistance?
13. What surgical airway options are available in this case?
14. What maintenance anesthetics are indicated or contraindicated in this patient?
15. What complications will the surgical plan introduce?

D. Postoperative Management

1. What are the criteria for extubation?
2. What techniques may be used during extubation?
3. How does alcohol abuse affect postoperative management?
4. What pain medication should be used?

A. Medical Disease and Differential Diagnosis

A.1. What variables mitigate injury from motorcycle collisions?

Trauma involving motorcycles accounts for 2% to 5% of all motor vehicle trauma, but there is a higher proportion of death and serious injury because of the relative exposure of the motorcycle rider to the environment. Factors such as youth, high speed, and intoxication contribute to motorcycle collisions just as they do for automobiles. Motorcycle riders also are much more susceptible to factors beyond their own control, such as lack of vigilance on the part of automobile and truck drivers, road conditions (oil or debris), and the weather.

Factors that can reduce the seriousness of motorcycle collisions when they do occur include helmets and protective clothing. Reenactment of a mandatory helmet law in the state of Washington in 1990 resulted in a decline in serious brain injury in motorcycle trauma victims from 20% to 9% and a reduction in mortality from 10% to 6%. Full leather or synthetic “armor” reduces the risk of massive skin and soft-tissue injuries in the event of a high-speed collision.

Liu BC, Ivers R, Norton R, et al. Helmets for preventing injury in motorcycle riders. *Cochrane Database Syst Rev*. 2008;(1):CD004333.

Meredith L, Brown J, Ivers R, et al. Distribution and type of crash damage to motorcyclists' clothing: validation of the zone approach in the European Standard for motorcycle protective clothing, EN13595. *Traffic Inj Prev*. 2014;15(5):501-507.

A.2. What other significant trauma may be present?

Motorcycle collisions are high-energy trauma that can result in injury to any organ system or region of the body. This patient will need a complete head-to-toe assessment and a number of diagnostic studies to establish the full extent of injury. Common injuries in motorcyclists include brain trauma from direct impact with the road and with other vehicles, pelvic fractures

from impact with the frame of the motorcycle, abdominal trauma from impact with the handlebars, and lower extremity orthopedic and soft-tissue trauma from impact with the road.

A.3. How is the initial assessment of a trauma patient organized?

The initial management of trauma patients is best described by the tenets of the Advanced Trauma Life Support course, written by the American College of Surgeons Committee on Trauma. This course provides a unified philosophy and common language to organize practitioners from different specialties in the care of complex patients with the potential for multiple injuries. Assessment of the seriously injured patient begins with the ABCs: *A*irway, *B*reathing, and *C*irculation;

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followed by a brief neurologic examination and a catalogue of visible injuries. This “primary survey” is followed by diagnostic testing and a more detailed secondary survey to discover all of the patient's injuries. One important principle of Advanced Trauma Life Support is interruption of the diagnostic sequence as necessary to provide life-saving resuscitative care, up to and including surgery for airway management or hemorrhage control prior to completion of diagnostic studies.

American College of Surgeons Committee on Trauma. *Advanced Trauma Life Support for Doctors*. 8th ed. Chicago: American College of Surgeons; 2008.

A.4. How would you evaluate airway and breathing?

On first contact with the patient, the provider should attempt verbal communication: “How are you?” A patient who answers coherently in a normal voice has no immediate airway issue, adequate circulatory function, and minimal traumatic brain injury. In an unconscious patient, initial assessment is by looking, listening, and feeling for airflow. If airflow is absent, the airway should be opened by jaw thrust (*not* head tilt, as this may exacerbate a cervical spinal column injury), cleared of any visible foreign bodies or secretions, and should have the placement of an oral or nasopharyngeal airway.

Breathing is assessed by observation of the chest wall and diaphragm once the airway is open and by immediate placement of a pulse oximeter probe. Patients who are not breathing adequately should be assisted with bag-valve-mask ventilation while preparations are made for securing a definitive airway and instituting mechanical ventilation.

A.5. How would you evaluate the circulation?

Initial assessment for shock is by vital signs (HR, blood pressure, pulse oximetry) and physical examination (pallor, diaphoresis, peripheral circulation, visible or suspected hemorrhage). Mental status is also a useful sign; the patient in hemorrhagic shock will be first agitated and then lethargic. Young patients have significant compensatory reserves and will maintain a normal systolic blood pressure even in the face of hemorrhage as great as 40% of their blood volume. This state of compensated shock can be diagnosed by a narrowed pulse pressure (especially on automated sphygmomanometers), elevated HR, pallor, abnormal lactate, and a base deficit. Shock in this patient could be the result of hemorrhage from chest or abdominal trauma (including a great vessel injury associated with the impalement) or tension pneumothorax in either side of the chest.

American College of Surgeons Committee on Trauma. *Advanced Trauma Life Support for Doctors*. 8th ed. Chicago: American College of Surgeons; 2008.

Bouglé A, Harrois A, Duranteau J. Resuscitative strategies in traumatic hemorrhagic shock. *Ann Intensive Care*. 2013;3(1):1.

Dutton RP. Initial resuscitation of the hemorrhaging patient. In: Speiss B, Shander A, eds. *Perioperative Transfusion Medicine*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:289-300.

Glorsky SL, Wonderlich DA, Goei AD. Evaluation and management of the trauma patient for the interventional radiologist. *Semin Intervent Radiol*. 2010;27(1):29-37.

A.6. How would you evaluate mental status and neurologic condition?

The quick neurologic examination consists of questions to determine alertness and orientation (assuming the patient is responsive) followed by gross assessment of voluntary motion in all extremities. In the less responsive patient, the Glasgow Coma Score (GCS) (Table 33.1) is

used to stratify the degree of impairment: GCS 3 to 8 is a severe injury, GCS 9 to 13 is moderate traumatic brain injury, and GCS 14 to 15 is mild injury. Cranial nerve, spinal cord, and peripheral nervous system function is assessed by specific motor and sensory testing of each extremity during the secondary survey.

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TABLE 33.1 Glasgow Coma Scores[a]

EYE-OPENING RESPONSE	VERBAL RESPONSE	MOTOR RESPONSE
4 = Spontaneous	5 = Oriented to name	6 = Follows commands
3 = To speech	4 = Confused	5 = Localizes to painful stimuli
2 = To pain	3 = Inappropriate speech	4 = Withdraws from painful stimuli
1 = None	2 = Incomprehensible sounds	3 = Abnormal flexion (decorticate posturing)
	1 = None	2 = Abnormal extension (decerebrate posturing)
		1 = None

[a]The GCS is the sum of the best scores in each of three categories.

Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. *Lancet*. 1974;2:81-84.

A.7. What diagnostic tests are indicated for this patient based on the mechanism of injury?

Because of the high energy mechanism of injury, this patient must be assessed from head to toe. Ultrasonography examination of the abdomen and chest is used to diagnosis free peritoneal fluid, pneumothorax (in the hands of a skilled operator), and pericardial tamponade. Chest and pelvis plain-film radiography will reveal fractures, pneumothoraces, and hemothorax. CT scanning should include the head, neck, chest, abdomen, and pelvis; newer technology will allow for three-dimensional (3D) reconstructions of organs and vasculature with sensitivity and specificity equivalent to more traditional angiographic imaging.

This patient's obvious injury—to zone I of the neck—will necessitate a focused assessment of the trachea, great vessels, esophagus, and bilateral pleural cavities. Traditionally, this has been accomplished by a combination of plain-film radiography, angiography, bronchoscopy, and esophagoscopy. Increasing CT speed and resolution is leading to the increased use of this test at centers with experienced radiographers and traumatologists. The sequencing of diagnostic studies will depend on the patient's stability. In this case, he is likely to require intubation and perhaps exploratory surgery first. A noninvasive study such as contrast-enhanced CT (with angiographic reconstructions) may help to guide the surgical approach to removal of the impaling object if the patient is calm and stable enough to tolerate the test.

Wilson CT, Clebone A. Initial assessment and management of the trauma patient. In: Scher CS, ed. *Anesthesia for Trauma: NewEvidence and NewChallenges*. New York: Springer; 2014:1-15.

A.8. What are the zones of the neck, and what is their clinical significance?

Zone I of the neck includes the area from the inferior aspect of the cricoid cartilage down to the thoracic outlet. Zone I injuries require the complex diagnostic workup described in the previous section, followed by a surgical approach that allows access to both the neck and chest. Partial or complete median sternotomy is often necessary to access an injured great vessel or to repair the trachea or esophagus.

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Zone II of the neck includes the area from the angle of the mandible down to the cricoid cartilage. Injuries in zone II are addressed through a lateral or transverse cervical incision, with the surgeon able to achieve both proximal and distal control of the carotid or jugular vessels before exploring the wound itself.

Zone III of the neck includes the area from the angle of the mandible upward to the base of the skull. Zone III vascular injuries pose a significant operative risk because distal control of an injured vessel cannot be achieved. Injuries in zone III are therefore approached angiographically or as part of a more complex neurosurgical operation.

Britt LD, Weireter LJ, Cole FJ. Management of acute neck injuries. In: Feliciano DV, Mattox KL, Moore EE, eds. *Trauma*. 6th ed. New York: McGraw-Hill; 2008:467-478.

A.9. What immediate treatment is necessary before diagnostic studies?

The key to this case will be control of the patient's airway. Once hemodynamic stability is confirmed, the timing and sequence of diagnostic studies will be determined by the patient's degree of cooperation and ability to spontaneously ventilate. Although a CT scan before a controlled intubation in the operating room (OR) would be ideal, it is possible that the patient will decompensate before this can be accomplished. Preemptive airway control will allow for a more secure and safer diagnostic workup before the OR.

A.10. When and where should the impaling object be removed?

All things being equal, the impaling tree branch is best removed in the OR in an anesthetized patient. All of the personnel and equipment should be present to perform an emergent median sternotomy and major vascular and/or tracheal surgery if necessary.

B. Preoperative Evaluation and Preparation

B.1. What laboratory tests would you want?

The patient should have a full set of laboratory studies, both to identify abnormalities and to establish a baseline for future changes. Hemoglobin and hematocrit will not indicate hemorrhage on the initial draw—the bleeding trauma patient is losing whole blood—but will drop with subsequent fluid resuscitation. Arterial blood gas and arterial or venous lactate measurement will be the most sensitive indicators of hypoperfusion and shock. Serum electrolytes will reveal baseline abnormalities, if any, and the effects of alcohol consumption and dehydration. Clotting studies are important to rule out congenital abnormalities or the effects of liver disease before what could be a major surgical procedure; coagulopathy at the time of trauma center admission is an indicator of substantial blood loss and severe hemorrhagic shock. Toxicology screening is indicated in every trauma patient and is important to rule out the use of drugs of abuse, such as heroin or cocaine, that have implications for the anesthesiologist.

Initial laboratory studies also should include a sample for the blood bank with the request for an urgent crossmatch of red blood cells and plasma. If there has been a major vascular injury, substantial blood loss is a possibility and should be treated with immediate transfusion of blood and coagulation factors.

American College of Surgeons Committee on Trauma. *Advanced Trauma Life Support for Doctors*. 8th ed. Chicago: American College of Surgeons; 2008.

Hess JR, Lindell AL, Stansbury LG, et al. The prevalence of abnormal results of conventional coagulation tests on admission to a trauma center. *Transfusion*. 2009;49(1):34-39.

B.2. What x-ray studies are most important to the anesthesiologist?

Although all of the studies described in the preceding text will have some relevance, there are a few that have particular implications for the anesthesiologist. The chest radiograph and/or CT scan will suggest the degree of tracheal involvement of the impaling object, the risk that there is of a major vascular injury, or the presence of a pneumothorax. Plain radiographs or a CT scan of the cervical spine will be useful in ruling out bony or ligamentous injury that might be exacerbated by manipulation of the neck during airway management.

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B.3. Is an electrocardiogram (ECG) necessary?

In the absence of dysrhythmias on the cardiac monitor, the criteria for ordering a preoperative ECG are the same as in any other surgical candidate, that is, patients presenting with

symptoms or with a history suggestive of coronary artery disease. Dysrhythmias or visible injury to the precordium would be an indication for a baseline ECG and cardiac enzyme assay.

B.4. Should this patient be intubated before going for computed tomographic (CT) scanning?

The answer to this question involves an assessment of risks and benefits. If the patient is cooperative, vital signs are stable, CT scanner is close at hand, and anesthesia personnel are available to accompany the patient, then an immediate CT scan would be indicated. If the patient is deteriorating in any way, his degree of cooperation is in doubt, or a CT scan would place the patient far from expert resources for an extended period of time, then it would be wise to secure the airway first. In this case, there is a possibility that successful airway management will precipitate patient deterioration (e.g., hemorrhage, conversion from simple to tension pneumothorax), which suggests that if airway management is attempted before CT, it should probably be done in the OR with the surgical team on hand.

One approach to this kind of complex decision is to define an ideal course of care that provides the best information for each of the experts involved while minimizing risk to the patient and maximizing flexibility in dealing with changing circumstances. In this case, the surgeon and anesthesiologist might define a plan that includes transport to the OR; induction, intubation, and mechanical ventilation in this (safest possible) environment; transport to CT or angiography with the anesthesiologist in attendance for diagnostic studies; and then return to the OR for definitive surgery.

B.5. When and where should this patient's airway be managed?

Because of the potential for rapid deterioration and the desire to examine the airway closely before and during the intubation process, the patient should be moved as rapidly as possible to the OR before airway management is attempted. The surgical team should be on hand from the start and instruments should be available for video laryngoscopy and bronchoscopy, emergent tracheostomy, control of large vessel bleeding, and median sternotomy.

B.6. Are any prophylactic medications indicated?

Tetanus toxoid treatment is indicated for any trauma patient with an open wound who is more than 5 years removed from his or her last booster. Any patient with a significant open wound should receive prophylactic antibiotic therapy that covers gram-positive organisms for at least the first 24 hours following injury.

Prophylactic treatment to reduce the consequences of aspiration would be considered but probably rejected in this case. Promotility agents such as metoclopramide and H_2 antagonists such as ranitidine will not have time to work before definitive airway control is achieved and the more immediate approach of administering oral Bicitra would be contraindicated because of the possibility of esophageal injury.

Because of the patient's history of intoxication, prophylactic intravenous administration of vitamins and thiamine is indicated. Prophylaxis against alcohol withdrawal and deep venous thrombosis are indicated in the immediate postoperative period.

C. Intraoperative Management

C.1. What monitors would you use? Is invasive monitoring necessary before definitive airway control?

Blood pressure, electrocardiography, capnography, and pulse oximetry should be employed as with any patient. A Foley catheter should be inserted once the patient is anesthetized, although urine output is not an accurate measure of intravascular volume status in a recently intoxicated patient. An arterial line is useful for moment-to-moment measurement of blood pressure and for easy access to blood for laboratory assay including arterial blood gases. A central venous catheter should be placed if there is need to monitor central venous intravascular volume, in anticipation of the need for rapid intravascular expansion (using a large-bore catheter such as a pulmonary artery introducer), and for the administration of

vasoactive drugs. A pulmonary artery catheter is rarely indicated and seldom used acutely for resuscitation, although it may be helpful in selected patients with known coronary artery or valvular disease. Because of the potential for great

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vessel injury in this case, initial central access should be through the femoral vein.

Invasive monitoring lines usually are best placed after induction and intubation, when the patient is anesthetized and both surgeons and anesthesiologists can be working at the same time. Delaying surgical hemostasis in an unstable patient is unwise. In the case under discussion, it would be appropriate to place an arterial line in the OR before airway management, as long as the patient remains cooperative and stable, and to place a femoral central line thereafter. Placing the arterial line on the right side also will allow for assessment of blood flow in the innominate artery during surgical exploration.

McCunn M, Grissom TE, Dutton RP. Anesthesia for trauma. In: Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2423-2459.

C.2. What is the surgical approach to a zone I neck injury?

In the present case, the surgery is likely to start with a collar incision through the impalement wound to allow for better visualization of the path of injury. If injury to the trachea or a great vessel is discovered, a partial or complete median sternotomy would be the next step. It is the uncertain nature of this patient's injuries that makes preoperative diagnostic information so valuable, which is why a CT scan before definitive surgery (but after airway management) is a strong consideration.

C.3. Is the patient likely to require tube thoracostomy? Should this be placed before managing the airway?

Pneumothorax and hemothorax are common in trauma patients and should be suspected and definitively ruled out following any high-energy blunt trauma (e.g., motor vehicle collision, pedestrian struck, fall from a height) or any penetrating trauma to the neck, thorax, or upper abdomen. Immediate temporizing needle decompression and/or tube thoracostomy are indicated in any hemodynamically unstable patient with a suspicious injury, even before chest radiograph. Intubation and the change to positive pressure ventilation may precipitate decompensation in a patient with chest injury, due to either decreased preload in the setting of hemorrhage or increased intrathoracic pressure caused by conversion from a simple to tension pneumothorax.

In this case, there is the possibility of pathology in either or both hemithoraces. A portable anterior-posterior chest radiograph should be obtained at the earliest moment, followed by CT of the chest as outlined previously. If a simple pneumothorax is present, it is most prudent to prepare for chest tube placement (personnel, equipment) before airway management but to wait until the airway is secure before actually placing the chest tube.

C.4. What are the options for managing this patient's airway?

Choices for induction of anesthesia should be considered in concert with choices for securing the airway and transitioning to positive pressure ventilation. Airway management can occur with the patient awake under topical anesthesia or asleep, with either continued spontaneous ventilation (a “breathe down” induction with a volatile anesthetic) or an immediate transition to positive pressure, as in a rapid sequence induction.

C.5. What are the risks of rapid sequence induction in this patient?

Although most trauma patients are best managed with rapid sequence induction and intubation, this case may represent an exception. Swelling or bleeding in the airway may make intubation physically difficult and the impaling object itself may prevent distal passage of an endotracheal tube. Further, dislodgment due to patient agitation or intubation attempts could precipitate hemorrhage or airway disruption. Finally, the transition from spontaneous to positive pressure ventilation could precipitate a tension pneumothorax.

Stephens CT, Kahntroff S, Dutton RP. The success of emergency endotracheal intubation in trauma patients: a 10-year experience at a major adult trauma referral center. *Anesth Analg*. 2009;109:866-872.

C.6. What anesthetic agents would you use for a rapid sequence induction?

Succinylcholine is the key component of a rapid sequence intubation (RSI). No other relaxant provides as consistently

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good intubating conditions as quickly and as reversibly as succinylcholine. The usual dose for a trauma patient is 1.5 mg per kg—somewhat greater than normal to compensate for a potentially lower cardiac output due to hemorrhage.

Because succinylcholine has no amnestic or analgesic properties, an induction sedative is also indicated in most patients. Any induction agent, including ketamine or etomidate, will precipitate hypotension in the hypovolemic patient with a high endogenous catecholamine level; so care with dosing is required. In young and previously healthy patients, sodium thiopental in a titrated dose from 1 to 5 mg per kg or propofol 0.5 to 2 mg per kg are effective and inexpensive. Etomidate (0.1 to 0.4 mg per kg) is a reasonable choice in elderly patients or in those with known cardiovascular disease.

McCunn M, Grissom TE, Dutton RP. Anesthesia for trauma. In: Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2423-2459.

C.7. How can you minimize the risk of exacerbating cervical spine trauma?

Appropriate precautions must be taken to avoid worsening an occult spinal cord injury. In the worst case, fractures or ligamentous injury can leave the cervical spine so unstable that the normal manipulation of a direct laryngoscopy will injure the spinal cord. This is a low probability event but is of concern to the health care team because quadriplegia is a catastrophic complication.

Manual in-line cervical stabilization has been shown to be safe and effective in protecting the cervical spine over tens of thousands of direct laryngoscopies and is the common approach to urgent intubations in the trauma population. Another option commonly used only in patients with known cervical instability is an awake intubation over a fiberoptic bronchoscope. This approach allows for the least manipulation of the neck but requires a cooperative patient who can tolerate the time required for topical anesthesia of the airway and a slower intubation. Awake fiberoptic intubation also may increase the risk of aspiration in patients with a full stomach, especially if topical anesthesia of the pharynx and vocal cords is provided.

Other intubation devices may also decrease the need for manipulation of the neck. Good results have been achieved with the newer generation of video laryngoscopes, lighted stylet intubations, and use of an intubating stylet with a less forceful laryngoscopy. Manual cervical stabilization is recommended with each of these approaches. In a difficult case such as the present one, the intubation technique chosen should be one that the anesthesiologist is experienced and comfortable with; this factor may be more relevant than the specific technology used.

Cranshaw J, Nolan J. Airway management after major trauma. *Contin Educ Anaesth Crit Care Pain*. 2006;6(3):124-127.

McCunn M, Grissom TE, Dutton RP. Anesthesia for trauma. In: Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2423-2459.

Pierre EJ, McNeer RR, Shamir MY. Early management of the traumatized airway. *Anesthesiol Clin*. 2007;25(1):1-11.

C.8. How can you minimize the risks of aspiration?

Because any significant injury is associated with decreased gastrointestinal motility, all trauma patients are considered to have full stomachs. The risk of aspiration is further increased by intoxication with drugs or alcohol, obesity, the use of analgesics, and injuries to the face, neck, or abdomen that may lead to bleeding within the gastrointestinal tract.

Minimization of risk is a function of how quickly the intubation must be accomplished. One component of prophylaxis is the normal use of rapid sequence induction to minimize the time during which the airway is at risk. Another is the use of cricoid pressure (the Sellick maneuver) to obstruct the upper esophagus against passive reflux, although recent magnetic resonance imaging research has shown significant variability in the relative anatomy of the

cricoid ring and the esophagus, casting doubt on the efficacy of cricoid pressure. Application of cricoid pressure for patients undergoing RSI is controversial. Not only might cricoid pressure not be effective in preventing aspiration, it may worsen laryngoscopic view and impair bag-valve-mask ventilation. Some experts think that cricoid pressure should be

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applied in trauma patients and patients at risk for aspiration; however, cricoid pressure, if necessary, should be altered or removed to facilitate intubation. In the case under consideration, there would be a risk of dislodging the impaling object, making cricoid pressure inadvisable. It would be reasonable to administer an H_2 antagonist such as cimetidine and a promotility agent such as metoclopramide if time allowed, but these agents would require 1 to 2 hours to have any substantial effect. An oral antacid is contraindicated because of the potential injury to the esophagus.

Smith KJ, Dobranowski J, Yip G, et al. Cricoid pressure displaces the esophagus: an observational study using magnetic resonance imaging. *Anesthesiology*. 2003;99(1):60-64.

Stewart JC, Bhanaker S, Ramaiah R. Rapid-sequence intubation and cricoid pressure. *Int J Crit Illn Inj Sci*. 2014;4(1):42-49.

C.9. How would you anesthetize the airway for an awake intubation?

Innervation of the airway can be separated into three neural pathways. If nasal intubation is planned, some method of anesthetizing maxillary branches from the trigeminal nerve is required. Involvement of the posterior tongue will require blockade of the glossopharyngeal nerve. Structures more distal in the airway to the epiglottis will require blockade of vagal branches, with the superior laryngeal nerve supplying the pharyngeal apparatus and the recurrent laryngeal nerve supplying the vocal cord and the tracheal mucosa.

The trigeminal nerve, which supplies sensory innervation to the nasal mucosa, can be anesthetized by inserting a nasal airway lubricated with lidocaine jelly into the patent naris. Mixing the lidocaine jelly with oxymetazoline 0.05%, phenylephrine 10 mg, or 4% cocaine may help vasoconstrict the nasal blood vessels and diminish bleeding from the nasal mucosa. The liquid local anesthetic and vasoconstrictor may also be applied in droplet form from a syringe.

The glossopharyngeal nerves of interest are the tonsillar nerves, which provide sensation to the mucosa overlying the palatine tonsil and continuous parts of the soft palate, and the sensory branches to the posterior one-third of the tongue. First, one must provide topical intraoral anesthesia with local anesthetic spray or nebulized lidocaine. Following topical anesthesia of the tongue, the mouth is opened wide and the posterior tonsillar pillar (palatopharyngeal fold) is identified. Then, a 22-gauge needle can be inserted at the caudad portion of the tonsillar pillar. The needle tip is inserted submucosally and following careful aspiration for blood, 5 mL of 0.5% lidocaine is injected. The block is then repeated on the contralateral side. A similar block can be performed with direct application of anesthetic soaked cotton to the bilateral tonsillar fossae.

The vagus nerve supplies innervation to the mucosa of the airway from the level of the epiglottis to the distal airways through both the superior and recurrent laryngeal nerves. A superior laryngeal nerve block and a translaryngeal block can be useful in anesthetizing these pathways. With the patient lying supine, the superior laryngeal block is done with a 22-gauge needle attached to a syringe, which is directed at the most posterior palpable part of the hyoid bone, near the greater cornu, and anterior to the carotid sheath. The needle must be parallel to the table and never directed posteriorly for fear of penetrating the carotid sheath. When the needle strikes the hyoid, it is carefully walked caudad until it just slips off the hyoid and then advanced a short distance through the hyothyroid membrane. Aspiration should produce nothing. Then, 2 mL of 2% lidocaine is injected and the block repeated on the opposite side.

The translaryngeal block is performed with a 20- or 22-gauge needle attached to a syringe. The needle is inserted through the cricothyroid membrane in the midline and air is aspirated. The patient is asked to inhale deeply and then to exhale fully. At the end of expiration, 4 mL of 2% to 4% lidocaine is injected rapidly and the needle is quickly removed. The resultant coughing will ensure a wide distribution of local anesthetic droplets throughout

the airway. If stability of the cervical spine is in doubt, then in-line stabilization should be held while the block is performed and coughing occurs. In the present case, both superior laryngeal and transtracheal blocks would be difficult to perform, and induced coughing might exacerbate the injury. Administration of nebulized lidocaine might be a safer choice.

Brown DL. *Atlas of Regional Anesthesia* . 4th ed. Philadelphia, PA: WB Saunders; 2010:191-196.

Gotta AW, Sullivan CA. Anaesthesia of the upper airway using topical anaesthetic and superior laryngeal nerve block. *Br J Anaesth*. 1981;53:1055-1058.

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C.10. What are the risks of awake fiberoptic intubation?

The greatest risk of awake fiberoptic intubation is deterioration of the patient's airway and/or mental status during the procedure. Ineffective topical anesthesia can lead to agitation and combativeness, which in turn leads to increased use of intravenous sedatives. Blood and secretions in the airway can cause coughing, laryngospasm, or aspiration. Oversedation causes respiratory depression and desaturation, which can pressure the anesthesia providers and lead to hasty decisions. More uncommon complications include injury to nerves or vessels during local nerve blocks, toxicity from local anesthesia ingestion, and direct injury to the laryngeal or pharyngeal mucosa.

This particular case also includes the possibility of inadvertent dislodgment of the impaling tree branch during sedation and topicalization or during the intubation effort itself. Bleeding from a loss of tamponade or open disruption of the airway could necessitate a sudden change in anesthetic and surgical plans. Although awake fiberoptic intubation in the OR is a reasonable starting point for this case, the anesthesiologists and surgeons involved must be prepared for other eventualities. These would include both RSI and emergency surgical airway access.

C.11. If the patient cannot be ventilated, what options are available?

Failure of awake fiberoptic intubation in this case should be followed by an immediate attempt at RSI. If RSI is not possible and the patient cannot be ventilated by mask or LMA, then a surgical airway may be required. An alternate technique involves placing a 14-gauge catheter over a needle through the cricothyroid membrane, removing the needle and using the catheter for jet ventilation. This technique provides a temporary route for oxygenation, as a bridge to a surgical airway, but is highly tenuous. Kinking or dislodgment of the jet catheter are common complications, with tension pneumothorax a possibility if the catheter tip is displaced into the paratracheal tissues. In this case, accessibility to the trachea or cricoid cartilage may be difficult or impossible due to the impaling object.

Benumof JL, Scheller MS. The importance of transtracheal jet ventilation in the management of the difficult airway. *Anesthesiology*. 1989;71:769-778.

C.12. Would a laryngeal mask airway (LMA) or other pharyngeal airway be of assistance?

Although an LMA or other supraglottic airway support device is often a great help in the difficult airway algorithm, this case may represent an exception. Establishing an efficient mask airway is beneficial if the cause of patient distress is neurologic (diminished respiratory drive due to anesthesia or traumatic brain injury) or related to pharyngeal anatomy (obstruction after muscle relaxation). Supraglottic ventilation will not help with more distal causes of airway obstruction, such as laryngospasm, tracheal disruption, or massive aspiration. Although an LMA or equivalent device should be on hand when this patient is brought to the OR, it is less likely to be of use.

C.13. What surgical airway options are available in this case?

As with the LMA, surgical airway access is beneficial when the cause of airway obstruction is proximal to the intervention. Cricothyroidotomy—the fastest and most readily performed surgical airway procedure—is therefore of benefit in patients who cannot be intubated and have

airway obstruction involving the pharynx or larynx. This procedure may be accomplished by surgical opening of the cricothyroid membrane and placing an endotracheal tube into the trachea. Operative cricothyrotomy can be performed more rapidly than conventional tracheostomy; however, it is more traumatic to the larynx, and the cricothyrotomy tube should be removed after 24 hours. If the patient cannot be decannulated at this time, a conventional tracheostomy should replace the cricothyrotomy.

Tracheostomy, performed lower in the airway, requires more extensive surgical dissection, takes longer, and carries a greater risk of hemorrhage secondary to thyroid tissue trauma. Surgical access to the lower trachea might be necessary in the present case if the impaling object has transected or significantly disrupted the airway. This would be accomplished essentially through the wound itself but would require a partial or complete median sternotomy and the full resources of the OR.

Britt LD, Weireter LJ, Cole FJ. Management of acute neck injuries. In: Feliciano DV, Mattox KL, Moore EE, eds. *Trauma*. 6th ed. New York: McGraw-Hill; 2008:467-478.

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C.14. What maintenance anesthetics are indicated or contraindicated in this patient?

If the initial awake fiberoptic examination of the trachea (at the time of intubation) rules out an airway injury, then muscle relaxation to facilitate surgical exploration would be appropriate for the duration of the case. Any of the commonly used intermediate-acting nondepolarizing relaxants could be used. If an airway injury is present, then management of the patient using inhalational anesthesia alone, with continued spontaneous ventilation, offers additional security in the event of airway discontinuity during the course of surgical repair. Sevoflurane, because of its greater palatability, is the easiest volatile anesthetic to administer without interrupting the patient's ventilation. Care must be taken to ensure adequate fluid volume replacement during a pure inhalational anesthetic since hemodynamic instability is possible. Nitrous oxide is contraindicated when the potential for pneumothorax exists or when airway continuity is in doubt.

Narcotics certainly will be required for postoperative analgesia and may offer some intraoperative advantages as well. Once airway patency is assured, a narcotic-based anesthetic provides for the lowest level of circulating catecholamines, making it easier to assess and manage fluid resuscitation. The usual concern with delayed emergence in a patient receiving a large dose of narcotics is not relevant in this case, as the patient will most likely require postoperative mechanical ventilation. The only caveat to intraoperative narcotics is the potential need to sustain spontaneous ventilation while the airway is assessed; narcotic administration should, therefore, be delayed until the anesthetic and surgical plans have become clear.

C.15. What complications will the surgical plan introduce?

Maintenance of homeostasis in the face of surgical provocations is the theme of many anesthetics, and the present case is no exception. At some point—ideally after anesthetic induction, successful airway management, and placement of lines and monitors—the impaling object is going to be removed from the patient's neck. Blunt object impalements in patients seen alive in the trauma center may produce less organ-specific damage than predicted from the location and course of the injury due to the ability of mobile anatomic structures to deform away from low-speed penetrations. Even so, it is entirely possible that this object has injured one of the great vessels or the trachea and that removing it might lead to torrential bleeding or significant disruption of the airway. The anesthesia team must be prepared to change course rapidly from a spontaneous breathing inhalational approach (assuming that airway continuity is the initial concern) to a hemodynamically friendly narcotic-based approach if blood loss and hemorrhagic shock become the major issue. An open team discussion of both surgical and anesthetic plans, including likely contingencies, is highly recommended before beginning definitive treatment.

Dutton RP. Shock management. In: Smith CE, ed. *Trauma Anesthesia*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2015:65-78.

D. Postoperative Management

D.1. What are the criteria for extubation?

Assuming that the case goes well and the patient's anatomic injuries are successfully repaired, it is appropriate to consider emergence and extubation when the following criteria are satisfied:

- Hemodynamic stability with complete cessation of bleeding and normal systemic coagulation.
- Adequate respiratory drive and reserve including complete return of neuromuscular function and minimal requirement for ventilator support.
- Acceptable mental status. The patient should be calm, cooperative, comfortable, not overly sedated, and recovered from acute intoxication. The patient should be able to follow commands.
- Evidence of airway patency. Edema at the site of injury will not be an issue with an endotracheal tube in place but might obstruct the airway quickly following extubation. Although not 100% predictive, the presence of an air leak around the endotracheal tube when the cuff is deflated is very reassuring.
- Completion of the diagnostic workup for high-energy trauma, including indicated CT scans, laboratory studies, and completion of all procedures that are likely to require general anesthesia. It would be poor judgment to extubate the patient after tracheal repair only to have the orthopedic surgeons schedule him for urgent pelvic surgery.

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McCunn M, Grissom TE, Dutton RP. Anesthesia for trauma. In: Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2423-2459.

D.2. What techniques may be used during extubation?

The best results from extubation will be achieved when the patient is most calm and comfortable and when the extubation itself is as nonstimulating as possible. The appropriate level of sedation and analgesia is a complicated, controversial, and very important question. Sedative agents, such as benzodiazepines and propofol, will diminish the patient's respiratory drive, cooperation, and ability to protect the airway, and should be minimized. The right level of narcotics, on the other hand, will allow for a comfortable patient with diminished airway reactivity, who can open his eyes and follow commands but is not otherwise distressed by the endotracheal tube or ventilator. The endotracheal tube should be suctioned ahead of time, and extubation deferred if there are copious secretions. Enough time should be allowed after suctioning for the stimulation to pass and the patient to relax. The posterior pharynx is then suctioned; the patient is asked to inhale deeply; the cuff is deflated, and the endotracheal tube is removed in one swift motion as the patient exhales.

The airway is in jeopardy immediately after extubation because edema and secretions may compromise respiratory function. Continuous pulse oximetry in a monitored setting is required and humidified oxygen should be administered for 24 hours postextubation.

D.3. How does alcohol abuse affect postoperative management?

Symptomatic withdrawal from alcohol usually occurs within 24 hours and manifests as agitation, tachycardia, and hypertension. Delirium tremens can occur thereafter if prophylactic therapy is not initiated. Prophylaxis should consist of a small basal dose of benzodiazepines or a low-dose intravenous alcohol infusion, with frequent assessment of mental status and the willingness to provide supplemental short-acting benzodiazepines if symptoms develop. The plan for delirium tremens prophylaxis should be coordinated with the pain management plan, ideally under the direction of a single individual, to provide for overall consistency and to avoid oversedation and respiratory arrest secondary to polypharmaceutical administration.

D.4. What pain medication should be used?

Postoperative analgesia in this case will depend on the extent of the surgical procedure and on the individual tolerance of the patient. Soft-tissue exploration of the neck, including surgery

on the trachea or major vessels, requires relatively little postoperative analgesia. Titrated intravenous narcotics can be used in the first 24 hours with a rapid transition to an oral narcotic/acetaminophen preparation thereafter. Median sternotomy or other significant extension of the surgery into the chest will necessitate more intensive postoperative analgesia, including a continuous narcotic infusion while the patient remains intubated, followed by intravenous patient-controlled analgesia after emergence and extubation. Nonsteroidal anti-inflammatory drugs are an appropriate adjuvant therapy once the risk of traumatic hemorrhage is past.

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Chapter 34
Open-Eye Injury

Theresa T. Kudlak

A 28-year-old, otherwise, healthy man presented to the emergency room with a fishhook embedded in his eye. He ate a full meal just before the fishing accident.

A. Medical Disease and Differential Diagnosis

1. Why is this patient a particular challenge to the anesthesiologist?
2. What are the determinants of intraocular pressure (IOP) under normal circumstances? What is the normal range? What was the expected IOP in this patient's injured eye?
3. How is aqueous humor formed and eliminated?
4. How is IOP affected by arterial PCO_2, systemic blood pressure, coughing and vomiting, deep inspiration, and hypoxemia?
5. What is the role of the central nervous system (CNS) on IOP?
6. What is glaucoma?
7. Is atropine contraindicated in patients with glaucoma?
8. How do carbonic anhydrase inhibitors work to decrease IOP? By what mechanism may osmotic agents decrease IOP?
9. Are carbonic anhydrase inhibitors or osmotic diuretics indicated in open-globe injuries?
10. Are topically applied ophthalmic medications absorbed systemically? How can this absorption be reduced? Which eyedrops may have effects that are of concern to the anesthesiologist?

B. Preoperative Evaluation and Preparation

1. Is an open-globe injury always a surgical emergency?
2. What preoperative evaluation would you require?
3. The patient ate shortly before the accident. Would you attempt to pass a nasogastric tube or to administer emetics to empty the stomach?
4. Could this case be done with topical anesthesia or a retrobulbar block?
5. How would you premedicate this patient?

C. Intraoperative Management

1. What are some factors that may increase the risk of vitreous herniation during induction and maintenance of anesthesia?
2. Will you intubate this patient? Would you consider a laryngeal mask airway? How does intubation affect IOP? How can this effect be minimized?
3. Would you consider an awake intubation?
4. Is succinylcholine contraindicated in open-globe injuries? How does succinylcholine affect IOP?

5. Does pretreatment with nondepolarizing muscle relaxants prevent the succinylcholine-induced elevation in IOP?
6. How do nondepolarizing muscle relaxants affect IOP?

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7. How will you perform a rapid sequence induction and intubation without using succinylcholine?
8. What are the effects of ketamine on the eye?
9. Would you consider the use of etomidate as an induction agent? What about propofol?
10. How do inhalation agents affect IOP and by what mechanism?
11. During the procedure, the patient's pulse suddenly dropped to 40 beats per minute. What do you think was happening? What is the oculocardiac reflex (OCR)?
12. What are the afferent and efferent pathways of the OCR?
13. What factors contribute to the incidence of the OCR?
14. How do you diagnose and treat the OCR?
15. Is atropine useful for the OCR?
16. Can a retrobulbar block prevent the OCR? Is it appropriate in this patient?

D. Postoperative Management

1. Would you reverse the neuromuscular blockade in this patient?
2. Do reversal doses of atropine affect IOP?
3. What would you do before extubating this patient?
4. When would you extubate this patient?
5. The patient awakened in the recovery room and complained of pain and tearing in the opposite eye. The conjunctiva was inflamed. What was the likely cause?
6. Will taping the eyes shut or applying ointment prevent corneal abrasions? Are there any contributing factors?
7. What should you do when you suspect your patient might have a corneal abrasion?
8. A month after the surgical repair, the patient complained of impaired vision in the operative eye. He was examined and found to have a detached retina. As part of the surgical treatment, the ophthalmologist injected a gas bubble into the patient's posterior chamber. Why is this important to an anesthesiologist?

A. Medical Disease and Differential Diagnosis

A.1. Why is this patient a particular challenge to the anesthesiologist?

The combination of a full stomach and an open-globe injury presents a unique challenge to the anesthesiologist. In addition to the increased risk of aspiration of gastric contents, any drug or maneuver that raises IOP in the injured, open eye may cause extrusion of the vitreous humor and loss of vision when the globe is opened.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

Holloway KB. Control of the eye during general anaesthesia for intraocular surgery. *Br J Anaesth*. 1980;52:671-679.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2521.

A.2. What are the determinants of intraocular pressure (IOP) under normal circumstances? What is the normal range? What was the expected IOP in this patient's injured eye?

IOP is determined by the balance between production and drainage of aqueous humor, by changes in choroidal blood volume, and by vitreous volume and extraocular muscle tone. Resistance to outflow of aqueous humor in the trabecular tissue is probably the factor that maintains IOP within physiologic range, but the mechanism of homeostasis is unknown.

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Normal IOP is 12 to 16 torr in the upright posture and increases by 2 to 4 torr in the supine position. IOP has been observed to nearly double in steep head-down position in the operating room.

When the globe is open, the IOP is lowered and may be as low as ambient pressure. The concern in this case is for the relative volume of choroid and vitreous humor within the eye. If this volume increases while the eye is open, the vitreous humor may be lost. Any deformation of the eye by external pressure in the globe may cause an increase in IOP.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

Jay JL. Functional organization of the human eye. *Br J Anaesth*. 1980;52:649-654.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83-98.

Kumar C, Dodds C, Fanning G, eds. *Ophthalmic Anaesthesia*. Lisse, The Netherlands: Swets & Zeitlinger BV; 2002:23-25.

LeMay M. Aspects of measurement in ophthalmology. *Br J Anaesth*. 1980;52:655-662.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2513-2514.

A.3. How is aqueous humor formed and eliminated?

Aqueous humor is a clear fluid that occupies the anterior and posterior chambers of the eye. Its total volume is 0.3 mL. Aqueous humor is produced primarily by an active secretory process from the ciliary body in the posterior chambers at an equilibrium rate of 2 μL per minute. The aqueous humor then circulates through the pupil to the anterior chamber, passes through the trabeculated Fontana spaces, and enters Schlemm canal. From here, the fluid drains into the episcleral veins and finally into the cavernous sinus or jugular venous systems (Fig. 34.1).

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

Jay JL. Functional organization of the human eye. *Br J Anaesth*. 1980;52:649-654.

LeMay M. Aspects of measurement in ophthalmology. *Br J Anaesth*. 1980;52:655-662.

McGoldrick K, ed. *Anesthesia for Ophthalmic and Otolaryngologic Surgery*. Philadelphia, PA: WB Saunders; 1992:180-182.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2513-2514.

A.4. How is IOP affected by arterial PCO_2, systemic blood pressure, coughing and vomiting, deep inspiration, and hypoxemia?

The choroidal arterioles vasodilate in response to hypercapnia and constrict during hypocapnia, thereby changing intraocular volume and pressure. However, the effect is minimal within the normal physiologic range of PCO_2.

Minor fluctuations in arterial blood pressure also have minimal effects on IOP, although IOP may be seen to increase when hypertension is sustained and can fall significantly with induced hypotension. Changes in venous pressure, on the other hand, have a major impact on IOP. Vomiting, coughing, and bucking on the endotracheal tube cause a dramatic

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increase in IOP by 30 to 40 torr. These actions, and also Valsalva maneuver, cause congestion in the venous system, which impedes the outflow of aqueous humor and increases the volume of choroidal blood. A deep inspiration may reduce IOP by 5 torr. Hypoxemia may increase IOP through choroidal vasodilatation.

Beulen P, Rotteveel J, de Haan A, et al. Ultrasonographic assessment of congestion of the choroid plexus in relation to the carbon dioxide pressure. *Eur J Ultrasound*. 2000;11:25-29.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin*. 1990;28(2):83-88.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2513-2514.

Murphy DF. Anesthesia and intraocular pressure. *Anesth Analg*. 1985;64:520-530.

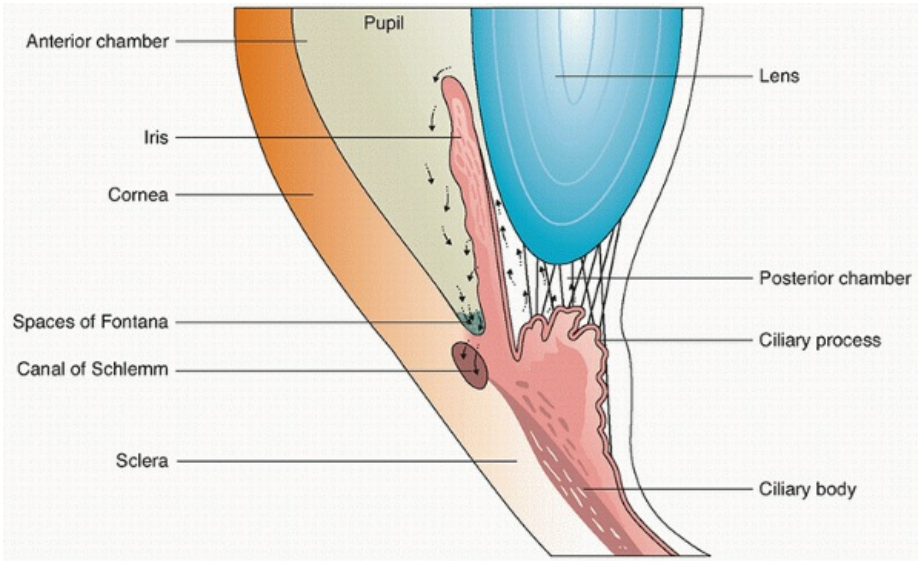


FIGURE 34.1 Sites of formation, circulation, and drainage of aqueous humor. (Modified from Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J.* 1986;33:197, with permission.)

A.5. What is the role of the central nervous system (CNS) on IOP?

The CNS influences IOP through alterations in extraocular muscle tone or, indirectly, by hormonal or hemodynamic changes.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2513-2514.

A.6. What is glaucoma?

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Glaucoma is a pathologic elevation of IOP caused by increased resistance to outflow of aqueous humor from the anterior chamber of the eye. It is classified as either open- or closed-angle glaucoma, depending on the anatomy and pathophysiology. Chronic elevation of IOP interferes with the intraocular blood supply and normal metabolism of the cornea. It can result in corneal opacities or decreased retinal blood flow.

The pathophysiology in open-angle glaucoma involves increased resistance to the flow of aqueous humor through Fontana spaces as a result of scarring of the trabecular network or thickening of the endothelial covering of these channels. In closed-angle glaucoma, the iris bulges forward blocking the access of aqueous humor to the trabecular network. This may occur with pupillary dilation or an acutely swollen lens.

Johnson DH, Brubaker RF. Glaucoma: an overview. *Mayo Clin Proc*. 1986;61:59-67.

LeMay M. Aspects of measurement in ophthalmology. *Br J Anaesth*. 1980;52:655-662.

A.7. Is atropine contraindicated in patients with glaucoma?

Topical atropine in the eye is generally contraindicated in patients with glaucoma, especially in those with closed-angle glaucoma. Atropine, studied in a single dose of 0.01 mg per kg, administered intramuscularly (IM), or given orally as 0.6 mg in two doses 4 hours apart,

caused no increase in IOP in either open- or closed-angle glaucoma because by calculation, only approximately 0.0001 mg reaches the eye, which is far less than topical dose. Intravenous atropine is associated with mydriasis and might be contraindicated in patients with glaucoma; however, preemptive topical use of pupillary constrictors such as pilocarpine and timolol avoid this problem.

Adams AK, Jones RM. Anaesthesia for eye surgery: general considerations. *Br J Anaesth*. 1980;52:663-669.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1376-1377.

Greenstein SH, Abramson DH, Pitts WR III. Systemic atropine and glaucoma. *Bull N Y Acad Med*. 1984;60:961-968.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2513-2514.

Schwartz B. Current concepts in ophthalmology: the glaucomas. *N Engl J Med*. 1978;299:182-184.

A.8. How do carbonic anhydrase inhibitors work to decrease IOP? By what mechanism may osmotic agents decrease IOP?

Carbonic anhydrase inhibitors, such as acetazolamide, interfere with the sodium-pump mechanism necessary for secretion of aqueous humor. An intravenous dose acts in 5 minutes, with maximal effect in 20 to 30 minutes. Chronic acetazolamide therapy may result in potassium depletion.

Osmotic agents, such as mannitol, increase plasma oncotic pressure relative to that of aqueous humor and produce an acute, transient drop in IOP. The maximum reduction in IOP occurs after 30 to 45 minutes and the effect lasts 5 to 6 hours.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1376.

McGoldrick KE. Ocular drugs and anesthesia. *Int Anesthesiol Clin*. 1990;28(2):72-77.

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A.9. Are carbonic anhydrase inhibitors or osmotic diuretics indicated in open-globe injuries?

No. If the globe is open, the IOP is low and these agents are not useful. In addition, they may cause transient choroidal congestion, which could lead to loss of ocular contents.

Smith GB. *Ophthalmic Anaesthesia*. Baltimore: University Park Press; 1983.

A.10. Are topically applied ophthalmic medications absorbed systemically? How can this absorption be reduced? Which eyedrops may have effects that are of concern to the anesthesiologist?

Topical ophthalmic drugs may be absorbed through the conjunctiva or may drain through the nasolacrimal duct and be absorbed through the nasal mucosa. Absorption is increased when the eye is instrumented, diseased, or traumatized. Finger pressure on the inner canthus for a few minutes after instillation of eyedrops will impede absorption by occluding the nasolacrimal duct.

Usage of the following topical medications may have implications for the anesthesiologist:

Atropine

Atropine is used to produce mydriasis and cycloplegia. The 1% solution contains 0.2 to 0.5 mg of atropine per drop. Systemic reactions, seen primarily in children and older adults, include tachycardia, flushing, thirst, dry skin, and agitation. Atropine is contraindicated in closed-angle glaucoma.

Scopolamine

One drop of the 0.5% solution has 0.2 mg of scopolamine. CNS excitement can be treated with physostigmine, 0.015 mg per kg intravenously (IV), repeated one or two times in a 15-minute period. Scopolamine is contraindicated in closed-angle glaucoma.

Cyclopentolate (Cyclogyl)

Cyclopentolate, a short-acting mydriatic and cycloplegic, may cause transient neurotoxic effects such as incoherence, visual hallucinations, slurred speech, ataxia, and seizures. It is contraindicated in closed-angle glaucoma.

Tropicamide (Mydriacyl)

Tropicamide is used to produce mydriasis for refraction or funduscopic examination. It may have CNS effects and can elevate IOP in closed-angle glaucoma.

Phenylephrine Hydrochloride (Neo-Synephrine)

Phenylephrine hydrochloride is used to produce capillary decongestion and pupillary dilatation. Applied to the cornea, phenylephrine hydrochloride can cause palpitations, nervousness, tachycardia, headache, nausea and vomiting, severe hypertension, reflex bradycardia, and subarachnoid hemorrhage. Solutions of 2.5%, 5%, and 10% (6.25-mg phenylephrine per drop) are available. The dose is one drop per eye per hour of the 2.5% solution (children) or the 5% solution (adults).

Epinephrine

Topical 2% epinephrine will decrease aqueous secretion, improve outflow, and lower IOP in open-angle glaucoma. Side effects include hypertension, palpitations, fainting, pallor, and tachycardia. The effects last approximately 15 minutes. One drop of 2% solution contains 0.5 to 1 mg of epinephrine. Epinephrine 1:200,000 in a balanced salt solution is sometimes continuously infused into the anterior chamber during cataract surgery. Systemic effects may occur.

Timolol Maleate (Timoptic)

Timolol maleate is a β-blocker used in the treatment of chronic glaucoma. Side effects include light-headedness, fatigue, disorientation, depressed CNS function, and exacerbation of asthma. Bradycardia and bronchospasm may occur as well as potentiation of systemic β-blockers.

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Betaxolol Hydrochloride (Betoptic)

Betaxolol HCl is a cardioselective (β_1) blocking agent used to treat glaucoma. It may be hazardous in patients with sinus bradycardia, heart block, or heart failure.

Acetylcholine

Acetylcholine may be injected intraoperatively into the anterior chamber to produce miosis. Side effects are due to its parasympathetic action and include hypotension, bradycardia, and bronchospasm. Intravenous atropine is an effective treatment.

Echothiophate Iodide (Phospholine Iodide)

Echothiophate iodide, a cholinesterase inhibitor, is used as a miotic agent. It may prolong the effect of both succinylcholine and ester-type local anesthetics. Levels of pseudocholinesterase decrease by 80% after 2 weeks on the drug. It takes 3 to 6 weeks for return to normal pseudocholinesterase activity after stopping the drug (4 weeks for return to 75% activity). Succinylcholine and ester-type local anesthetics should be avoided. Demecarium is another such cholinesterase inhibitor.

Cocaine

Cocaine is used to produce vasoconstriction and to shrink mucous membranes during dacryocystorhinostomy. One drop of 4% solution contains approximately 1.5 mg of cocaine, and the maximum dose is approximately 3 mg per kg. Systemic effects may be seen with a dose as low as 20 mg and involve the CNS, respiratory, and cardiovascular systems.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1380-1381.

Fraunfelder FW, Fraunfelder FT, Jensvold B. Adverse systemic effects from pledgets of topical ocular phenylephrine 10%. *Am J Ophthalmol*. 2002;134:624-625.

Johnson DH, Brubaker RF. Glaucoma: an overview. *Mayo Clin Proc*. 1986;61:59-67.

McGoldrick KE. Ocular drugs and anesthesia. *Int Anesthesiol Clin*. 1990;28(2):72-77.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2514.

B. Preoperative Evaluation and Preparation

B.1. Is an open-globe injury always a surgical emergency?

No. In most cases, surgery is not required immediately and some time may be spent in adequately preparing the patient for anesthesia and surgery. However, the surgery should probably be performed within 12 hours to minimize the possibility of infection and other

complications. Delaying surgery for gastric emptying to occur is not reliable as gastric emptying may be prolonged in this stressful situation.

Arthur DS, Dewar KM. Anaesthesia for eye surgery in children. *Br J Anaesth*. 1980;52:681-688.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83-98.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2521.

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B.2. What preoperative evaluation would you require?

An accurate, thorough history and physical examination are the best means of evaluating this patient preoperatively and should reveal any existing medical problems that will guide your selection of preoperative laboratory tests.

In this otherwise healthy young patient, no routine laboratory tests are indicated, unless required by the institution in which you are practicing. In cases where more extensive trauma is suspected, other injuries must also be addressed such as fractures to the skull and orbit, intracranial hemorrhage, and any other injuries suggested by the history and physical examination.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1381-1383.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2514-2515.

B.3. The patient ate shortly before the accident. Would you attempt to pass a nasogastric tube or to administer emetics to empty the stomach?

Absolutely not. These procedures are contraindicated when there has been a perforation of the eye. Gagging, vomiting, and straining could cause a potentially disastrous increase in IOP and extrusion of intraocular contents. A cough can increase central venous pressure and choroidal blood volume and may raise IOP by 34 to 40 torr.

Adams AK, Jones RM. Anaesthesia for eye surgery: general considerations. *Br J Anaesth*. 1980;52:663-669.

Arthur DS, Dewar KM. Anaesthesia for eye surgery in children. *Br J Anaesth*. 1980;52:681-688.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83-98.

B.4. Could this case be done with topical anesthesia or a retrobulbar block?

General anesthesia is the preferred technique for open-globe injuries. The patient is completely immobilized, and there is no time limit for the procedure. In this case, because the patient is not fasting, an endotracheal tube will guard against aspiration.

A retrobulbar or peribulbar injection has the potential to increase IOP because of the volume of local anesthetic used and the likelihood of the patient squeezing his eyes during the injection. However, there have been reports of blocks being used successfully for the repair of open-globe injuries. Topical anesthesia with intravenous sedation also has been used to repair the globe in select patients with limited injury when general anesthesia is contraindicated.

Boscia F, La Tegola MG, Columbo G, et al. Combined topical anesthesia and sedation for open-globe injuries in selected patients. *Ophthalmology*. 2003;110:1555-1559.

Lo MW, Chalfin S. Retrobulbar anesthesia for repair of ruptured globes. *Am J Ophthalmol*. 1997;123:833-835.

Scott IU, Mccabe CM, Flynn HW, et al. Local anesthesia with intravenous sedation for surgical repair of selected open globe injuries. *Am J Ophthalmol*. 2002;134:707-711.

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B.5. How would you premedicate this patient?

Premedications should be given parenterally because gastrointestinal absorption is unreliable. Sedatives and anxiolytics may be given as necessary. Metoclopramide (0.15 mg per kg IM or IV) may be used to facilitate gastric emptying and to increase the tone of the cardiac, lower esophageal, sphincter. Narcotics should be used cautiously because they may cause nausea and vomiting. Nonparticulate antacids and H_2 receptor antagonists (cimetidine 2 mg

per kg IM) should be considered to reduce the risk of aspiration pneumonitis. Intravenous droperidol (0.01 mg per kg) or ondansetron (0.1 mg per kg) can be given for antiemesis.

Atropine or glycopyrrolate will be useful to reduce secretions and gastric acidity, and they may also inhibit the OCR.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1383.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

C. Intraoperative Management

C.1. What are some factors that may increase the risk of vitreous herniation during induction and maintenance of anesthesia?

Factors that may increase the risk of vitreous herniation during induction and maintenance of anesthesia include the following:

- Face mask pressing on the eyeball
- Increased pressure from coughing, straining, bucking, and head-down position
- Extraocular muscle spasm induced by depolarizing muscle relaxants or surgical stimulation during light anesthesia
- Poorly applied cricoid pressure that blocks venous drainage from the eye
- Choroidal congestion from hypercarbia, hypoxia, osmotic diuretics, intubation, or increases in blood pressure

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

Holloway KB. Control of the eye during general anaesthesia for intraocular surgery. *Br J Anaesth*. 1980;52:671-679.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83-98.

Libonati MM, Leahy JJ, Ellison N. The use of succinylcholine in open eye surgery. *Anesthesiology*. 1985;62:637-640.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2512-2518.

C.2. Will you intubate this patient? Would you consider a laryngeal mask airway? How does intubation affect IOP? How can this effect be minimized?

It is imperative that this patient be intubated not only to maintain the airway, which is close to the surgical field, but also to avoid pressure by a face mask on the eyeball and to minimize the risk of aspiration. Although the laryngeal mask airway has been used successfully in ophthalmologic anesthesia, it is not appropriate in this case because it does not protect the airway from aspiration. Many studies have demonstrated a significant increase in IOP caused by laryngoscopy and

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intubation under varying states of anesthetic depth and muscle relaxation. IOP may be increased even when there is no visible reaction to intubation. This increase in IOP can be attenuated by topical laryngeal anesthesia and by increased depth of anesthesia to reduce coughing, straining, and increases in blood pressure. The cardiovascular response to intubation can also be reduced by intravenous lidocaine (1.5 mg per kg), β-blockers, α_2-agonists, or calcium channel blockers. Topical anesthesia of the larynx is not recommended in a full-stomach situation because of the increased risk of aspiration.

Akhtar TM, McMurray P, Kerr WJ, et al. A comparison of laryngeal mask airway with tracheal tube for intraocular ophthalmic surgery. *Anaesthesia*. 1992;47:668-671.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1383-1387.

Cook JH. The effect of suxamethonium on intraocular pressure. *Anaesthesia*. 1981;36:359-365.

Gefke K, Andersen LW, Friesel E. Lidocaine given intravenously as a suppressant of cough and laryngospasm in connection with extubation after tonsillectomy. *Acta Anaesthesiol Scand*. 1983;27:111-112.

Libonati MM, Leahy JJ, Ellison N. The use of succinylcholine in open eye surgery. *Anesthesiology*. 1985;62:637-640.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2521.

C.3. Would you consider an awake intubation?

Awake intubation is frequently accompanied by coughing and bucking and is risky in an open-globe injury when other safe methods of intubation are available. However, when dealing with a possible compromised airway or difficult intubation, an awake fiberoptic intubation expertly done under careful sedation may be indicated to safely secure the airway.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin*. 1990;28(2):83-88.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83-98.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2512-2518.

C.4. Is succinylcholine contraindicated in open-globe injuries? How does succinylcholine affect IOP?

The use of succinylcholine in open-globe injuries is controversial. In the intact eye, following thiopental induction, succinylcholine has been shown to increase IOP by 6 to 8 torr between 1 and 4 minutes after administration. Tracheal intubation further increases IOP. IOP returns to baseline in 5 to 7 minutes. In open-globe injuries, succinylcholine use has been associated with loss of ocular contents. The increase in IOP may be mediated by prolonged tonic contraction of the extraocular muscles, although IOP has been shown to rise after succinylcholine even when the extraocular muscles have been severed. Other factors that may be contributory include choroidal blood flow, increased central venous pressure, and increased resistance to outflow of aqueous humor resulting from the cycloplegic effects of succinylcholine.

The hemodynamic response to laryngoscopy or intubation may have a much more significant effect on IOP than succinylcholine alone. Simply blinking will raise the IOP in a normal eye by 10 to 15 torr, similar to the effect of succinylcholine. Pretreatment with nifedipine or lidocaine may attenuate the increase in IOP following succinylcholine and intubation.

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Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin*. 1990;28(2):83-88.

Cook JH. The effect of suxamethonium on intraocular pressure. *Anaesthesia*. 1981;36:359-365.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

Holloway KB. Control of the eye during general anaesthesia for intraocular surgery. *Br J Anaesth*. 1980;52:671-679.

Kelly RE, Dinner M, Turner LS, et al. Succinylcholine increases intraocular pressure in the human eye with the extraocular muscles detached. *Anesthesiology*. 1993;79:948-952.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83-98.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2512-2518.

Moreno RJ, Kloess P, Carlson DW. Effect of succinylcholine on the intraocular contents of open globes. *Ophthalmology*. 1991;98:636-638.

Murphy DF, Davis NJ. Succinylcholine use in emergency eye operation. *Can J Anaesth*. 1987;34:101-102.

Smith RB, Babinski M, Leano N. The effect of lidocaine on succinylcholine-induced rise in intraocular pressure. *Can Anaesth Soc J*. 1979;26:482-483.

C.5. Does pretreatment with nondepolarizing muscle relaxants prevent the succinylcholine-induced elevation in IOP?

Available data are contradictory on this question, probably reflecting different methods of IOP measurement under varying depths of anesthesia with a variety of anesthetic adjuvant agents. Many techniques have been tried to prevent succinylcholine-induced elevation of IOP, and none has been consistently effective. However, there are no published reports of the loss of ocular contents when succinylcholine use has been preceded by pretreatment with a

nondepolarizing relaxant and barbiturate for induction, and many anesthesiologists feel this is a safe combination for rapid sequence induction in the open-eye, full-stomach situation.

Bourke DL. Open eye injuries. *Anesthesiology*. 1985;63:727.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin*. 1990;28(2):83-88.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

Hartman GS, Fiamengo SA, Riker WF Jr. Succinylcholine: mechanism of fasciculations and their prevention by d-tubocurarine or diphenylhydantoin. *Anesthesiology*. 1986;65:405-413.

Holloway KB. Control of the eye during general anaesthesia for intraocular surgery. *Br J Anaesth*. 1980;52:671-679.

Konchigeri HN, Lee YE, Venugopal K. Effect of pancuronium on intraocular pressure changes induced by

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succinylcholine. *Can Anaesth Soc J*. 1979;26:479-481.

Libonati MM, Leahy JJ, Ellison N. The use of succinylcholine in open eye surgery. *Anesthesiology*. 1985;62:637-640.

McGoldrick KE. The open globe: is an alternative to succinylcholine necessary? *J Clin Anesth*. 1993;5:1-4.

Meyers EF, Krupin T, Johnson M, et al. Failure of nondepolarizing neuromuscular blockers to inhibit succinylcholine-induced increased intraocular pressure: a controlled study. *Anesthesiology*. 1978;48:149-151.

Miller RD, Way WL, Hickey RF. Inhibition of succinylcholine-induced increased intraocular pressure by non-depolarizing muscle relaxants. *Anesthesiology*. 1968;29:123-126.

Murphy DF. Anesthesia and intraocular pressure. *Anesth Analg*. 1985;64:520-530.

C.6. How do nondepolarizing muscle relaxants affect IOP?

Nondepolarizing muscle relaxants either decrease or have no effect on IOP.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin*. 1990;28(2):83-88.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2512-2518.

Schneider MJ, Stirt JA, Finholt DA. Atracurium, vecuronium, and intraocular pressure in humans. *Anesth Analg*. 1986;65:877-882.

C.7. How will you perform a rapid sequence induction and intubation without using succinylcholine?

The safety of the patient always must be the primary concern; the preservation of the injured eye is secondary. Measures must be taken to guarantee adequate anesthetic depth and to blunt the hemodynamic responses to laryngoscopy and endotracheal intubation. Pretreatment measures such as narcotics, β-blockers, calcium channel blockers, lidocaine, or midazolam should be considered. Before induction, the patient should breathe 100% oxygen for several minutes, administered by a gently applied face mask. Anesthesia can then be induced using carefully applied cricoid pressure with intravenous methohexital (1 to 2 mg per kg) or propofol (2 to 3 mg per kg) and a nondepolarizing muscle relaxant. Several options exist:

- Atracurium (0.5 mg per kg) will allow safe intubation in 3 minutes. A larger bolus (1.5 mg per kg) will allow intubation in 60 to 90 seconds but may cause hypotension, tachycardia, and histamine release.
- Cisatracurium—because of its intermediate onset of action, cisatracurium (0.10 to 0.15 mg per kg) is not recommended for rapid sequence endotracheal intubations. Cisatracurium (0.4 mg per kg) 8 × ED95 will allow intubation in 90 seconds without histamine release, but duration of action may exceed for 60 minutes.
- Vecuronium (0.2 mg per kg) should provide adequate intubating conditions after 90 seconds.
- Rocuronium (0.8 to 1.0 mg per kg) gives excellent intubating conditions at 60 to 70 seconds. Time to recovery is variable and may take 45 to 60 minutes.
- An alternative is to pretreat the patient with a small dose of the nondepolarizing relaxant several minutes before induction, which may shorten the onset of action and lessen the dose required of subsequently administered relaxant. This has been referred to as a priming dose. Its use is controversial in that it may lead to diplopia, muscle weakness, respiratory distress, and aspiration while offering no definite advantage over the use of larger initial doses of nondepolarizing muscle relaxants. The doses for rapid tracheal intubation with succinylcholine or various nondepolarizing relaxants are listed in Chapter 15, section C.4 and Table 15.4.

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Whatever technique is selected, it is essential to monitor the degree of muscle relaxation with a neuromuscular blockade monitor. It is also possible to intubate the patient without any muscle relaxant at all after a deep level of anesthesia has been reached, but this is not a recommended technique. Not only is the airway unprotected for a long period but also prevention of bucking cannot be guaranteed, and positive pressure ventilation by face mask may exert pressure on the eye.

Abbott MA, Samuel JR. The control of intra-ocular pressure during the induction of anaesthesia for emergency eye surgery. A high-dose vecuronium technique. *Anaesthesia*. 1987;42:1008-1012.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1389-1390.

Lennon RL, Olson RA, Gronert GA. Atracurium or vecuronium for rapid sequence endotracheal intubation. *Anesthesiology*. 1986;64:510-513.

Mehta MP, Choi WW, Geris SD, et al. Facilitation of rapid endotracheal intubations with divided doses of nondepolarizing neuromuscular blocking drugs. *Anesthesiology*. 1985;62:392-395.

Musich J, Walts LF. Pulmonary aspiration after a priming dose of vecuronium. *Anesthesiology*. 1986;64:517-519.

Rich AL, Witherspoon CD, Morris RE, et al. Use of nondepolarizing anesthetic agents in penetrating ocular injuries. *Anesthesiology*. 1986;65:108-109.

Sosis MB. On use of priming with vecuronium in a patient with an open globe and a full stomach. *Anesth Analg*. 1990;70:336-337.

C.8. What are the effects of ketamine on the eye?

Ketamine may cause nystagmus and blepharospasm and is, therefore, not suitable for ophthalmic surgery. Studies with respect to the effect of ketamine on IOP have shown both increased and decreased IOP in children and no change in IOP in adults premedicated with diazepam and meperidine. This may depend on whether ketamine is administered through the IM or IV route.

Antal M, Mucsi G, Faludi A. Ketamine anesthesia and intraocular pressure. *Ann Ophthalmol*. 1978;10: 1281-1289.

Ausinsch B, Rayburn RL, Munson ES, et al. Ketamine and intraocular pressure in children. *Anesth Analg*. 1976;55:773-775.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

Peuler M, Glass DD, Arens JF. Ketamine and intraocular pressure. *Anesthesiology*. 1975;5:575-578.

Yoshikawa K, Murai Y. The effect of ketamine on intraocular pressure in children. *Anesth Analg*. 1971;50:199-202.

C.9. Would you consider the use of etomidate as an induction agent? What about propofol?

Although etomidate has been associated with a decrease in IOP when used as an induction agent, the unpredictable incidence of generalized myoclonus seen with etomidate use and resultant elevation of IOP may preclude its use in open-globe injuries, unless rapid and complete prior muscle relaxation can be guaranteed. Propofol, with its antiemetic

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properties and ability to decrease IOP, would be an excellent choice for induction.

Berry JM, Merin RG. Etomidate myoclonus and the open globe. *Anesth Analg*. 1989;69:256-259.

Calla S, Gupta A, Sen N, et al. Comparison of the effects of etomidate and thiopentone on intraocular pressure. *Br J Anaesth*. 1987;59:437-439.

Ferrari LR, Donlon JV. A comparison of propofol, midazolam, and methohexital for sedation during retrobulbar and peribulbar block. *J Clin Anesth*. 1992;4:93-96.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83-98.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2512-2518.

C.10. How do inhalation agents affect IOP and by what mechanism?

Inhalation agents cause dose-related decreases in IOP as a consequence of the following:

- Reduced aqueous humor production
- Depression of the CNS control center
- Facilitation of aqueous humor outflow

- Decreased extraocular muscle tension
- Lowered arterial blood pressure

The degree of IOP reduction is proportional to the depth of anesthesia.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2517-2518.

C.11. During the procedure, the patient's pulse suddenly dropped to 40 beats per minute. What do you think was happening? What is the oculocardiac reflex (OCR)?

The OCR may be manifested by bradycardia, bigeminy, ectopy, nodal rhythms, atrioventricular block, and cardiac arrest. It is caused by traction on the extraocular muscles (especially medial rectus), ocular manipulation, or manual pressure on the globe. The OCR is commonly seen during eye muscle surgery, detached retina repair, enucleation, or whenever there is extensive traction or rotation of the eyeball.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1379-1380.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2513.

C.12. What are the afferent and efferent pathways of the OCR?

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The OCR is trigeminovagal. The afferent pathway is by way of the ciliary ganglion to the ophthalmic division of the trigeminal nerve and through the gasserian ganglion to the main sensory nucleus in the fourth ventricle. The efferent pathway is the vagus nerve.

Adams AK, Jones RM. Anaesthesia for eye surgery: general considerations. *Br J Anaesth*. 1980;52:663-669.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1379-1380.

C.13. What factors contribute to the incidence of the OCR?

Preoperative anxiety, light general anesthesia, hypoxia, hypercarbia, and increased vagal tone because of age or drugs are associated with an increased incidence of the OCR. The reported incidence of cardiac rhythm changes during eye muscle surgery is 32% to 82%. The incidence is higher in children.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2513.

C.14. How do you diagnose and treat the OCR?

- Monitor the electrocardiogram intraoperatively and during any eye manipulation.
- Stop the surgical stimulus immediately.
- Ensure that ventilation is adequate.
- Ensure sufficient anesthetic depth.

The OCR may fatigue with repeated stimulation.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2513.

C.15. Is atropine useful for the OCR?

Atropine use is controversial. Atropine, 0.4 mg IM, as a premedicant has no vagolytic effect after 60 minutes and is of no value in preventing or treating the OCR. Atropine, 0.4 mg IV, is effective for 30 minutes in preventing bradycardia associated with the OCR. Doses greater than 0.5 mg IV can cause tachycardia that may be detrimental in certain patients with heart disease. At least 2 to 3 mg is required to ensure a total vagal block.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2513.

C.16. Can a retrobulbar block prevent the OCR? Is it appropriate in this patient?

Retrobulbar block injection is not only unreliable in preventing the OCR but may, during the injection, cause the OCR, a cardiac arrest, or a retrobulbar hemorrhage.

Local infiltration of the recti muscles and a delicate operating technique may decrease the incidence of the OCR. In this patient, a retrobulbar block is relatively contraindicated because it may increase IOP.

Allen ED, Elkington AR. Local anesthesia and the eye. *Br J Anaesth*. 1980;52:689-694.

McGoldrick KE. Complications of regional anesthesia for ophthalmic surgery. *Yale J Biol Med*. 1993;66:443-445.

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Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2513.

D. Postoperative Management

D.1. Would you reverse the neuromuscular blockade in this patient?

There is no contraindication to reversal provided that efforts are made to minimize coughing or bucking on the endotracheal tube.

D.2. Do reversal doses of atropine affect IOP?

Reversal doses of atropine, when given in conjunction with neostigmine, do not significantly alter IOP. This combination may be safely used even in patients with glaucoma.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1376-1377.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195-208.

D.3. What would you do before extubating this patient?

- Empty the stomach with an orogastric tube while the patient is still paralyzed.
- Suction the pharynx with the patient still paralyzed or deeply anesthetized.
- Give an antiemetic, such as droperidol 0.01 mg per kg IV or ondansetron 0.1 mg per kg IV, 20 to 30 minutes before the end of surgery.
- Give lidocaine 1.5 mg per kg IV or remifentanil 0.5 to 0.8 μg per kg IV to prevent coughing during emergence.

Gefke K, Andersen LW, Friesel E. Lidocaine given intravenously as a suppressant of cough and laryngospasm in connection with extubation after tonsillectomy. *Acta Anaesthesiol Scand*. 1983;27:111-112.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2517-2518.

D.4. When would you extubate this patient?

There may be a conflict between the desire to extubate awake because of the full stomach and the desire to extubate deep to prevent coughing and bucking. Because modern techniques of eye repair involve minimal risk of suture disruption with coughing, one may extubate awake, thereby protecting the airway.

D.5. The patient awakened in the recovery room and complained of pain and tearing in the opposite eye. The conjunctiva was inflamed. What was the likely cause?

General anesthesia decreases tear production and reduces normal mechanical eyelid closure. Corneal abrasions are the most common perioperative ocular injury, and this patient's complaints are consistent with that diagnosis.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1393.

Grixti A, Sadri M, Watts MT. Corneal protection during general anesthesia for nonocular surgery. *Ocul Surf*. 2013;11(2):109-118.

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Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2517-2518.

D.6. Will taping the eyes shut or applying ointment prevent corneal abrasions? Are there any contributing factors?

There is no guarantee that an eye that has been taped shut or lubricated will not sustain a corneal abrasion. Most anesthesiologists protect the eyes in some way; abrasions, however, still occur. Corneal abrasions represent the most common ophthalmic complication associated with general anesthesia. The incidence may be as high as 44% when no preventative measures have been taken and the cornea is exposed. The mechanism is thought to be drying of or direct trauma to exposed cornea. Possible contributing factors may be mask anesthesia, the prone, lateral or Trendelenburg position, or having the patient's face in the surgical field.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1393.

Bronheim D, Abel M, Neustein S. Corneal abrasions following non-ophthalmic surgery: a retrospective view of 35,253 general anesthetics. *Anesthesiology*. 1995;83:A1071.

Gild WM, Posner KL, Caplan RA, et al. Eye injuries associated with anesthesia. A closed claims analysis. *Anesthesiology*. 1992;76:204-208.

Nair PN, White E. Care of the eye during anaesthesia and intensive care. *Anaesth Intensive Care Med*. 2014;15(1):40-43.

D.7. What should you do when you suspect your patient might have a corneal abrasion?

Prompt consultation with an ophthalmologist should be solicited for precise diagnosis and treatment. The patient should be reassured that corneal abrasions usually heal and that relief of pain occurs within 24 to 48 hours. Possible treatments include eye patching and topical administration of antibiotics, short-acting cycloplegics, or anti-inflammatory agents. The use of eye patches is controversial.

A topical anesthetic for the cornea should never be given to a patient for self-administration. Misuse may cause delayed wound healing and keratopathy.

Hulbert MF. Efficacy of eyepad in corneal healing after corneal foreign body removal. *Lancet*. 1991;337:643.

Kaiser PK. The Corneal Abrasion Patching Study Group. A comparison of pressure patching versus no patching for corneal abrasions sue to trauma or foreign body removal. *Ophthalmology*. 1995;102:1936-1942.

Turner A, Rabiu M. Patching for corneal abrasion. *Cochrane Database Syst Rev*. 2006;(2):CD004764.

D.8. A month after the surgical repair, the patient complained of impaired vision in the operative eye. He was examined and found to have a detached retina. As part of the surgical treatment, the ophthalmologist injected a gas bubble into the patient's posterior chamber. Why is this important to an anesthesiologist?

If a patient with intraocular gas needs to undergo general anesthesia before the gas bubble resorbs, nitrous oxide must be avoided because the gas will expand thereby increasing IOP. The effects on the eye may be disastrous. Various types of gases may be injected, with different durations. Patients are usually given bracelets to inform anesthesiologists that they have gas in their eye and nitrous oxide must be avoided.

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Fu AD, McDonald HR, Eliott D, et al. Complications of general anesthesia using nitrous oxide in eyes with preexisting gas bubbles. *Retina*. 2002;22(5):569-574.

Hart RH, Vote BJ, Borthwick JH, et al. Loss of vision caused by expansion of intraocular perfluoropropane (C_3F_8) gas during nitrous oxide anesthesia. *Am J Ophthalmol*. 2002;134(5):761-763.

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Chapter 35
Laser Treatment for Laryngeal Lesions

Marcus Gutzler

Franklin B. Chiao

A 7-year-old girl with a past history of recurrent respiratory papillomatosis (RRP) is scheduled for direct laryngoscopy and possible reexcision. The patient has had 10 papilloma reexcisions in the past 2 years. Currently, she is undergoing adjuvant treatment with α-interferon but now presents with slowly progressive hoarseness.

A. Medical Disease and Differential Diagnosis

1. What is the cause of RRP?
2. Does a cesarean section delivery prevent the maternal transmission of the human papilloma virus (HPV) to the neonate?
3. Is this an unusual presentation for RRP?
4. What are the available treatment options for RRP?
5. What are common adverse effects of α-interferon therapy?
6. What is the differential diagnosis of hoarseness in this child?

B. Preoperative Evaluation and Preparation

1. What are the key points of the preanesthetic history and physical examination in this patient?
2. What preoperative laboratory tests are necessary?
3. How should this child be premedicated before coming to the operating room (OR)?
4. What are the special considerations for anesthetic setup in this case?

C. Intraoperative Management

1. What is a laser, and how does it work?
2. What are the characteristics of laser radiation?
3. Discuss some advantages associated with the use of lasers for laryngeal surgery.
4. What are some disadvantages of lasers compared with microdebriders?
5. How would you protect the external surface of a conventional endotracheal tube (ETT) for use during laser microlaryngoscopy?
6. What are the disadvantages of foil-wrapped tubes?
7. What special ETTs are available for laser surgery?
8. How would you manage an airway fire?
9. What is the Venturi effect?
10. What is Venturi jet ventilation?
11. How would you institute and conduct manual jet ventilation?
12. How is anesthesia maintained during jet ventilation?
13. What are the complications of jet ventilation?

14. Are there contraindications for the use of jet ventilation?

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15. Discuss airway management options during laryngeal papilloma resection.
16. How would you plan to monitor this patient?
17. How would you induce anesthesia for an intermittent apnea technique?
18. What supplemental medication and techniques would you use during this case?

D. Postoperative Management

1. After uneventful laser microlaryngeal resection using jet ventilation, the patient was extubated in the OR and then transferred to the recovery room. What are the common postoperative complications?

A. Medical Disease and Differential Diagnosis

A.1. What is the cause of RRP?

RRP, a disease of the respiratory mucosa characterized by benign nonkeratinizing squamous papillomata, is caused by the human papilloma virus (HPV). On the basis of shared genetic code homologies, HPV are grouped and numbered. Although there are approximately 100 different HPV types identified to date, with respect to RRP, two types stand out: HPV 6 and 11. They are not only the causative agents for RRP but are also responsible for 90% of genital warts (*Condylomata acuminata*). Recently, there has been evidence implicating infections with non-HPV agents in the pathogenesis of RRP.

Donne AJ, Hampson L, Homer JJ, et al. The role of HPV type in recurrent respiratory papillomatosis. *Int J Pediatr Otorhinolaryngol*. 2010;74(1):7-14.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142-3157.

Venkatesan NN, Pine HS, Underbrink MP. Recurrent respiratory papillomatosis. *Otolaryngol Clin North Am*. 2012;45(3):671-694.

A.2. Does a cesarean section delivery prevent the maternal transmission of the human papilloma virus (HPV) to the neonate?

HPV has been estimated to be present in the genital tract of as many as 25% of all women of childbearing age worldwide. Although RRP is the most common benign neoplasm of the larynx in children, its true incidence and prevalence are uncertain. It is estimated that each year, 1,500 to 2,500 new cases of childhood-onset RRP occur in the United States. Therefore, only a minority of children of virus-carrying mothers will become symptomatic, although the number of virus-carrying children may be much higher. Even in parturients with an active genital condyloma lesion, the neonate's risk of contracting the disease when normal spontaneous vaginal delivery is chosen is only approximately 1 in 400.

The route of transmission (i.e., transplacental, perinatal, or postnatal) is not completely understood, and the preventive value of cesarean sections in parturients carrying the virus is unknown. Cesarean section with the sole intention of preventing the disease in the newborn is therefore not recommended. For reasons unknown, genital warts often increase in number and size during pregnancy and may make a vaginal delivery difficult leading to excessive maternal bleeding or pelvic outlet obstruction. In these cases, maternal considerations may make a cesarean delivery the delivery method of choice.

It is hoped that with the wider availability of vaccines effective against HPV 6 and 11 (GARDASIL, Merck & Co, Inc, Whitehouse Station, NJ), the incidence of RRP will decrease in the future.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:1221-1222, 1275.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142-3157.

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A.3. Is this an unusual presentation for RRP?

Recurrence of voice changes despite repeated surgical interventions is unfortunately not that rare in patients with respiratory papillomatosis. Hoarseness, stridor, and—if severe enough—the development of respiratory distress from airway obstruction are the most consistent signs and symptoms of patients with RRP. Oral, tracheobronchial, and pulmonary involvements also are known to occur.

At present, there is no cure for RRP and no modality that would lead to eradication of the virus from the respiratory mucosa. Local recurrences are therefore to be expected.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142-3157.

A.4. What are the available treatment options for RRP?

As stated in the preceding text, there is no cure but only disease control for relentless and recurrent papillomatosis. The current standard of care is surgical therapy with the goal of complete removal of papillomata and preservation of normal structures as much as possible.

Because scarring from overaggressive laryngeal resections may lead to precisely the adverse clinical outcome that surgical therapy seeks to avoid or minimize (dysphonia, airway compromise), most experienced surgeons will accept incomplete papilloma resection, especially when near delicate structures such as the anterior laryngeal commissure. Even with the removal of all clinically evident papilloma, not all latent virus particles will have been eradicated.

With respect to surgical technique, the CO_2 laser had been the mainstay of therapy since the 1970s. According to a recent survey by the American Society of Pediatric Otolaryngology, this may be changing. Most members participating in this survey seem to rely on the use of the microdebrider as the preferred surgical therapy. The microdebrider is considered to be just as precise a surgical tool as the CO_2 laser; it may be easier to use and may limit the damage to underlying tissue, allowing for greater preservation of normal epithelium.

There continues to be an application for laser-based resections. Certain lesions, such as sessile ones, those with ventricular involvement, or those in the area of significant scarring, are still best dealt with by CO_2-, potassium titanyl phosphate (KTP), or pulsed-dye laser (PDL).

In addition, there seems to be an increasing role for adjuvant medical therapy: *α*-interferon and various antiviral agents, of which the most commonly used one is intralesional cidofovir.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142-3157.

Gallagher TQ, Derkay CS. Recurrent respiratory papillomatosis: update 2008. *Curr Opin Otolaryngol Head Neck Surg*. 2008;16:536-542.

Schraff S, Derkay CS, Burke B, et al. American Society of Pediatric Otolaryngology members' experience with recurrent respiratory papillomatosis and the use of adjuvant therapy. *Arch Otolaryngol Head Neck Surg*. 2004;130:1039-1042.

Venkatesan NN, Pine HS, Underbrink MP. Recurrent respiratory papillomatosis. *Otolaryngol Clin North Am*. 2012;45(3):671-694.

A.5. What are common adverse effects of α-interferon therapy?

Interferons (IFNs) are potent cytokines that possess antiviral, immunomodulating, and antiproliferative activities. Of the three known major classes of IFNs (*α*, *β*, and *γ*), only *α*-interferon is clinically used in RRP. A common therapeutic regimen entails daily subcutaneous applications for a month, followed by a 6-month period of injections three times a week, and

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then further slow weaning as tolerated. Known adverse effects associated with systemic application are an acute, relatively benign influenza-like syndrome, characterized by fever, chills, headache, myalgia, arthralgia, nausea, vomiting, and diarrhea, as well as more serious dose-limiting comorbidities, namely, myelosuppression and neurotoxicity. Neurotoxicity is characterized by somnolence, confusion, behavioral disturbance, and rarely,

seizures, debilitating neurasthenia, and depression. Alopecia and personality change are common in IFN-treated children. Cardiovascular toxicity (hypotension and tachycardia) and hepatotoxicity seem to be more rare.

Brunton LL, Chabner BA, Knollmann BC, eds. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw Hill; 2011:1593-1622.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142-3157.

A.6. What is the differential diagnosis of hoarseness in this child?

Hoarseness always indicates some abnormality of laryngeal structure or function. Given the patient's previous history, local papilloma recurrence and/or postoperative scarring of laryngeal structures seem likely causes in this patient. A broader differential diagnosis for hoarseness in children would be as follows:

- Anatomic and congenital causes
  - Cystic lesions (laryngocele, thyroglossal cyst)
  - Vocal fold nodules
  - Glottic webs
- Neoplastic causes
  - Squamous cell carcinoma
  - RRP
- Neurologic causes
  - Central (e.g., intracerebral hemorrhage, hydrocephalus)
  - Peripheral neuropathies
- Inflammatory
  - Gastroesophageal reflux
  - Rheumatoid arthritis
  - Angioneurotic edema
- Infectious
  - Croup syndrome
  - Laryngotracheobronchitis
  - Epiglottitis

McMurray JS. Disorders of phonation in children. *Pediatr Clin North Am*. 2003;50:363-380.

B. Preoperative Evaluation and Preparation

B.1. What are the key points of the preanesthetic history and physical examination in this patient?

First and foremost, it is important to quickly detect and address any serious respiratory compromise in this patient. In the

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absence of severe respiratory distress, a detailed history should be obtained. A review of previous anesthetic experiences with particular emphasis on problems pertaining to airway management would be a good starting point. Are there signs of obstruction? Does the patient snore at baseline? What position does the child sleep in? Sleep position can assist the team in maintaining airway patency particularly for masking. Weight, general health, associated comorbidities, recent respiratory infections, allergies, medications, and nothing-by-mouth status are all of obvious importance. A search for serious adverse effects from IFN therapy should be done.

With respect to the voice changes, a more in-depth investigation may offer some clues regarding the suspected location: A low-pitched, coarse, fluttering voice suggests a subglottic lesion, whereas a high-pitched, cracking voice, aphonia, or breathy voice suggests a glottic lesion. Associated high-pitched stridor also suggests a glottic or subglottic lesion. Because of the precision of laryngeal mechanics, hoarseness may result from a remarkably small lesion. On the other hand, if the origin of the lesion is remote from the vocal cords, hoarseness may result from a significantly larger lesion.

The concern here is to recognize a lesion that may potentially result in complete airway obstruction once anesthesia has been induced. A preoperative flexible nasopharyngoscopy examination is now routinely performed in most ear, nose, and throat (ENT) offices. If, however, it has not already been done before the patient's arrival to the OR, an immediate preoperative flexible nasopharyngoscopic examination should be considered.

Derkay CS. Recurrent respiratory papillomatosis. *Laryngoscope*. 2001;111:57-69.

B.2. What preoperative laboratory tests are necessary?

In recent years, the value of routine preoperative laboratory screening has been questioned. For a surgical procedure not associated with significant intraoperative blood loss in a child who is not at increased risk for severe and physiologic important anemia, no laboratory tests are required.

This patient may however no longer fall into this latter category. After all, α-interferon is associated with serious side effects, such as neurotoxicity and myelosuppression. Because the effects of myelosuppression may not be diagnosed easily by history and physical examination, a preoperative complete blood count may be beneficial in this particular patient.

Coté CJ, Lerman J, Anderson MB, eds. *Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:31-63.

B.3. How should this child be premedicated before coming to the operating room (OR)?

Children with RRP are often quite anxious and apprehensive coming back to the OR for yet another reexcision. A reassuring preoperative visit by the anesthesiologist should help allay fears. Sedative premedication should be used very carefully, especially in the child with significant respiratory distress. It should not be administered without close monitoring and the immediate availability of oxygen, suction, and positive pressure ventilation. Dexmedetomidine, an α_2-agonist, given intranasally has no effect on respiration and has anxiolytic properties. Anticholinergic premedication may be used to dry up oral secretions.

Coté CJ, Lerman J, Anderson MB, eds. *Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:31-63.

B.4. What are the special considerations for anesthetic setup in this case?

Before the initiation of anesthesia, the anesthesiologist should discuss the case with the surgeon. The anesthesiologist should have a thorough understanding of the surgical plan and must keep in close communication with the surgeon throughout the procedure. A strategy for maintaining oxygenation and ventilation during the case, while working around surgical needs, must be devised. Special equipment (e.g., laser, jet ventilator, bronchoscopes) must be present and in good working condition.

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The use of a laser greatly impacts airway management. The biggest concern here is prevention of an airway fire. Also, a plan to deal effectively with a fire, if it occurs, needs to be firmly established beforehand. Aside from that, all OR staff must wear protective eye gear and laser masks when working around the laser.

Derkay CS. Recurrent respiratory papillomatosis. *Laryngoscope.* 2001;111:57-69.

C. Intraoperative Management

C.1. What is a laser, and how does it work?

Electromagnetic radiation consists of photons, and photons have properties consistent with both particles and waves. Like radio waves and Roentgen waves, visible light is another form of electromagnetic radiation.

The characteristic features of these different forms of radiation are their respective wavelengths. Visual light is electromagnetic radiation with wavelengths in the range from 385 to 760 nm, shorter wavelengths are ultraviolet, and longer wavelengths are infrared.

Laser is an acronym for light amplification by stimulated emission of radiation. What makes laser special is the high energy density that it provides and its ability to quickly transfer large quantities of energy to remote locations, be it through fiberoptic channels (e.g., with the potassium titanyl phosphate laser) or through free air, as is usually the case with the CO_2 laser.

Several concepts are important for a basic understanding of the phenomenon of laser:

- *The photoelectric effect*. Light of a certain wavelength (e.g., blue) causes metal to eject electrons at a rate proportional to the brightness of this light. Intense light of different colors (e.g., red, orange, yellow) cannot do that.
- *The orbital model*. Electrons circling the nuclei of atoms are limited to a few specific orbital patterns and radii. Each orbital has its specific energy level. The energy differences between electron orbitals are characteristic for specific atoms. The only way an electron can move from one orbital to another of higher or lower energy is to either absorb or emit an amount of energy equivalent to the difference in energy between the two orbitals.
- *Stimulated absorption*. The process by which a photon's energy is captured by an electron, thereby lifting the electron into a higher energy orbital (the electrons get “excited”).
- *Spontaneous emission.* The opposite phenomenon during which an electron drops to a lower orbital by emitting a photon to carry away the excess energy.
- *Population inversion*. Many (as opposed to one single) electrons achieve a higher energy level (higher orbital). Once initiated by a single photon, a chain reaction of stimulated emission sets in (amplification).

The necessary components of a laser system consist of a laser medium (gaseous or solid) containing the atoms whose electrons create the laser light, resonating mirrors to enhance laser efficiency, and an energy source to excite the atoms of the laser medium into generating laser light. An energy source provides the means for obtaining a population inversion of orbital electrons of the laser medium. A pair of axial mirrors permits repeated passes of collimated photons through the medium, allowing maximum amplification by stimulated emission. One of the mirrors is partially transmitting, finally allowing the laser beam to emerge.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2598-2611.

C.2. What are the characteristics of laser radiation?

The high energy density of a laser is the result of three characteristics:

- There is a high degree of monochromaticity which means that all of the photons in a laser beam have the same wavelength.
- Electromagnetic fields of all photons in the laser beam oscillate in identical phase. Unlike ordinary light where the electromagnetic fields are randomly phased, this phenomenon of synchronous oscillation is called *coherence*.

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- Whereas ordinary light beams spread out in all directions from a point source, laser light remains in a narrow collimated beam with the elements of the laser beam being nearly parallel.

These characteristics permit lasers to deliver intense energy via powerful light beams efficiently and accurately through lenses to small targets.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2598-2611.

C.3. Discuss some advantages associated with the use of lasers for laryngeal surgery.

With laser light, tissue penetration is mostly a function of wavelength. Long-wavelength laser light, such as that from CO_2 (operating at 10,600 nm), is completely absorbed by water in the first few layers of cells. The thermal effect is therefore largely limited to the point of entry into the target tissue. This results in explosive vaporization of the surface tissue of the target with surprisingly little damage to underlying cells. When coupled to an operating microscope, the

laser vaporizes the lesions with precision, causing minimal bleeding and edema, an obvious advantage, especially in small pediatric airways.

As mentioned in section A.4, in certain situations, a laser-based resection technique is the surgical method of choice: Sessile lesions, lesions in scarred areas, and those located near or in the laryngeal ventricle often are treated with PDL. Other than the CO_2 laser, this is a laser with a shorter wavelength that typically *spares* the epithelium but specifically targets the microvascular supply of the overriding lesion. This has obvious advantages, where the epithelium of one wall is in proximity to epithelium from an opposing wall, such as is the case in the anterior laryngeal commissure. Not denuding the epithelium is beneficial from a functional standpoint, as it should limit fibrotic changes from abutting raw surfaces that might interfere with the delicate interplay of laryngeal substructures. An added benefit at least in the adult patient population is that the PDL can be used with just topical anesthesia alone (delivery is typically via fiberoptic means), thereby avoiding many of the complicating considerations for laser surgery under general anesthesia.

Derkay CS. Recurrent respiratory papillomatosis. *Laryngoscope*. 2001;111:57-69.

Gallagher TQ, Derkay CS. Recurrent respiratory papillomatosis: update 2008. *Curr Opin Otolaryngol Head Neck Surg*. 2008;16:536-542.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2598-2611.

C.4. What are some disadvantages of lasers compared with microdebriders?

There are significant risks associated with the use of laser for laryngeal surgery. Extra staff is typically required for the safe operation of the laser equipment, adding to the overall cost of the procedure. Special eye protection for both patient and staff are indispensable because the powerful laser beam may cause serious ocular injury. Other body parts need also to be carefully protected from inadvertent laser exposure in order to prevent tissue injury.

The biggest concern with laser use, however, revolves around the generation of an airway fire through ignition of the endotracheal tube (ETT) by inadvertent laser strike. This is a potentially fatal complication if not managed quickly. To minimize the risk of an airway fire, the oxygen concentration should be kept as low as clinically feasible; the aim is to keep the fraction of inspired oxygen (FIO_2) below 30%. Nitrous oxide is not a suitable diluting gas; it is flammable.

Inappropriate and aggressive use of the laser may cause injury to the patient's mucosa that is unaffected by disease and create an environment suitable for implantation of viral particles and thereby may actually promote spread of the disease. Laser-induced pneumothorax has been reported after a laryngeal procedure. Although the thermal effect is largely limited to the point of entry into the target tissue, if not used judiciously especially near delicate structures such as the anterior or posterior laryngeal commissure, the laser may cause unacceptable scarring and subsequent abnormal vocal fold function.

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Laser smoke contains water vapor and destroyed tissue material. It has been found to contain active viral DNA, a potential source of infection for OR personnel. Smoke may also obstruct the surgeon's view during the resection. The staff should protect themselves with N95 face masks.

When comparing the microdebrider to the CO_2 laser, there is evidence suggesting that removing papillomas using the microdebrider is associated with better short-term improvement in voice quality and a shorter procedure time, which may ultimately translate to reduced operative cost. Heat-induced scarring of nearby tissues is not a concern; there is no need for protection from an inadvertent laser strike, and the risk for an airway fire is no higher than in a standard case.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142-3157.

Gallagher TQ, Derkay CS. Recurrent respiratory papillomatosis: update 2008. *Curr Opin Otolaryngol Head Neck Surg*. 2008;16:536-542.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2598-2611.

Pasquale K, Wiatrak B, Woolley A, et al. Microdebrider versus CO_2 laser removal of recurrent respiratory papillomas: a prospective analysis. *Laryngoscope*. 2003;113(1):139-143.

Werkhaven JA. Microlaryngoscopy-airway management with anaesthetic techniques for CO_2 laser. *Paediatr Anaesth*. 2004;14:90-94.

C.5. How would you protect the external surface of a conventional endotracheal tube (ETT) for use during laser microlaryngoscopy?

An inadvertent laser strike can ignite and burn any hydrocarbon material in the airway, including ETTs. Because of their proximity to the operative field, ETTs pose a serious fire hazard during laser use, especially in the oxygen-enriched environment of a general anesthetic.

All commonly used ETTs are potentially flammable, but to some degree, flammability is a function of the material used to manufacture the tube. Unfortunately, the common clear polyvinylchloride (PVC) plastic tubes seem to catch fire much more easily than older red rubber tubes. Also, red rubber tubes seem to lead to less toxic combustion products once ignited.

In addition to limiting the amount of oxygen used to ventilate the patient to as low as tolerated, one strategy to make the use of conventional PVC tubes safer is to guard it with reflective tape. Conventional aluminum or copper tape is an inexpensive (although not U.S. Food and Drug Administration [FDA]-approved) way to offer some protection against a brief laser strike. FDA-approved tape is also available (Merocel Laser-Guard, Medtronic, Minneapolis, MN).

Should a regular cuffed tube be used, the cuff unfortunately cannot be protected from laser strike in this manner because it is impractical to wrap the cuff with tape. Cuff breakage needs to be recognized immediately because it increases the fire hazard significantly; it allows oxygen-enriched gas mixtures into the hypopharynx. One strategy here to reduce risk is to fill the cuff with an indicator dye (e.g., methylene blue in normal saline) to detect a break early and hopefully douse small fires at the same time. The cuff should also be covered from above with wet gauze or neurosurgical sponges to retard heating.

To wrap a PVC tube with tape, the tube should be clean and oil-free, thereby facilitating tape adhesion. The tube diameter should be chosen 1 to 2 mm smaller than usual. Mastisol will further enhance the stickiness to the ETT. Wrapping should start at the distal end or just proximal to the cuff and be continued up to the level of the uvula. The distal end of the tape should be cut at a 60-degree angle, and the tube should then be wrapped in a spiral with approximately 30% overlap, avoiding sharp edges and leaving no PVC exposed.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2598-2611.

Wöllmer W, Schade G, Kessler G. Endotracheal tube fires still happen—a short overview. *Med Laser Appl*.

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2010;25(2):118-125.

C.6. What are the disadvantages of foil-wrapped tubes?

Disadvantages of metallic foil-wrapped tubes include risk of trauma to pharyngeal and laryngeal tissues by sharp edges. The tube will lose elasticity and be more prone to kink. If foil becomes detached, the protective effect is lost and aspirated foil may lead to airway obstruction. The reflective surface enhances the risk of inadvertent laser strike of surrounding tissues.

Gregory GA, Androupoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:798.

Wöllmer W, Schade G, Kessler G. Endotracheal tube fires still happen—a short overview. *Med Laser Appl*. 2010;25(2):118-125.

C.7. What special ETTs are available for laser surgery?

The FDA-approved specialized tubes for laser surgery are commercially available. Although these laser-resistant ETTs may withstand laser strikes longer than conventional tubes, they will all ignite with longer exposure. In essence, laser-resistant tubes are made of metal or have a metallic overlay on a nonmetal core.

The Laser-Shield II (Medtronic, Minneapolis, MN) has a silicone-based core wrapped with laser-reflective aluminum topped with a smooth fluoroplastic overwrap on the outside. Other laser-resistant tubes with a metallic overlay on a nonmetal core are the Sheridan Laser-Trach (Teleflex, Limerick, PA) and the Rüsch Lasertubus (Teleflex, Germany).

The Covidien Mallinckrodt Laser Oral/Nasal Tracheal Tube (Medtronic, Minneapolis, MN) is a metal tube model; it has an airtight stainless steel spiral tube with two independent distal PVC cuffs. If one ruptures, the second unruptured cuff will still limit egress of oxygen-rich gas. The Bivona Fome-Cuf (Smiths Medical, Dublin, OH) was an aluminum spiral tube with an outer silicone coating that is no longer available; it had a specially designed self-inflating foam sponge-filled cuff that remained expanded even after laser puncture. Currently, there are no ETTs with cuffs that remain inflated after puncture. Not surprisingly, the rigidity and bulkiness of these tubes are practical disadvantages that discourage their routine use, especially in pediatric patients.

Green JM, Gonzalez RM, Sonbolian N, et al. The resistance to carbon dioxide laser ignition of a new endotracheal tube: Xomed Laser-Shield II. *J Clin Anesth*. 1992;4(2):89-92.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2598-2611.

Wöllmer W, Schade G, Kessler G. Endotracheal tube fires still happen—a short overview. *Med Laser Appl*. 2010;25(2):118-125.

C.8. How would you manage an airway fire?

In case of an airway fire, rapid and effective action is required. When suddenly faced with this frightening situation, the "4 *E*s" mnemonic may help you to stay focused:

- *E*xtract
- *E*liminate
- *E*xtinguish
- *E*valuate

All combustible materials (ETT, pledgets) must be *e*xtracted from the airway at once. Oxygen supply through the tube must be quickly *e*liminated by disconnection from the circuit. Continued flow through a burning tube would lead to a blowtorch

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effect. Any residual fires need to be *e*xtinguished with normal saline. Ventilation with 100% oxygen should then be provided by mask, and anesthesia should be continued. *E*valuation of the injury is then in order and should be done with direct laryngoscopy and rigid bronchoscopy to assess the upper and lower airway. Any apparent airway damage makes reintubation the most prudent approach. For severe injury, a low tracheotomy may be indicated.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2598-2611.

Werkhaven JA. Microlaryngoscopy-airway management with anaesthetic techniques for CO_2 laser. *Paediatr Anaesth*. 2004;14:90-94.

C.9. What is the Venturi effect?

The Venturi effect originally described the impact of constricted channels on fluid flow. As fluid passes through the constriction of a Venturi tube (a tube with two open ends and a narrowing in its midsection), it must speed up. At the same time, its hydrostatic pressure drops. This pressure drop is proportional to flow and can, for example, be used to measure flow in pipes without interfering with flow.

Ihra G, Aloy A. On the use of Venturi's principle to describe entrainment during jet ventilation [letter to the editor]. *J Clin Anesth*. 2000;12:417-419.

C.10. What is Venturi jet ventilation?

The jet injector technique of ventilation for upper airway surgery was introduced by Sanders in 1967. A high-pressure gas source is connected to a stiff, narrow cannula positioned at the inlet of the laryngoscope. With a manual switch, gas boluses are delivered. In the lumen of the laryngoscope, the high-velocity stream of gas encounters stationary gas, which it pushes forward. Each jet bolus entrains ambient air through the open laryngoscope entrance, substantially augmenting the volume of the bolus and diluting the oxygen fraction of the jet.

Whether or not it is truly based on the phenomenon known as the *Venturi effect*, the jet injector provides a simple approach to deliver physiologic tidal volumes in a non-gas tight

delivery system. Venturi ventilation has become synonymous with jet ventilation in the medical literature.

Ihra G, Aloy A. On the use of Venturi's principle to describe entrainment during jet ventilation [letter to the editor]. *J Clin Anesth*. 2000;12:417-419.

McRae K. Anesthesia for airway surgery. *Anesthesiol Clin North America*. 2001;19(3):497-541.

C.11. How would you institute and conduct manual jet ventilation?

We recommend observation of chest rise with the patient breathing spontaneously before induction. Then we gently mask to get a feel for chest wall compliance. This helps gather information about how much chest rise to expect on jet ventilation.

Before effective jet ventilation can begin, the operating laryngoscope must be inserted, the larynx adequately exposed and evaluated for appropriateness for jet ventilation, the suspension system installed, and the jet injector needle attached to the laryngoscope in alignment with the axis of the trachea. All of this takes time in an anesthetized apneic patient. Therefore, it is our preference at the New York-Presbyterian Hospital/Weill Cornell Medical Center to begin with laryngoscopy and intubation using a standard PVC ETT if the airway appears appropriate for jet ventilation. Uninterrupted ventilation can now be performed while the operating laryngoscope and jet injector are positioned. When ready, the ETT is removed, and jet ventilation begun. Alternatively, following anesthesia induction and demonstration of adequate mask airway ventilation, the patient is paralyzed and the operating laryngoscope and jet injector are inserted and positioned while the patient is apneic.

Ventilation begins with a jet pressure of 5 to 10 psi in infants and children and 15 to 20 psi in adults. The jet pressure is gradually increased until adequate chest excursions are noted. Jet ventilation should produce good clinical expansion of

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the chest at a rate appropriate for the patient's age. The inspiratory-to-expiratory (I:E) ratio should allow for complete passive exhalation in between jet applications. Monitoring of peripheral arterial saturation is mandatory as is monitoring ventilation both by auscultation and palpation.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142-3157.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2598-2611.

C.12. How is anesthesia maintained during jet ventilation?

The leak around the scope is smaller in children having jet ventilation, but the delivery of inhalational anesthetics is not optimal because of OR pollution and the inability to precisely regulate gas concentrations. Most clinicians, therefore, favor a total intravenous technique. Combining a hypnotic agent such as propofol with a short-acting opioid (ideally remifentanil), hypnosis, amnesia, and analgesia can all be achieved, while allowing for a rapid recovery of the patient at the end of the procedure. Temporary muscle relaxation can be achieved with either a short-acting or intermediate-duration muscle relaxants.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2523-2549.

C.13. What are the complications of jet ventilation?

Complications associated with jet ventilation include dehydration of the mucosa, inadequate oxygenation and ventilation, gastric distention, regurgitation, and barotrauma. Pneumomediastinum and pneumothorax have been reported and seem to occur most frequently when jet ventilation is used in a patient with a (partially) obstructed airway. This is best avoided by using muscle relaxation during jet ventilation. In addition, particulate matter and virus particles can be spread down the distal airway. End-tidal carbon dioxide measurements are also inaccurate.

Borland LM. Airway management for CO_2 laser surgery on the larynx: Venturi jet ventilation and alternatives. *Int Anesthesiol Clin*. 1997;35(3):99-106.

Jaquet Y, Monnier P, Van Melle G, et al. Complications of different ventilation strategies in endoscopic laryngeal surgery: a 10-year review. *Anesthesiology*. 2006;104(1):52-59.

C.14. Are there contraindications for the use of jet ventilation?

Jet ventilation is most suited for patients with normal, unobstructed airways and normal lung and chest wall compliance.

The ability to fully exhale in between jet applications is crucial. If this is not possible (glottic lesion, significant interarytenoid scarring, laryngospasm), jet ventilation may not be appropriate. Decreased chest wall compliance, such as in obese patients, may lead to inadvertent gastric distension, further worsening respiratory compliance. Advanced chronic obstructive pulmonary disease with its inherent prolonged exhalation phase may again make jet ventilation unpractical and in the presence of pulmonary bullae even hazardous. Significant overbite especially when combined with retrognathia makes orolaryngotracheal alignment challenging and accidental gastric hyperinflation likely.

Borland LM. Airway management for CO_2 laser surgery on the larynx: Venturi jet ventilation and alternatives. *Int Anesthesiol Clin*. 1997;35(3):99-106.

Jaquet Y, Monnier P, Van Melle G, et al. Complications of different ventilation strategies in endoscopic laryngeal surgery: a 10-year review. *Anesthesiology*. 2006;104(1):52-59.

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C.15. Discuss airway management options during laryngeal papilloma resection.

In addition to (manual) Venturi jet ventilation, there are three different widely accepted methods for managing the airway during papilloma resection—controlled mechanical ventilation through a small ETT, spontaneous ventilation, and an apnea technique with intermittent ventilation.

Except for the first option, all methods require an unsecured, unprotected airway during parts of the surgical resection. As reassuring as a secured airway may feel to the anesthesiologist, the use of an ETT during airway laser surgery presents the aforementioned risk of an airway fire. Also, surgical exposure is often suboptimal in the presence of an ETT because the tube limits access to parts of the larynx.

Access to all parts of the laryngeal mucosa using spontaneous ventilation without an additional airway device (e.g., tube, laryngeal mask airway) is naturally superior. And, depending on the type of laser used, in the *nonpediatric* population, all that is sometimes required is *topical* anesthesia allowing for office-based treatments. In pediatric patients though, maintenance of spontaneous ventilation under general anesthesia is usually the more successful strategy. For obvious reasons, muscle relaxation is not an option, and the moving surgical field is somewhat of a drawback of this technique, potentially making the resection more demanding.

Intermittent apnea offers a solution to this problem. During apnea with intermittent ventilation, the patient is repeatedly hyperventilated, either by mask or after reintubation. Use of 100% oxygen will extend the tolerable apnea time to follow. Inadvertent movement is best avoided using muscle relaxants. If an ETT is used, it is removed periodically, respirations are held while the surgeon operates for brief periods of time, and the peripheral oxygen saturation is closely monitored. Before desaturation occurs, the patient is then either reintubated or just masked and readied for another period of apnea to allow for further resection as needed. Spreading the virus to more distal parts of the airway by repeated reintubations is a concern with this technique.

Spontaneous ventilation and intermittent apnea techniques seem to be favored by most members of the American Society of Pediatric Otolaryngology.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142-3157.

Gallagher TQ, Derkay CS. Recurrent respiratory papillomatosis: update 2008. *Curr Opin Otolaryngol Head Neck Surg*. 2008;16:536-542.

Jaquet Y, Monnier P, Van Melle G, et al. Complications of different ventilation strategies in endoscopic laryngeal surgery: a 10-year review. *Anesthesiology*. 2006;104(1):52-59.

C.16. How would you plan to monitor this patient?

Routine monitors include a pulse oximeter, noninvasive blood pressure measurements, an electrocardiogram, a precordial stethoscope, a temperature probe, an oxygen analyzer,

a CO_2 detector, and a neuromuscular blockade monitor. Placement of a hand on the chest also aids the clinician to assess respiration. In this otherwise healthy patient without the potential for significant blood loss or fluid shifts, no additional monitoring is necessary.

American Society of Anesthesiologists. Standards for basic anesthetic monitoring. Reaffirmed July 1, 2011. http://www.asahq.org/search.aspx?q=standards+basic+anesthetic+monitoring. Accessed October 15, 2015.

C.17. How would you induce anesthesia for an intermittent apnea technique?

The choice of anesthetic induction is critically dependent upon the presence of signs and symptoms suggesting possible airway compromise on induction. If present, the logical choice in an adult patient is an awake fiberoptic intubation which not only secures the airway but also enables evaluation of the subglottic airway before ETT placement.

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In children and uncooperative adults, an inhalation induction using sevoflurane is the next safest option. Maintenance of spontaneous ventilation is again critical. In this scenario, muscle relaxants are unsafe, until it is clear that the patient can be ventilated and/or intubated. If severe compromise is present, an awake tracheotomy under local anesthesia may be the best means of managing the airway.

Blind techniques (lightwand, blind oral or nasal intubation) cannot be recommended in this setting because they carry the risk of bleeding and loss of the airway due to an obstructing lesion.

A word of caution here: Papillomas are dynamic lesions in a sense that they may grow rapidly. The endoscopic airway examination should be pertinently current. Also, the absence of suggestive signs and symptoms does not truly guarantee a patent airway once anesthesia has been induced. Hence, extreme caution in managing these patients is essential.

If the patient truly has no airway compromise, any routine induction technique (intravenous or inhalational) can be used safely. An intermittent apnea technique will allow the surgeons to have a full view without an ETT in place.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2523-2549.

C.18. What supplemental medication and techniques would you use during this case?

The use of antiemetics would be prudent. Dexamethasone will help to reduce postoperative edema in the airway.

These patients are frequently in the OR and may benefit from the advent of new video recording technology. Chiao and Resta-Flarer created and presented the concept of the “airway passport” which involves collecting videos of each patient's airway to track their therapeutic progress. Clinicians and patients can store these videos and use them at future appointments.

Chiao F, Bolash R, Lesser J, et al. The difficult airway in patients with vascular anomalies of the head and neck: a case series of 238 video laryngoscopies using GlideScope. Paper presented at: International Society for the Study of Vascular Anomalies Biannual Conference; June 16-19, 2012; Malmo, Sweden.

Chiao F, Resta-Flarer F, Lesser J, et al. Airway vascular malformation and dyspnea in blue rubber bleb nevus syndrome. Paper presented at: American Society of Anesthesiology Annual Conference; October 15-19, 2011; Chicago, IL.

Resta-Flarer F, Lesser J, Chiao F, et al. Airway vascular malformation and dyspnea in blue rubber bleb nevus syndrome. In: *The 19th International Workshop on Vascular Anomalies*. Amsterdam, Germany: International Society for the Study of Vascular Anomalies; 2012:141.

D. Postoperative Management

D.1. After uneventful laser microlaryngeal resection using jet ventilation, the patient was extubated in the OR and then transferred to the recovery room. What are the common postoperative complications?

Laryngeal edema can occur early in the postoperative period and is usually manifested by retractions and inspiratory stridor in the recovery room. After microlaryngeal surgery, patients may benefit from humidified oxygen, intravenous steroids (e.g., dexamethasone), and racemic epinephrine inhalation. Laryngospasm may develop because of laryngeal hyperactivity. To reduce the incidence of laryngospasm, lidocaine may be sprayed in the oropharynx. If laryngospasm develops postoperatively, it is treated with the standard maneuvers, including

positive pressure ventilation and Larson's maneuver. Care must be taken not to insufflate the stomach with the use of greater than 20 mm Hg pressure. Often, 5 to 10 mm Hg pressure will suffice. More severe forms of laryngospasm may require the use of small doses of succinylcholine (1/10 of a normal intubation dose, i.e., 0.2 mg per kg for pediatic patients and 0.1 mg per kg for adult patients intravenously). Pulmonary complications can result from retained secretions, atelectasis, or barotrauma (if jet ventilation was used).

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Jaquet Y, Monnier P, Van Melle G, et al. Complications of different ventilation strategies in endoscopic laryngeal surgery: a 10-year review. *Anesthesiology*. 2006;104(1):52-59.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2523-2549.

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Chapter 36
Tracheoesophageal Fistula

Jacques H. Scharoun

A 12-hour-old full-term infant weighing 2.5 kg presents with choking and cyanosis during his first feed. Neonatal intensive care unit (NICU) staff is unable to pass a feeding tube into the stomach. The baby also has copious oral secretions. Before birth, polyhydramnios was seen.

A. Pathophysiology and Differential Diagnosis

1. What is the diagnosis? What are the clinical features of this disease?
2. What is the pathophysiology of this disease?
3. Describe the normal development of the foregut.
4. How are tracheoesophageal fistula (TEF) and esophageal atresia (EA) inherited?
5. How are the different types of TEF/EA classified?
6. What other problems may this child have, and when should these be investigated?
7. What should the parents be told regarding perioperative risk? Risk of recurrence?

B. Preoperative Evaluation and Preparation

1. What laboratory workup should be obtained before surgery?
2. What options are there if patient has severe lung disease?
3. Describe management in the NICU before surgery.
4. Should this patient be routinely intubated preoperatively for airway protection?

C. Intraoperative Management

1. What intravenous (IV) access and monitoring are appropriate before induction? After induction?
2. Discuss fluid and temperature management for this baby.
3. What are the options regarding induction and intubation?
4. What is the role of rigid and fiberoptic bronchoscopy in this patient prior to incision?
5. Describe the steps of an open repair of EA/TEF.
6. What are common intraoperative problems, and how can they be managed?
7. If the surgeon decides to proceed thoracoscopically, how will you perform your anesthetic? Is one-lung ventilation required? How can you isolate the lung safely in a newborn? What are some complications unique to thoracoscopy and one-lung ventilation in the newborn?

D. Postoperative Management

1. When should the baby be extubated?
2. What pain control options are available?
3. What are early and late complications of TEF repair?

A. Pathophysiology and Differential Diagnosis

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A.1. What is the diagnosis? What are the clinical features of this disease?

This patient has EA with a TEF. This occurs in 1 per 3,000 live births. The diagnosis is suspected prenatally by the presence of polyhydramnios, which is caused by the failure of the fetus to swallow amniotic fluid (secondary to EA). Polyhydramnios is a nonspecific prenatal finding that can also be caused by other defects, including duodenal atresia, anencephaly, congenital diaphragmatic hernia, and trisomy 18. Only 10% to 20% of fetuses with polyhydramnios will have other anomalies. There will be an absence of a fluid-filled stomach bubble on prenatal ultrasound. After birth, the neonate will have copious drooling. Attempts to feed the baby will result in coughing and cyanosis. An orogastric tube (OGT) will coil up in the upper esophageal pouch rather than pass into the stomach.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092-1099.

Spitz L. Esophageal atresia. Lessons I have learned in a 40-year experience. *J Pediatr Surg*. 2006;41:1635-1640.

A.2. What is the pathophysiology of this disease?

In this abnormality, there are two distinct problems: TEF and EA. In TEF, the trachea is connected to the esophagus through a fistula. This causes two problems. First, inhaled air can bypass the lungs through the fistula into the stomach and cause hypoventilation and gastric distension. If the lungs are especially noncompliant or the fistula is large, attempts to institute positive pressure ventilation (PPV) can lead to severely compromised ventilation due to gastric expansion or even rupture. Second, there is the continual risk of acidic stomach contents refluxing via the fistula back into the trachea causing aspiration pneumonitis. With EA, the esophagus is divided into a proximal and distal portion. The proximal portion ends in a blind pouch. Secretions from the hypopharynx pool here and cause drooling, coughing, and choking with feeds. The child is unable to feed orally.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092-1099.

Houben CH, Curry JI. Current status of prenatal diagnosis, operative management and outcome of esophageal atresia/tracheo-esophageal fistula. *Prenat Diagn*. 2008;28:667-675.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

A.3. Describe the normal development of the foregut.

The lung bud emerges from the embryonic foregut beginning at the fourth week of gestation. This bud gives rise to the trachea and lung tissue. There are two competing theories about how this happens. The first possibility is that the trachea simply grows rapidly out of the lung bud longitudinally. The second possibility, currently more favored, is a septation model in which the lateral sides of the foregut converge and pinch off two separate compartments that will become the trachea and esophagus; this septation process begins at the lung bud and proceeds cranially. Abnormal separation of the trachea from the foregut results in a residual fistula between the esophagus and trachea.

There are multiple genes involved in the separation of trachea from foregut (future esophagus) making it unlikely that a single genetic error accounts for all cases of TEF/EA. Rats exposed to Adriamycin during development develop TEF/EA of the type most common in humans as well as associated defects in the cardiovascular, skeletal, and gastrointestinal systems that are also seen in humans afflicted with TEF/EA. (These associated defects are described in the following sections.) Aberrant patterns of gene expression gradients from dorsal to ventral in the primitive foregut may be involved. Involved genes include sonic hedgehog

and FOX. Studying rats prenatally exposed to Adriamycin has led to a greater understanding of the process of compartmentalization of the foregut, which is incompletely understood in humans, and hopefully, this knowledge will shed light on the human variety of TEF/EA.

Fausett SR, Klingensmith J. Compartmentalization of the foregut tube: developmental origins of the trachea and

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esophagus. *Wiley Interdiscip Rev Dev Biol*. 2012;1:184-202.

Shaw-Smith C. Genetic factors in esophageal atresia, tracheo-esophageal fistula and the VACTERL association: roles for FOXF1 and the 16q24.1 FOX transcription factor gene cluster, and review of the literature. *Eur J Med Genet*. 2010;53:6-13.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

A.4. How are tracheoesophageal fistula (TEF) and esophageal atresia (EA) inherited?

TEF/EA is believed to be multifactorial in etiology and sporadic. Rarely, it is associated with a specific genetic mutation or syndrome. These include trisomy 18, CHARGE syndrome, anophthalmia-esophageal-genital (AEG) syndrome, Feingold syndrome, and 16q24.1 deletion syndrome. Most of the cases, however, are non-familial. There is a 1% chance of recurrence in each sibling of someone with EA. EA is twice as common in twins.

Shaw-Smith C. Genetic factors in esophageal atresia, tracheo-esophageal fistula and the VACTERL association: roles for FOXF1 and the 16q24.1 FOX transcription factor gene cluster, and review of the literature. *Eur J Med Genet*. 2010;53:6-13.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

A.5. How are the different types of TEF/EA classified?

There are five types of TEF according to the classic Gross's classification (Fig. 36.1). Type A is pure EA with no involvement of the respiratory tree; this occurs in 8% of cases. Gross type B has EA and a fistula connecting the proximal esophageal pouch to the trachea; this occurs in less than 1%. The most common is type C, with EA and fistula linking the distal esophagus to the trachea; this occurs in 75% to 80% of cases. Rarely, type D occurs with two fistula connecting both proximal and distal esophagus to the trachea (2%). Type E, known as an H-type fistula, has no atresia. Instead, an intact esophagus has a linkage with trachea through a fistula, and it occurs in 4%.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092-1099.

Houben CH, Curry JI. Current status of prenatal diagnosis, operative management and outcome of esophageal atresia/tracheo-esophageal fistula. *Prenat Diagn*. 2008;28:667-675.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

A.6. What other problems may this child have, and when should these be investigated?

Unfortunately, TEF often does not occur in isolation. Fifty percent of children with EA/TEF will have additional anomalies. Most often, they occur in the spectrum known as *VACTERL* (formerly known as *VATER*):

V = vertebral anomalies (10%)

A = anal canal defect (anal atresia) (14%)

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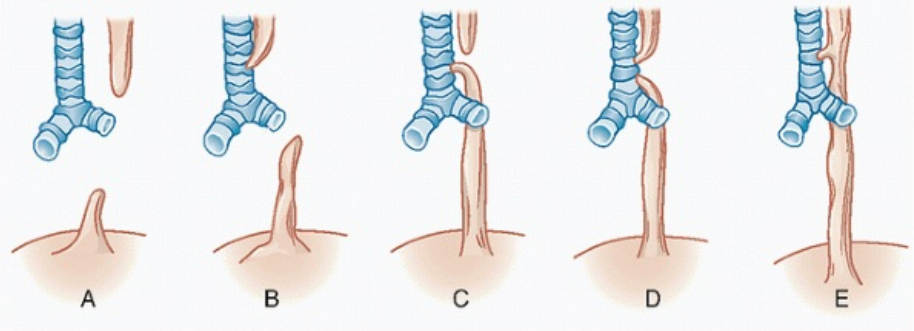


FIGURE 36.1 Gross's classification of esophageal atresia and tracheoesophageal fistula. (Modified from Gregory GA, ed. *Pediatric Anesthesia*. 2nd ed. New York: Churchill Livingstone; 1989:921, with permission.)

C = cardiac malformations (29%), including ventricular septal defect, atrial septal defect, tetralogy of Fallot, right-sided arch, patent ductus arteriosus

TE = tracheoesophageal fistula

R = renal dysplasia

L = limb defect (radial aplasia)

A patient is considered to have VACTERL association with the presence of three or more of these lesions. Nearly one-third of TEF patients will have an additional VACTERL lesion, and an additional one-fifth will have two VACTERL problems. Other possible gastrointestinal problems include malrotation of the midgut and duodenal atresia. Renal problems can include malposition, hydronephrosis, and ureteral abnormalities.

Because the existence of these associated defects may alter the surgical or anesthetic plan, and because the TEF is an urgent but not emergent procedure, these other possible defects should be assessed *prior* to TEF repair.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092-1099.

Diaz LK, Akpek EA, Dinavahi R, et al. Tracheoesophageal fistula and associated congenital heart disease: implications for anesthetic management and survival. *Paediatr Anaesth*. 2005;15:862-869.

A.7. What should the parents be told regarding perioperative risk? Risk of recurrence?

The survival of TEF babies has improved over the years because of improvements in intensive care unit care, anesthesia, and surgical technique. Waterston developed the first classification of prognosis of TEF in 1962 as follows:

- Group A: weight greater than 2.5 kg, healthy, survival 95%
- Group B: weight 1.8 to 2.5 kg and healthy, or greater than 2.5 kg with moderate pneumonia, or other anomalies, survival 68%
- Group C: weight less than 1.8 kg, or greater than 1.8 kg with severe pneumonia or severe congenital anomaly, survival 6%

With improvements in neonatal care, the survival in Waterston groups A and B both approached 100%. So Spitz developed a new classification system in the 1990s to better stratify the surgical risk incorporating the realization that cardiac disease is a leading cause of mortality in the TEF group:

- Spitz group I: birth weight more than 1.5 kg, no major cardiac disease, survival 97%
- Spitz group II: birth weight less than 1.5 kg, or major cardiac disease, survival 59%

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- Spitz group III: birth weight less than 1.5 kg and major cardiac disease, survival 22%

Okamoto et al. in 2009 suggested an updating of Spitz grouping as follows:

- Okamoto group I: weight more than 2.0 kg, no major cardiac disease, survival 100%
- Okamoto group II : weight less than 2.0 kg, no major cardiac disease, survival 82%
- Okamoto group III: weight more than 2.0 kg and major cardiac disease, survival 72%
- Okamoto group IV: weight less than 2.0 kg and major cardiac disease, survival 27%

The risk of recurrence in a sibling is 1%.

Lopez PJ, Keys C, Pierro A, et al. Oesophageal atresia: improved outcome in high-risk groups? *J Pediatr Surg*. 2006;41:331-334.

Okamato T, Takamizawa S, Arai H, et al. Esophageal atresia: prognostic classification revisited. *Surgery*. 2009;145:675-681.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

B. Preoperative Evaluation and Preparation

B.1. What laboratory workup should be obtained before surgery?

First, one must assess the presence and severity of pulmonary disease, especially looking for aspiration pneumonia and respiratory distress associated with prematurity. Plain

chest x-ray may show infiltrates. It may also show the presence of congestive heart failure in the setting of associated cardiac disease, which may be optimized by administering a diuretic. A radiopaque OGT will be coiled in the proximal esophageal pouch, whereas an abdominal x-ray may show air in the bowels entering through the fistula. Because of the risk of aspiration, the use of contrast dye to delineate the fistula should be used only when there is diagnostic uncertainty. Ideally, contrast would be given under fluoroscopy, so that any aspiration can be immediately detected. This should only be done if the baby is stable enough to be transported to the fluoroscopy suite. Of note, an OGT that appears to enter the stomach may also reflect esophageal perforation caused by repeated traumatic insertion attempts.

Second, an echocardiogram is *mandatory* since major cardiac defects strongly influence survival and may have an impact on anesthetic management. If the child has severe tetralogy of Fallot, he may require placement of a temporary shunt between the systemic arterial and pulmonary circulation prior to repair of the TEF. In addition, one wants to look for presence of a right-sided aortic arch because this will require positioning the infant with the opposite side down from usual.

Spinal plain films should be done to exclude vertebral anomalies, especially if epidural pain management is being considered. Renal ultrasound should be done to rule out abnormalities, especially hydronephrosis. In addition, complete blood count (CBC), arterial blood gas, and electrolytes should be drawn, and at least 1 unit of packed red blood cells should be type and crossed.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092-1099.

Houben CH, Curry JI. Current status of prenatal diagnosis, operative management and outcome of esophageal atresia/tracheo-esophageal fistula. *Prenat Diagn*. 2008;28:667-675.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

B.2. What options are there if patient has severe lung disease?

In the past, most children with TEF were routinely given a gastrostomy (under local anesthesia) followed by a staged

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repair. This would prevent critical gastric distension while child was being treated for the pneumonia that typically ensued when the diagnosis was delayed. It was discovered that this tripled the incidence of postoperative gastroesophageal reflux disease (GERD) and is no longer routinely performed. Very early primary repair is considered standard of care. However, there remains a subset of neonates with either severe pneumonia or respiratory distress syndrome (from prematurity), who are poor anesthetic and surgical risks (Waterston type C) and who need to be intubated because of respiratory disease. One technique to optimize ventilation in these babies while minimizing gastric distension (through the fistula) without creating a gastrostomy is to employ high frequency oscillator ventilation to minimize the peak inspiratory pressure. If this is insufficient, a simple gastrostomy is placed to allow drainage of gastric fluid (to minimize further aspiration) and to prevent or relieve gastric distension that can occur with PPV in the setting of a type C TEF. This procedure can be performed under local anesthesia and obviates the need for a thoracotomy. The problem with this approach is that by decompressing the stomach, gas from the trachea can now bypass the lungs and exit through the stomach. This is especially a concern if the baby's lungs are noncompliant from pneumonia or respiratory distress syndrome. This can make it difficult or impossible to ventilate the baby adequately. In this situation, the priority is to perform an emergency occlusion or ligation of the fistula from an abdominal or thoracic approach, and the esophageal repair is deferred until the patient is more stable.

More recently, Ratan et al. describe another salvage technique, which involves occluding the fistula retrograde through a gastrostomy. The child is given local anesthetic over the incision site and a styletted no. 10 French Foley catheter is advanced through a gastrostomy to a position just above the gastroesophageal junction using fluoroscopy. The balloon is then inflated and the catheter is either clamped or placed under water seal. In this way, the baby can be ventilated with positive pressure while avoiding gastric distention or inadequate

ventilation from gas bypassing the lungs. This technique runs the risk of esophageal rupture if the catheter is not placed properly.

Lampland AL, Mammel MC. The role of high-frequency ventilation in neonates: evidence-based recommendations. *Clin Perinatol*. 2007;34:129-144.

Orford J, Cass DT, Glasson MJ. Advances in the treatment of oesophageal atresia over three decades: the 1970s and the 1990s. *Pediatr Surg Int*. 2004;20:402-407.

Ratan SK, Rattan KN, Ratan J, et al. Temporary transgastric fistula occlusion as salvage procedure in neonates with esophageal atresia with wide distal fistula and moderate to severe pneumonia. *Pediatr Surg Int*. 2005;21:527-531.

Spitz L. Esophageal atresia. Lessons I have learned in a 40-year experience. *J Pediatr Surg*. 2006;41:1635-1640.

B.3. Describe management in the NICU before surgery.

After the diagnosis of TEF is established and other coexisting anomalies investigated, the baby should be immediately placed on nothing-by-mouth (NPO) status. He should be kept in a warmed isolette with the head elevated at least 30 degrees to minimize reflux through the fistula. A nasogastric tube should be placed in the proximal esophageal pouch and kept on intermittent suction to minimize aspiration of oral secretions. Antibiotics to treat aspiration pneumonia should be given when appropriate. Ampicillin and gentamicin should be given to those patients who have coexisting cyanotic cardiac disease as prophylaxis. Ensure that blood is available from the blood bank. Because the patient will require a thoracotomy with lung retraction and intermittent compression of the trachea and great vessels, an arterial line is mandatory for the case. This should ideally be placed in the NICU. An umbilical artery line may be conveniently placed by a qualified neonatologist. Two additional IV lines should also be placed. Avoid placing lines in the right arm, as this arm will most likely be elevated during right thoracotomy and access will be limited.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092-1099.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

B.4. Should this patient be routinely intubated preoperatively for airway

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protection?

Unless mandated by severe pulmonary disease, the child is not intubated routinely preoperative to minimize the possibility of gastric distension from PPV through the fistula. Intubation does not protect the child from aspiration of gastric contents through the fistula.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092-1099.

C. Intraoperative Management

C.1. What intravenous (IV) access and monitoring are appropriate before induction? After induction?

At least one peripheral IV should be in place before induction. A second may be placed after the patient is anesthetized. If the surgeon intends to give the child total parenteral nutrition postoperatively, a central line may be placed. Arterial line (a-line) placement for blood gas and hemodynamic monitoring should be placed before incision if it has not already been inserted in the NICU. An a-line is especially useful if thoracoscopy is planned. If a peripheral a-line is not feasible, an umbilical a-line may be placed by someone experienced in this technique. Electrocardiogram, oxygen saturation, end-tidal carbon dioxide (CO_2), and rectal temperature should also be monitored. A precordial stethoscope should be placed over the left axilla to assess breath sounds in case of inadvertent movement of the endotracheal tube (ETT) during surgical retraction or positioning. A second stethoscope placed over the stomach may be useful to assess if the fistula is being ventilated.

If a gastrostomy tube is present, the end may be placed underneath a water seal. The presence of bubbling indicates ventilation through the fistula, which will occur if the tip of

the ETT is proximal to the opening of the fistula. A capnograph inserted into the gastrostomy tube will indicate the same thing.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092-1099.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:577.

Krosnar S, Baxter A. Thoracoscopic repair of esophageal atresia with tracheoesophageal fistula: anesthetic and intensive care management of a series of eight neonates. *Paediatr Anaesth*. 2005;15:541-546.

C.2. Discuss fluid and temperature management for this baby.

As with all neonates undergoing surgery, meticulous attention to fluid management and temperature is essential. The child should be transported to the operating room (OR) (in a head-up position) in a warmed isolette, with a stocking cap on his head to minimize temperature shifts. The OR should be prewarmed to at least 85°F. Surgical irrigation, IV crystalloid solutions, and any blood products should be warmed. Using a forced-air convective warming system is strongly recommended. An appropriate size heat-moisture exchanger placed in the airway can be useful. Keep in mind that the neonate is more prone to develop hypothermia for a number of reasons including limited subcutaneous fat. One way the baby compensates is with brown fat nonshivering thermogenesis. When choosing an anesthetic technique, keep in mind that volatile anesthetics including halothane and isoflurane can decrease thermogenesis by up to 70%.

Considering that the patient has been on NPO since birth and whatever was fed probably did not reach the stomach because of esophageal atresia, it is advisable to administer a dextrose-containing solution at a controlled rate during the operation. D10/0.2 normal saline (NS) administered IV at a maintenance rate using a controlled-infusion pump is an excellent way to avoid hypoglycemia. Insensible losses should be estimated at 3 to 4 mL/kg/hr and replaced with an isotonic solution. Urine output (ideally 1 mL/kg/hr) may be difficult to assess accurately in a low birth weight baby.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA:

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Mosby Elsevier; 2011:577.

Krosnar S, Baxter A. Thoracoscopic repair of esophageal atresia with tracheoesophageal fistula: anesthetic and intensive care management of a series of eight neonates. *Paediatr Anaesth*. 2005;15:541-546.

C.3. What are the options regarding induction and intubation?

The goal is to intubate the baby to allow adequate gas exchange with the lowest possible inspiratory pressure needed to inflate the lungs, avoid atelectasis, and minimize gas flow through the fistula. Avoidance of PPV until the fistula is ligated is one approach. One can intubate awake or after inhalation induction while maintaining spontaneous ventilation. Awake intubation used to be common, but attention must be paid to the possibility of increased intracranial pressure or intraventricular hemorrhage in the premature infant as well as the obvious discomfort to the child. If one chooses to intubate after induction, this will requires a deep inhalational technique with gentle assisting of each breath to minimize atelectasis. In either case, the lowest inspiratory pressure is used, minimizing distension of the stomach. Gentle positive pressure mask ventilation followed by intubation may be tolerated provided airway pressure is kept low. If the lungs are suspected of being poorly compliant due to pneumonia or prematurity, then mask ventilation should be avoided. Good intubating conditions can be achieved with deep volatile agent, but maintaining adequate ventilation and surgical conditions during a thoracotomy without relaxant may be challenging. Rapid sequence IV induction and intubation (to minimize face-mask ventilation) is another option provided that attention is paid to minimizing inspiratory pressure.

The most important aspect of the intubation is the correct positioning of the ETT. The goal is to have the tip of the ETT distal to the fistula yet proximal to the carina. If the tube is deliberately placed deep (into the right mainstem) with the bevel facing forward, then slowly pulled back just until breath sounds occur on the left equal to the right, the tube is likely to be in good position. If the tube is in good position, then the child can be paralyzed and normal

PPV maintained. The difficulty lies in maintaining good position of the ETT during surgical manipulation and turning the patient lateral. Alabbad et al. describe a disastrous scenario in which a neonate with TEF was intubated and ETT position confirmed by breath sounds; yet after turning the patient, the ETT migrated *into* the fistula without being recognized. This resulted in failure to ventilate the baby and eventual cardiac arrest.

Yet another option, to avoid the risk of ETT malposition, is to deliberately keep the tip of the tube *above* the fistula (if it is shown by bronchoscopy to be small) and keep ventilation pressures low until the fistula is ligated.

Alabbad SI, Shaw K, Puligandla PS, et al. The pitfalls of endotracheal intubation beyond the fistula in babies born with type C esophageal atresia. *Semin Pediatr Surg*. 2009;18(2):116-118.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092-1099.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:577.

Krosnar S, Baxter A. Thoracoscopic repair of esophageal atresia with tracheoesophageal fistula: anesthetic and intensive care management of a series of eight neonates. *Paediatr Anaesth*. 2005;15:541-546.

C.4. What is the role of rigid and fiberoptic bronchoscopy in this patient prior to incision?

Perioperative bronchoscopy before commencing TEF repair has become common. First, the airway can be examined directly to help guide the surgical technique. A cervical level fistula does not require a thoracotomy to repair. Bronchoscopy can detect the presence of tracheomalacia or detect the presence of a second fistula (rare) which may indicate challenging airway management. Identifying the level of the fistula can assist in correctly positioning the ETT (11% may have it below the carina in one series). Second, if deemed appropriate, the fistula can be occluded using a 3.5 Fogarty occlusion catheter, thereby allowing normal PPV without distending the abdomen. This technique of isolating the trachea and esophagus before ligation may be useful in skilled hands. However, there is a real possibility that during positioning or

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surgical manipulation, the Fogarty balloon may slide back into the trachea. This could precipitate immediate complete airway obstruction if not promptly recognized and treated. Recurrent TEF can be treated endoscopically by placing fibrin glue directly into the fistula, precluding the need for a second thoracotomy.

Atzori P, Iacobelli BD, Bottero S, et al. Preoperative tracheobronchoscopy in newborns with esophageal atresia: does it matter? *J Pediatr Surg*. 2006;41:1054-1057.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:577.

Meier JD, Sulman CG, Almond PS, et al. Endoscopic management of recurrent congenital tracheoesophageal fistula: a review of techniques and results. *Int J Pediatr Otorhinolaryngol*. 2007;71:691-697.

Spitz L. Esophageal atresia. Lessons I have learned in a 40-year experience. *J Pediatr Surg*. 2006;41:1635-1640.

C.5. Describe the steps of an open repair of EA/TEF.

First, the patient is positioned in the lateral position, left side down. If the patient has a right-sided aortic arch (rare), the surgeon will position the patient with right side down. A retropleural approach is used which minimizes the danger from an anastomotic leak. The azygous vein is ligated to better visualize the fistula. The fistula is exposed and ligated, leaving a little stump; this usually occurs within 45 minutes. It is important to remember that a fistula stump remains after repair, at least initially. When the patient returns for follow-up surgery (e.g., esophageal dilations), during intubation, the ETT may be observed to pass through the vocal cords yet the tip end up in the stump, precluding effective ventilation. An anterior posterior chest x-ray (AP CXR) will not show this, but a lateral film will. This possibility should always be entertained if unable to ventilate one of these patients despite apparent successful intubation. If the patient is stable, then normal PPV can commence while the repair of the esophagus begins. The upper esophagus is mobilized, then the distal esophagus. The esophagus is joined together. Following this, a feeding tube is placed across the anastomosis to allow feeding (if the patient does not have a gastrostomy).

The lung should be carefully reexpanded to eliminate atelectasis before closure. Chest tubes are not routinely placed following repair.

Houben CH, Curry JI. Current status of prenatal diagnosis, operative management and outcome of esophageal atresia/tracheo-esophageal fistula. *Prenat Diagn*. 2008;28:667-675.

Spitz L. Esophageal atresia. Lessons I have learned in a 40-year experience. *J Pediatr Surg*. 2006;41:1635-1640.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

C.6. What are common intraoperative problems, and how can they be managed?

Interference with ventilation is the most common problem and can have many causes. Lung retraction with resulting atelectasis leads to frequent desaturation. It may be difficult if not impossible to maintain normocarbia. The PCO_2 may rise to 70 to 80 mm Hg despite all attempts to optimize ventilation. If the patient has a Fogarty catheter in the fistula, it may be displaced into the trachea causing total airway obstruction. Surgical manipulation of the soft trachea makes the ETT vulnerable to kinking or displacement distally into right mainstem or proximally above the fistula. Frequent compression of vital structures in the mediastinum can lead to profound hemodynamic compromise. Blood and secretions are a constant problem, which risk obstructing the tube. The ETT should be suctioned frequently, more so if blood is seen. (It does not require much blood to clog a 3.0 ETT.) The retracted lung may need to be intermittently reexpanded to avoid severe hypoxia. Severe gastric distension before ligation of the TEF may require emergent gastric needle decompression. It is crucial to maintain close communication with the surgeon. Avoid hypothermia.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*.

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2011;21:1092-1099.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:577.

C.7. If the surgeon decides to proceed thoracoscopically, how will you perform your anesthetic? Is one-lung ventilation required? How can you isolate the lung safely in a newborn? What are some complications unique to thoracoscopy and one-lung ventilation in the newborn?

Thoracoscopy to repair TEF/EA has gained increasing popularity over the past decade. Three major advantages are described. First, the approach provides excellent visualization of the fistula, which allows rapid ligation and stabilization of ventilation. Second, avoidance of thoracotomy results in less pain. Third, avoiding posterolateral thoracotomy results in better chest wall symmetry and less long-term scoliosis. A meta-analysis by Borruto et al. showed that the anastomosis leak rate was not increased in the thoracoscopic group.

To perform this anesthetic, an a-line is mandatory due to the significant gradient between end-tidal and arterial CO_2. Concerns regarding intubation, PPV, paralysis, fluid, and temperature management are identical to that for an open repair. Opioid requirements may be reduced. Isolating the right lung is *not* required for a successful thoracoscopy. Deliberate left mainstem ETT intubation to collapse the right lung may result in prolonged left upper lobe lung collapse. Krosnar describes a series of eight cases of thoracoscopic repair performed successfully with the tube positioned in the trachea. One-lung ventilation is created by insufflation of the right chest cavity with CO_2 to a pressure of 5 mm Hg. One can expect significant desaturation (to 84% to 90% initially), and the baby will need to be on 100% FIO_2. A sudden increase in end-tidal CO_2 ($ETCO_2$) suggests the possibility of surgical disruption causing escape of CO_2 into the airway.

Borruto FA, Impellizeri P, Montalto AS, et al. Thoracoscopy versus thoracotomy for esophageal atresia and tracheoesophageal fistula repair: review of the literature and meta-analysis. *Eur J Pediatr Surg*. 2012;22:415-419.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092-1099.

Dingemann C, Ure BM. Minimally invasive repair of esophageal atresia: an update. *Eur J Pediatr Surg*. 2013;23:198-203.

Krosnar S, Baxter A. Thoracoscopic repair of esophageal atresia with tracheoesophageal fistula: anesthetic and intensive care management of a series of eight neonates. *Paediatr Anaesth*. 2005;15:541-546.

D. Postoperative Management

D.1. When should the baby be extubated?

Although some surgeons prefer to have the baby extubated immediately in the OR to minimize tension on the suture line, this can be risky. Many infants with TEF have a deficiency of tracheal cartilage at the level of the fistula predisposing to tracheomalacia. This can precipitate airway obstruction requiring immediate reintubation. Many of the children have lung disease from prematurity or aspiration pneumonia; after receiving narcotics for pain, they may be prone to hypoventilation. If early extubation is planned, an epidural technique might be helpful. However, if the child is to remain intubated, care should be made to limit inspiratory pressure to protect the repair from disruption.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092-1099.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:578.

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D.2. What pain control options are available?

If the patient is going to remain intubated postoperative (most likely), then a narcotic technique is advisable. Fentanyl at 10 to 20 μg per kg with muscle relaxant will give hemodynamic stability and allow analgesia to be continued in the postoperative period. For experienced practitioners, an epidural can also be placed. An epidural catheter threaded through the caudal space can be threaded up to the thoracic dermatomes. Check the placement of the catheter with fluoroscopy before using it. This technique should only be undertaken by one who is highly experienced in regional anesthesia for children, with full awareness of the risks and ability to manage complications.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092-1099.

D.3. What are early and late complications of TEF repair?

Early anastomosis leakage occurs in up to 15% of patients. This may require immediate exploration or may be managed expectantly. Esophageal dysmotility and GERD are common. The dysmotility may be from abnormal innervation of the distal esophagus or may be related to vagal nerve injury during the repair. Stricture of the esophageal anastomosis may require repeated dilatations. Tracheomalacia may be evident postoperatively, and vocal cord paresis has been reported.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:578.

Houben CH, Curry JI. Current status of prenatal diagnosis, operative management and outcome of esophageal atresia/tracheo-esophageal fistula. *Prenat Diagn*. 2008;28:667-675.

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Chapter 37
Congenital Diaphragmatic Hernia

Peter M. Savard

Fun-Sun F. Yao

A full-term male baby was born with respiratory distress and cyanosis. Physical examination showed barrel chest and scaphoid abdomen. The breath sounds were absent in the left side of the chest; the heart sounds were best heard in the right side of the chest. Labored respiration, nasal flaring, and sternal retraction were found. The baby weighed 2,800 g. Blood pressure was 60/30 mm Hg; heart rate, 160 beats per minute; respiration, 70 breaths per minute; and temperature, 36°C (96.8°F). Arterial blood gas analysis on room air showed the following: pH, 7.20; $PaCO_2$, 55 mm Hg; PaO_2, 35 mm Hg; and CO_2 content, 19 mEq per L.

A. Medical Disease and Differential Diagnosis

1. What differential diagnoses are compatible with these signs and symptoms?
2. Describe the incidence and classification of congenital diaphragmatic hernia (CDH).
3. What are the causes of hypoxemia in patients with CDH?
4. How do you assess the severity of pulmonary hypoplasia?
5. How do you make a diagnosis of right-to-left shunting through the patent ductus arteriosus?
6. What other congenital anomalies are usually associated with CDH?

B. Preoperative Evaluation and Preparation

1. How would you interpret the following arterial blood gas analyses: pH, 7.20; $PaCO_2$, 55 mm Hg; PaO_2, 35 mm Hg; and CO_2 content, 19 mEq per L? How would you correct them?
2. What immediate treatment should be given to improve the newborn's respiratory status preoperatively?
3. Should CDH be repaired urgently once the diagnosis is made and confirmed?
4. What are the effects of nitric oxide (NO) on pulmonary and systemic circulation?
5. What is the current role of extracorporeal membrane oxygenation (ECMO) in the management of CDH?

C. Intraoperative Management

1. What monitors would you use for this neonate during surgery?
2. How would you induce and maintain anesthesia?
3. Would you use nitrous oxide for anesthesia? Why?
4. How would you ventilate the patient?
5. Is the infant with CDH more at risk from hypothermia?

6. The surgeon returned the intrathoracic stomach and intestine to the peritoneal cavity and the ipsilateral lung was found to be hypoplastic and collapsed. The resident anesthesiologist tried to expand the collapsed lung manually with positive airway pressure. Five minutes after the abdomen was closed, the blood pressure suddenly dropped from 70/40 to 30/20 mm Hg, the heart rate from 150 to 80 beats per minute, and the pulse oximeter from 95% down to 60% saturation. What would you do immediately?
7. Discuss fluid therapy in this patient.
8. At the conclusion of surgery, would you extubate the patient in the operating room?

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D. Postoperative Management

1. What is the mortality rate in patients with CDH? What postoperative problems would you expect in this patient?

A. Medical Disease and Differential Diagnosis

A.1. What differential diagnoses are compatible with these signs and symptoms?

The differential diagnosis of cyanosis and respiratory distress in the newborn is broad and includes respiratory distress syndrome, sepsis, meconium aspiration, diaphragmatic hernia, persistent pulmonary hypertension of the newborn (PPHN), cyanotic congenital heart disease, hypoglycemia, choanal atresia, and airway anomalies. The constellation of scaphoid abdomen (due to the absence of abdominal contents), barrel chest, bowel sounds in the chest, and the shift of heart sounds to the right is only consistent with CDH. To confirm the diagnosis, a chest radiograph should be performed to demonstrate gas-filled loops of bowel in the chest. The lung on the side of the hernia is compressed into the hilum, and the mediastinum is shifted to the opposite side of the chest. If in doubt, a radiopaque dye may be injected through a nasogastric tube to delineate the stomach and intestine in the chest.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2012:594-596.

Kliegman RM, Stanton BF, St Geme JW III, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier; 2015:862-864.

A.2. Describe the incidence and classification of congenital diaphragmatic hernia (CDH).

The incidence of CDH is estimated to be between 1 in 2,500 and 1 in 3,000 births. Eighty-five percent of lesions are on the left side. Ninety percent are posterolateral (Bochdalek hernia). Anteromedial and paraesophageal hernias and eventrations make up the remainder (Fig. 37.1).

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia, PA: Saunders/Elsevier Science; 2013:756-758.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby/Elsevier Science; 2011:567-574.

A.3. What are the causes of hypoxemia in patients with CDH?

Infants with CDH have deficient bilateral major airway and vessel branching not explained by simple compression of the ipsilateral and contralateral lungs. The mechanisms for these abnormalities and the resultant lung and vascular hypoplasia are not known. The severity of pulmonary vascular hypoplasia correlates with mortality in CDH. Airway maldevelopment leads to reduced total number of alveoli at birth, with resultant low lung compliance and decreases in both ventilation and surface area for gas exchange. Oxygenation is thus impaired. Pulmonary vascular hypoplasia results in pulmonary hypertension, causing right-to-left shunting through the patent ductus arteriosus, with resultant hypoxemia.

Bancalari E, Polin RA, eds. *The Newborn Lung: Neonatology Questions and Controversies*. Philadelphia, PA: Elsevier Health Sciences; 2012:381-406.

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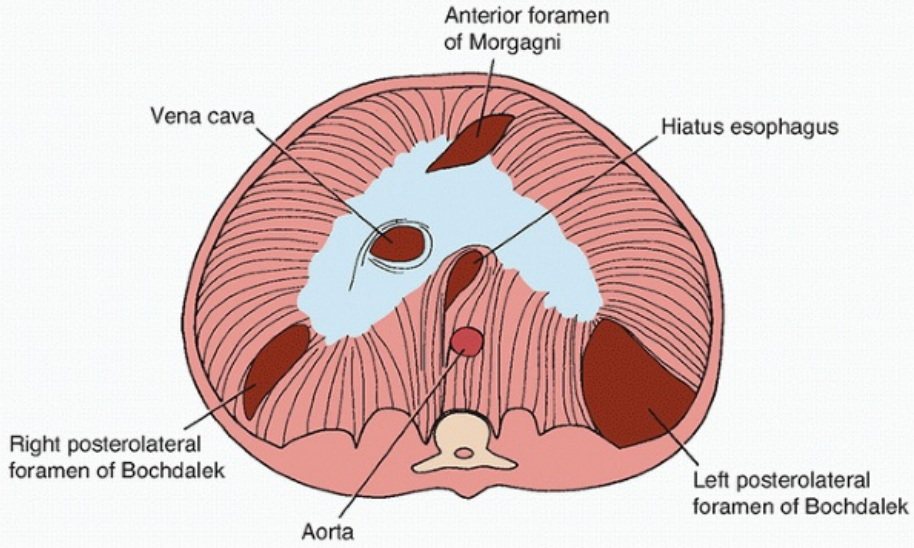


FIGURE 37.1 Potential sites of congenital diaphragmatic hernia.

A.4. How do you assess the severity of pulmonary hypoplasia?

Prenatally, the degree of pulmonary hypoplasia is estimated using ultrasound. Lung-to-head circumference and diameter of the proximal pulmonary artery indexed to the descending aorta are two measurements used to estimate risk of severe pulmonary hypoplasia. Intrathoracic position of the liver prenatally independently predicts poor outcome.

Postnatally, the severity of pulmonary hypoplasia is apparent in the clinical presentation of the infant, in that infants who are born with severe hypoplasia exhibit symptoms immediately after birth and require mechanical ventilation immediately. Inability to be resuscitated in the delivery room is a marker of lethal lung hypoplasia. Most centers will not attempt emergency ECMO in this situation.

Bancalari E, Polin RA, eds. *The Newborn Lung: Neonatology Questions and Controversies*. Philadelphia, PA: Elsevier Health Sciences; 2012:381-406.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Saunders/Elsevier Science; 2013:756-758.

A.5. How do you make a diagnosis of right-to-left shunting through the patent ductus arteriosus?

Pulse oximetry from the upper (preductal) and lower/umbilical (postductal) arteries can help identify a right-to-left shunt occurring through the ductus arteriosus. A difference in arterial PO_2 >20 mm Hg or oxygen saturation SpO_2 >10% should be considered significant.

Fuhrman B, Zimmerman J, eds. *Fuhrman and Zimmerman's Pediatric Critical Care*. Philadelphia, PA: Elsevier Health Sciences; 2011:666.

A.6. What other congenital anomalies are usually associated with CDH?

The incidence of other congenital anomalies in newborns with CDH is as follows:

- *Cardiovascular system*. 13% to 23%; for example, atrial septal defect, ventricular septal defect, coarctation of aorta, and tetralogy of Fallot
- *Central nervous system*. 28%; for example, spina bifida, hydrocephalus, and acephalus
- *Gastrointestinal system*. 20%; for example, malrotation and atresia

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- *Genitourinary system*. 15%; for example, hypospadias

Gregory GA, ed. *Gregory's Pediatric Anesthesia*. 5th ed. New York: Churchill Livingstone; 2012:510-512.

B. Preoperative Evaluation and Preparation

B.1. How would you interpret the following arterial blood gas analyses: pH, 7.20; $PaCO_2$, 55 mm Hg; PaO_2, 35 mm Hg; and CO_2 content, 19 mEq per L? How would you correct them?

The blood gas analyses showed mixed respiratory and metabolic acidosis and severe hypoxemia. Severe hypoxemia is caused by the pulmonary pathologies and persistent pulmonary hypertension (PPH). Hypoxemia stimulates respiratory chemoreceptors and causes hyperventilation, resulting in respiratory alkalosis initially. However, if hypoxemia is not corrected, the patient will become exhausted and CO_2 retention ensues. Severe pulmonary hypoplasia may also cause CO_2 retention. Severe hypoxemia induces anaerobic metabolism, resulting in lactic acidosis.

Hypoxemia and respiratory acidosis should be treated with mechanical ventilation and oxygen therapy. Metabolic acidosis should be corrected by administration of sodium bicarbonate and improvement of circulation with fluid therapy.

Kliegman RM, Stanton BF, St Geme JW III, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier; 2015:1989.

B.2. What immediate treatment should be given to improve the newborn's respiratory status preoperatively?

Immediate treatment should include intubation of the trachea and decompression of the stomach with an orogastric tube. Lung protective ventilation strategies should then be employed with the goal of establishing a period of stability prior to attempted surgical repair. Permissive hypercapnia with pressure limitation and permissive oxygenation (tolerating preductal SpO_2 values as low as the low 80s) allow protection of the vulnerable hypoplastic lungs from ventilator-associated injury during perinatal transition and ultimately promote growth and recovery.

Bancalari E, Polin RA, eds. *The Newborn Lung: Neonatology Questions and Controversies*. Philadelphia, PA: Elsevier Health Sciences; 2012:381-406.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia, PA: Saunders/Elsevier Science; 2013:756-758.

B.3. Should CDH be repaired urgently once the diagnosis is made and confirmed?

In the past, CDH was considered a surgical emergency in the belief that the herniated contents caused lung collapse and respiratory failure. However, recognition of the role of pulmonary hypertension, in addition to pulmonary hypoplasia and the effects of surgical repair on pulmonary function, has prompted critical reevaluation of that strategy. It is now clear that lung compression by the herniated viscera is a minor factor in the cardiopulmonary compromise compared with the pulmonary hypertension and hypoplasia. The consensus today is to delay surgery and concentrate on medical stabilization. The goals of medical management are improved oxygenation and correction of metabolic acidosis using the least aggressive ventilation possible. Optimizing hemodynamic and respiratory support rather than specific timing of surgery contributes to improving outcome.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia, PA: Saunders/Elsevier Science; 2013:756-758.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA:

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Mosby/Elsevier Science; 2011:567-574.

B.4. What are the effects of nitric oxide (NO) on pulmonary and systemic circulation?

When produced in vivo, NO is endothelium-derived relaxing factor producing smooth muscle relaxation and vasodilation. Inhaled NO is unique, as it is a selective pulmonary vasodilator and has no effect on systemic circulation because it is inactivated immediately on exposure to hemoglobin. In general, most patients with intractable pulmonary hypertension plus lung hypoplasia do not have a dramatic response to NO. Nonetheless, because some patients do

respond and the drug has a limited toxicity in lower doses, NO is often used in infants with CDH who require therapy beyond conventional ventilator support.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby/Elsevier Science; 2011:567-574.

B.5. What is the current role of extracorporeal membrane oxygenation (ECMO) in the management of CDH?

A 2008 Cochrane review concluded that in spite of short-term efficacy, improved long-term survival without major sequelae was not apparent with ECMO. Thus, many centers now reserve ECMO as a rescue therapy for infants who have persistent preductal hypoxemia in spite of inotropic and ventilator support.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby/Elsevier Science; 2011:567-574.

C. Intraoperative Management

C.1. What monitors would you use for this neonate during surgery?

Respiratory

- Two pulse oximeters, for preductal and postductal oxygen saturation
- Capnometry
- Inspiratory pressure measurement
- Inspiratory oxygen concentration
- Intraoperative arterial blood gas analysis

Cardiovascular

- Five-lead electrocardiogram
- Blood pressure cuff
- Arterial line: right radial artery for preductal PaO_2
- Central venous pressure (CVP) line for evaluating volume status and right ventricular performance

Thermoregulatory

- Esophageal or rectal temperature probe

C.2. How would you induce and maintain anesthesia?

Infants with a moderate or large CDH generally require ventilator support and sedation preoperatively, and many require neuromuscular blockade. In general, the preoperative care of the patient is continued in the operating room with the addition of high-dose opioids. Volatile agents may reduce systemic vascular resistance (SVR) more than peripheral

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vascular resistance (PVR), resulting in worsening right-to-left shunt. Adequate central access should be established. Frequent blood gas sampling will guide changes in respiratory management during closure of the diaphragm. Paradoxically, the compliance of the chest decreases after surgical correction of the hernia and return of the displaced abdominal organs to the abdomen. This is the result of the effect of the distended abdomen on the non-hypoplastic lung, without significant improvement of function of the hypoplastic lung.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Saunders/Elsevier Science; 2013:756-758.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby/Elsevier Science; 2011:567-574.

C.3. Would you use nitrous oxide for anesthesia? Why?

No. Nitrous oxide is avoided because many infants require high-inspired oxygen concentration and because it may distend the intrathoracic gut and compress the functioning lung tissue, further compromising pulmonary function. Moreover, a distended gut may cause

difficulty in abdominal closure and may increase abdominal pressure, compressing the inferior vena cava and resulting in hypotension.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby/Elsevier Science; 2011:567-574.

C.4. How would you ventilate the patient?

The goals of ventilation and oxygenation in the operating room are the same as preoperative: avoiding volutrauma by using small tidal volumes, appropriate positive end-expiratory pressure (PEEP) to avoid derecruitment at end expiration, adequate oxygenation without hyperoxia with goal saturation in the low to mid-90s, and permissive hypercapnia with maintenance of pH >7.25.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby/Elsevier Science; 2011:567-574.

C.5. Is the infant with CDH more at risk from hypothermia?

All neonates are susceptible to heat loss because of a high ratio of surface area-to-body weight, reduced subcutaneous fat, and an underdeveloped ability to shiver in response to cold. However, infants with CDH have dramatic risks associated with increased PVR due to hypothermia, which can set in motion a vicious cycle of decreased oxygen delivery, worsening acidosis, and continued increase in PVR.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby/Elsevier Science; 2011:567-574.

C.6. The surgeon returned the intrathoracic stomach and intestine to the peritoneal cavity and the ipsilateral lung was found to be hypoplastic and collapsed. The resident anesthesiologist tried to expand the collapsed lung manually with positive airway pressure. Five minutes after the abdomen was closed, the blood pressure suddenly dropped from 70/40 to 30/20 mm Hg, the heart rate from 150 to 80 beats per minute, and the pulse oximeter from 95% down to 60% saturation. What would you do immediately?

Any sudden deterioration in blood pressure, heart rate, oxygen saturation, or pulmonary compliance is suggestive of tension pneumothorax. Auscultation of the chest, particularly the contralateral side, should be done immediately. If absent

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or diminished breath sounds confirm the diagnosis, a chest tube should be inserted immediately. A large-bore intravenous catheter with needle may be inserted to release the tension pneumothorax if a chest tube is not immediately available.

The tension pneumothorax is usually on the contralateral side because the high airway pressure required to inflate the hypoplastic lung may rupture the normal alveoli on the contralateral side, resulting in pneumothorax. Moreover, the ipsilateral chest usually already has a chest tube after surgery.

If there is no pneumothorax, or if deterioration is not improved after insertion of a chest tube, inferior vena cava compression (causing decreased venous return and decreased cardiac output) should be considered. The peritoneal cavity is often underdeveloped and unable to fully accommodate the returned abdominal organs, which increases the intra-abdominal pressure. In this circumstance, the abdominal wound should be opened to relieve the compression on the vena cava and diaphragm. A patch closure of the abdomen can be attempted or rarely a chimney prosthesis or silastic pouch is placed.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby/Elsevier Science; 2011:567-574.

C.7. Discuss fluid therapy in this patient.

Fluid therapy should be aimed to correct the preoperative deficit, provide maintenance fluid, and replace intraoperative evaporative, third-space, and blood losses.

Kidneys are 80% to 90% mature by 1 month of age. Before that time, the infant cannot tolerate the extremes of renal stress. Neonates are obligate sodium losers; therefore, exogenous sodium should be supplied. In addition, neonates have decreased glycogen storage and are prone to hypoglycemia after brief periods of starvation. Therefore, glucose should also be provided. However, hyperglycemia may predispose the patient to intracranial hemorrhage and should be avoided. The preoperative fluid deficit may be evaluated by careful history taking, signs and symptoms of dehydration, urine output, and CVP monitoring. Maintenance fluids consisting of 5% dextrose in one-fourth to one-half strength saline are given at 4 mL/kg/hr. Intraoperative evaporative and third-space losses are replaced with Ringer's lactate or saline at approximately 6 to 8 mL/kg/hr. Each milliliter of blood loss is replaced with 3 mL of Ringer's lactate or 1 mL of 5% albumin. Blood pressure, heart rate, urine output, CVP, hematocrit, and sodium and glucose levels are monitored following the fluid therapy.

Kliegman RM, Stanton BF, St Geme JW III, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier; 2015:384-388.

C.8. At the conclusion of surgery, would you extubate the patient in the operating room?

No. The patient should not be extubated in the operating room because varying degrees of pulmonary dysfunction are always present postoperatively. The endotracheal tube should be left in place, and the baby should be transported to the intensive care unit for further postoperative care.

D. Postoperative Management

D.1. What is the mortality rate in patients with CDH? What postoperative problems would you expect in this patient?

The mortality in patients with CDH varies from 20% to 30%. About half of all survivors have chronic lung disease. Growth failure, oral aversions, and gastroesophageal reflux occur in 45% to 90% of infants with CDH. Neurocognitive delay and behavioral disorders are common, especially in survivors who required ECMO support. Sensorineural hearing loss occurs in up to 50% of survivors, likely resulting from a combination of hypoxemia and exposure to ototoxic drugs (e.g., aminoglycosides, furosemide). Finally, survivors often develop chest wall deformities and scoliosis.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia, PA: Saunders/Elsevier Science; 2013:756-758.

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Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby/Elsevier Science; 2011:567-574.

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Chapter 38
Tetralogy of Fallot

James A. DiNardo

A 5-month-old infant recently adopted from South America is being evaluated for stable persistent cyanosis with arterial oxygen saturation (SaO_2) of 70% to 80% since birth. She eats well and is in the 70th percentile for weight (6.5 kg). An echocardiogram, done before her arrival at your institution, suggests that she has tetralogy of Fallot (TOF). Although she has never been noted to have a "Tet spell," her SaO_2 was noted to decrease to 60% during a recent febrile episode. A repeat echocardiogram reveals TOF with severe valvular pulmonary stenosis (PS) and mild subvalvular PS, secondary to anterior deviation of the conal septum into the right ventricle outflow tract (RVOT). There is a peak instantaneous pressure gradient of 70 mm Hg across the RVOT, as determined by continuous wave Doppler.

A. Medical Disease and Differential Diagnosis

1. What is tetralogy of Fallot (TOF)?
2. What is the pathophysiology of TOF with pulmonary stenosis (TOF/PS)?
3. What is shunting and how is Q_P:Q_S calculated?
4. What is the pathophysiology of TOF with pulmonary atresia?
5. How is arterial O_2 saturation determined in single ventricle physiology?
6. What is a "pink Tet"?
7. What are hypercyanotic spells? How are they treated?
8. What palliative surgical procedures are available for treating this patient with TOF/PS?
9. What definitive surgical procedures are available for treating this patient with TOF/PS?
10. What palliative and definitive surgical procedures are available for treating a patient with TOF with pulmonary atresia?

B. Preoperative Evaluation and Preparation

1. What preoperative history and physical examination information do you want?
2. Which other abnormalities need to be considered in this patient?
3. In general, what nothing by mouth (NPO) guidelines will you follow and what premedication will you give to a child with congenital heart disease?

C. Intraoperative Management

1. How will you induce anesthesia in this patient if intravenous (IV) access cannot be obtained?
2. Why would end-tidal carbon dioxide ($ETCO_2$) monitoring be of particular use in a patient with TOF/PS?
3. What is near-infrared spectroscopy (NIRS) and what does it measure?

4. What are the important management issues during creation of a palliative shunt?
5. What is the effect of inhalation anesthetics on airway reflexes, myocardial contractility, systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR) in children?
6. What are the pre-cardiopulmonary bypass (CPB) anesthetic goals for a patient undergoing definitive surgical correction of TOF/PS?

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7. What interventions will reliably reduce PVR?
8. How does heparin administration and activated coagulation time (ACT) monitoring differ in children as compared with adults?
9. How is heparin reversed?
10. What is the incidence of protamine reactions in children?
11. What is the role of transesophageal echocardiography (TEE) in this patient?
12. What effect would a residual ventricular septal defect (VSD) have in this patient following separation from CPB?

D. Postoperative Management

1. How should postoperative ventilation be managed in this patient following placement of a transannular patch for TOF/PS?
2. Following complete repair of TOF/PS in an infant, what arterial oxygen saturation (SaO_2) is acceptable?
3. Following placement of a modified Blalock-Taussig shunt (MBTS) for TOF/PS in an infant, what SaO_2 is acceptable?
4. What is junctional ectopic tachycardia (JET)?

A. Medical Disease and Differential Diagnosis

A.1. What is tetralogy of Fallot (TOF)?

In 1888, Fallot described a congenital heart defect composed of four characteristics: (1) large VSD, (2) right ventricular (RV) outflow obstruction, (3) overriding aorta, and (4) right ventricle hypertrophy (RVH). Broadly defined, TOF is a complex of anatomic malformations consisting of a large, misaligned conoventricular VSD; a rightward and anterior displacement of the aorta, such that it overrides the VSD; and a variable degree of subvalvular RVOT obstruction due to anterior, superior, and leftward deviation of the conal (infundibular) ventricular septum. In addition, abnormalities in the septal and parietal bands of the crista supraventricularis further exacerbate the infundibular RVOT obstruction. RVH is the result of chronic RVOT obstruction. The most common associated lesion is a right aortic arch with mirror image arch vessel branching (innominate artery gives rise to left carotid and left subclavian arteries; right carotid and right subclavian arise separately) present in 25% of patients. Two broad subsets of TOF exist: TOF with PS (TOF/PS) and TOF with pulmonary atresia. A third much less common type of TOF known as *TOF with absent pulmonary valve* will not be considered here.

Tetralogy of Fallot with Pulmonary Stenosis

TOF/PS involves the features of TOF in conjunction with varying degrees of valvular PS. At one end of the spectrum of TOF/PS, the pulmonary valve may be mildly hypoplastic (reduced annulus size) with minimal fusion of the pulmonary valve leaflets (Fig. 38.1A). The pulmonary valve is almost always bileaflet. At the other end of the spectrum, the pulmonary annulus may be very small with near fusion of the pulmonary valve leaflets. It is important to point out that a valvular obstruction is a *fixed* obstruction, while a subvalvular obstruction is *dynamic.* If left uncorrected, RVOT obstruction from either valvular or subvalvular obstruction will progress to subvalvular obstruction, as compensatory RVH increases the mass of the RV and infundibulum. The anatomy of TOF/PS can almost always be definitively delineated (including coronary anatomy) by two-dimensional echocardiography. Cardiac catheterization is rarely necessary or indicated.

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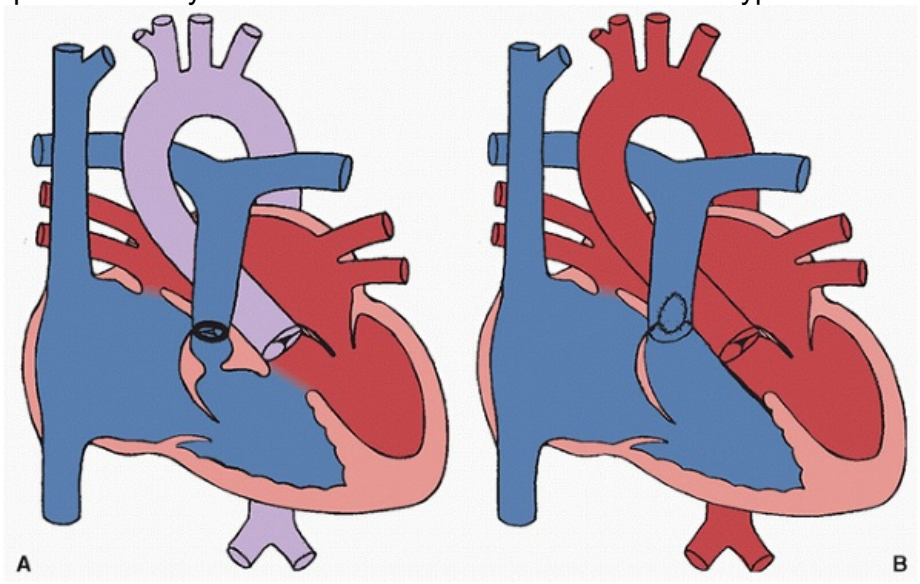


FIGURE 38.1 A. Uncorrected tetralogy of Fallot with pulmonary stenosis (TOF/PS) demonstrating malalignment ventricular septal defect (VSD) with aortic override, valvular and subvalvular (dynamic) PS. There is a left aortic arch. **B.** Definitively repaired TOF/PS with VSD closure creating left ventricle (LV) to aortic continuity, resection of subvalvular muscle bundles and deviated conal septum, and creation of a transannular patch (with pulmonary valvectomy) creating pulmonary insufficiency. A small atrial level communication has been left.

Tetralogy of Fallot with Pulmonary Atresia

TOF with pulmonary atresia involves the features of TOF and infundibular and pulmonary valvular atresia in conjunction with varying degrees of pulmonary arterial atresia. Four groups are said to exist. *Group 1* patients have isolated infundibular and pulmonary valve atresia with a main pulmonary artery (PA) and distal PAs of near normal size and architecture. In some of these patients, the main PA may extend to the atretic infundibulum. In others, atresia involves a short segment of the main PA (Fig. 38.2). Patients in this group have pulmonary blood flow supplied from a patent ductus arteriosus (PDA). In *group 2* patients, the main PA is absent, but the PAs are in continuity and supplied by a PDA. *Group 3* patients have severely hypoplastic native PAs; the left and right PA may not be in continuity. There are major aortopulmonary collateral arteries (vessels from the aorta to the PA) known as *MAPCAs.* A PDA may be present as well. Some segments of lung may be perfused from MAPCAs, some only by the native PAs, and others by both sources (Fig. 38.3). *Group 4* patients have no native PAs and all pulmonary blood flow is derived entirely from MAPCAs.

The anatomy of MAPCAs in TOF with pulmonary atresia can almost never be clearly delineated by two-dimensional echocardiography alone. Cardiac catheterization and/or magnetic resonance imaging or magnetic resonance angiography are necessary to delineate collateral anatomy and determine Q_P:Q_S.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

Jonas RA, ed. Tetralogy of Fallot with pulmonary atresia. In: *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:440-456.

A.2. What is the pathophysiology of TOF with pulmonary stenosis (TOF/PS)?

TOF/PS is a disease with a complex shunt in which a communication (VSD) and a partial obstruction to RV outflow (RV infundibular and valvular stenosis) are present. In complex

shunts, the resistance to outflow is a combination of the resistance from the obstructive lesions and the PVR. If the resistance from the RV obstructive lesions is high, changes in PVR will have little effect on shunt magnitude and direction. In most patients with TOF/PS, there is a fixed and a dynamic component to RV outflow obstruction. The fixed component

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is produced by the valvular stenosis. The dynamic component is produced by variations in the caliber of the RV infundibulum. The pathophysiology present in TOF/PS is physiologic rightto-left (R-L) shunting induced by the presence of a VSD and RVOT obstruction. In addition, because the aorta overrides the VSD and the RV, desaturated systemic venous blood tends to stream out of the aorta, even in the presence of mild RVOT obstruction.

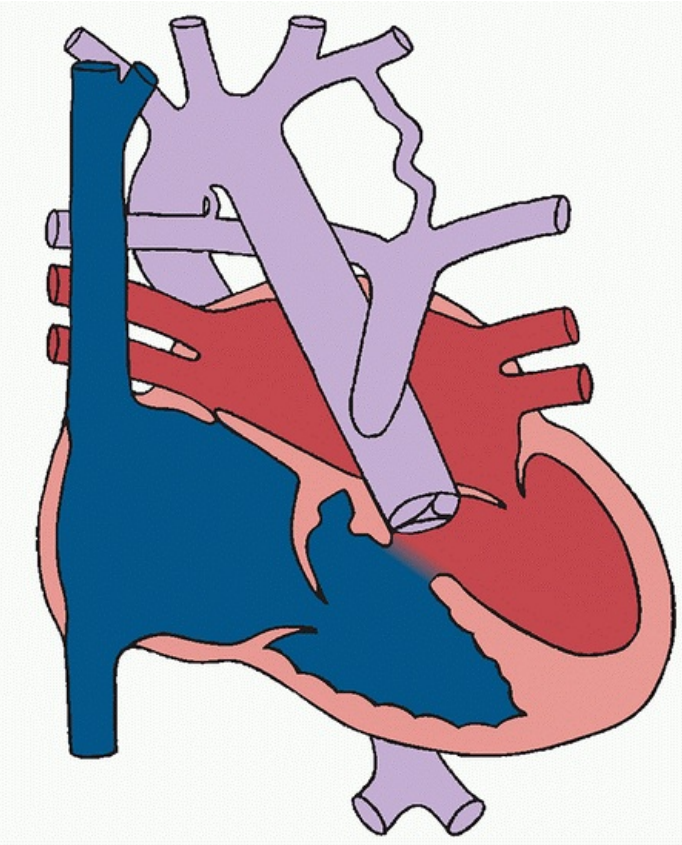


FIGURE 38.2 Illustration of tetralogy of Fallot with pulmonary atresia group 1 with short segment pulmonary artery, good-sized PAs in continuity supplied by a right-sided patent ductus arteriosus (PDA), and one major aortopulmonary collateral artery (MAPCA) from the left subclavian artery. There is a right aortic arch with mirror image arch vessel branching.

The SaO_2 is determined by the relative volumes and saturations of recirculated systemic venous blood and effective systemic blood flows that have mixed and reached the aorta. This is summarized in the following equation:

$$\text{Aortic } Sao_2 = \frac{[(\text{pulmonary venous } O_2 \text{ saturation} \times \text{effective systemic blood flow}] + (\text{systemic venous } O_2 \text{ saturation} \times \text{recirculated systemic venous blood flow})]}{(\text{total systemic blood flow})}$$

This is demonstrated in Figure 38.4 where the $SaO_2 = [(98 \times 0.5) + (65 \times 0.5)] / 1 = 81$. Notice that the patient has a Q_P:$Q_S = 0.5:1$.

A.3. What is shunting and how is Q_P:Q_S calculated?

Shunting is the process whereby venous return into one circulatory system is recirculated through the arterial outflow of the same circulatory system. Flow of blood from the systemic venous atrium (right atrium) to the aorta produces recirculation of systemic venous blood. Flow of blood from the pulmonary venous atrium (left atrium) to the PA produces

recirculation of pulmonary venous blood. Recirculation of blood produces a physiologic shunt. Recirculation of pulmonary venous blood produces a physiologic left-to-right (L-R), whereas recirculation of systemic venous blood produces a physiologic R-L shunt. A physiologic R-L or L-R shunt commonly is the result of an anatomic R-L or L-R shunt. In an anatomic shunt, blood moves from one circulatory system to the other through a communication (orifice) at the level of the cardiac chambers or great vessels. Physiologic shunts can exist in the absence of an anatomic shunt; transposition physiology is the best example.

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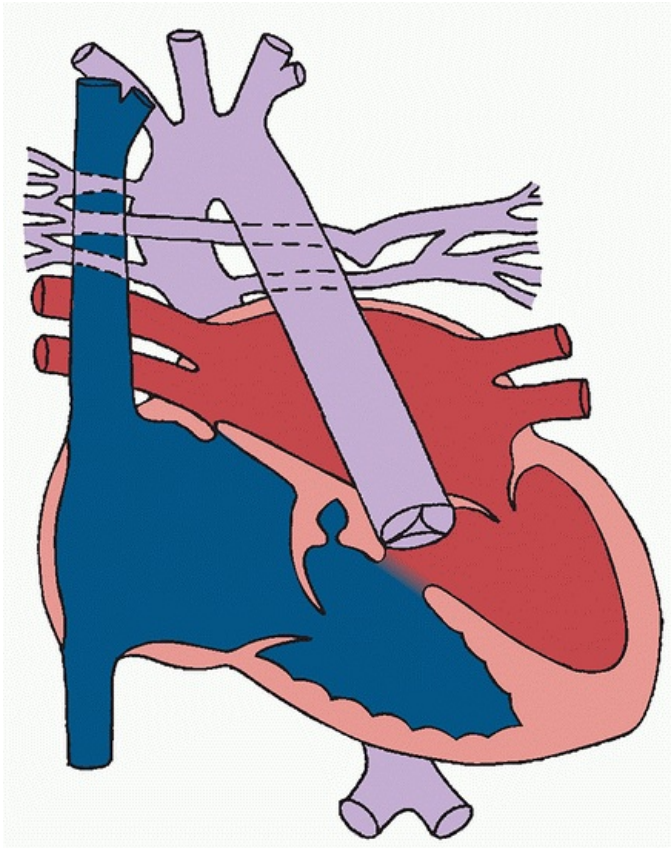


FIGURE 38.3 Illustration of tetralogy of Fallot with pulmonary atresia group 3 with no main PA, small branch PAs in continuity supplied by major aortopulmonary collateral arteries (MAPCAs). Some lung segments are supplied by the native PAs while others are supplied directly by MAPCAs. There is a right aortic arch with mirror image arch vessel branching.

Effective blood flow is the quantity of venous blood from one circulatory system reaching the arterial system of the other circulatory system. Effective pulmonary blood flow is the volume of systemic venous blood reaching the pulmonary circulation, whereas effective systemic blood flow is the volume of pulmonary venous blood reaching the systemic circulation. Effective pulmonary and effective systemic blood flows are the flows necessary to maintain life and are always equal, no matter how complex the lesions. Effective blood flow usually is the result of a normal pathway through the heart, but it may occur as the result of an anatomic R-L or L-R shunt.

Total pulmonary blood flow (Q_P) is the sum of effective pulmonary blood flow and recirculated pulmonary blood flow. Total systemic blood flow (Q_S) is the sum of effective systemic blood flow and recirculated systemic blood flow. Total pulmonary blood flow and total systemic blood flow do not have to be equal. Because Q_S (systemic cardiac output) tends to remain constant to supply end organs, a physiologic L-R shunt (pulmonary recirculation) causes pulmonary volume overload while a physiologic R-L shunt (systemic recirculation) allows Q_S to be maintained at the expense of SaO_2.

Calculation of Q_P:Q_S (the ratio of total pulmonary blood flow to systemic blood flow) is greatly simplified when the determination is made using low inspired concentrations of oxygen (fraction of inspired oxygen [FIO_2]). This allows the contribution of oxygen carried in

solution ($PO_2 \times 0.003$) to be ignored. Failure to account for this component when determination of Q_P:Q_S is made using an FIO_2 of 1.0 will introduce substantial (100%) error. If the FIO_2 is low, the determination of Q_P:Q_S can be simplified to the following equation using just oxygen saturations:

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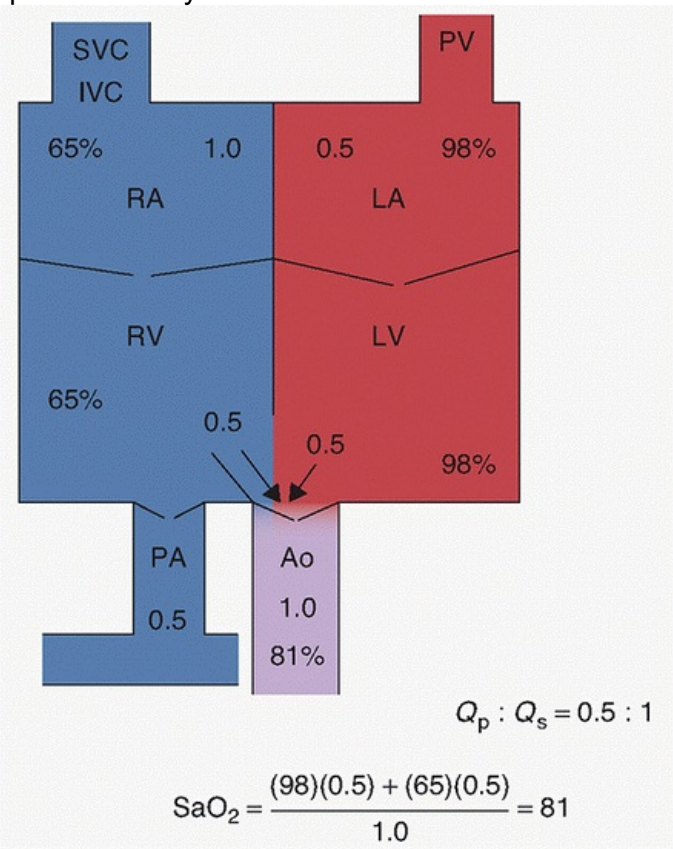


FIGURE 38.4 Chamber oxygen saturations and relative flows for a patient with uncorrected tetralogy of Fallot with pulmonary stenosis (TOF/PS). Arterial, oxygen saturation (SaO_2) and Q_P:Q_S are illustrated. Ao, aorta; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; PA, pulmonary artery; PV, pulmonary vein; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

$(S_AO_2 - S_{SVC}O_2) / (S_{PV}O_2 - S_{PA}O_2)$

where A = arterial, SVC = superior vena cava, PV = pulmonary vein that can be assumed to be 98% in the absence of significant pulmonary disease, and PA = pulmonary artery.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:45-65.

A.4. What is the pathophysiology of TOF with pulmonary atresia?

The pathophysiology of TOF with pulmonary atresia is similar to the single ventricle physiology. Single ventricle physiology describes the situation wherein complete mixing of pulmonary venous and systemic venous blood occurs at the atrial or ventricular level and the ventricle(s) then distributes output to both the systemic and pulmonary beds. As a result of this physiology, the following are observed:

- Ventricular output is the sum of pulmonary blood flow (Q_P) and systemic blood flow (Q_S).
- Distribution of systemic and pulmonary blood flow is dependent on the relative resistances to flow (both intracardiac and extracardiac) into the two parallel circuits.
- Oxygen saturations are the same in the aorta and the PA.

This physiology can exist in patients with one well-developed ventricle and one hypoplastic ventricle as well as in patients with two well-formed ventricles. In the case of a single anatomic ventricle, there is always obstruction to either pulmonary or systemic blood flow as the result of complete or near complete obstruction to inflow and/or outflow from the hypoplastic ventricle. In this circumstance, there must be a source of both systemic and pulmonary blood flow to ensure postnatal

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survival. In some instances of a single anatomic ventricle, a direct connection between the aorta and the PA through a PDA is the sole source of systemic blood flow (hypoplastic left heart syndrome) or of pulmonary blood flow (PA with intact ventricular septum). This is known as *ductal dependent circulation.* In other instances of a single anatomic ventricle, intracardiac pathways provide both systemic and pulmonary blood flow without the necessity of a PDA. This is the case in tricuspid atresia with normally related great vessels, a nonrestrictive VSD and minimal or absent PS.

In certain circumstances, single ventricle physiology can exist in the presence of two wellformed anatomic ventricles. This is generally the result of atresia or near atresia of outflow from one of the ventricles. Examples include the following:

- TOF with pulmonary atresia where pulmonary blood flow is supplied through a large PDA or MAPCAs
- Truncus arteriosus
- Severe neonatal aortic stenosis and interrupted aortic arch; in both lesions, a substantial portion of systemic blood flow is supplied through a PDA
- Heterotaxy syndrome

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:45-65.

A.5. How is arterial O_2 saturation determined in single ventricle physiology?

With single ventricle physiology, the SaO_2 will be determined by the relative volumes and saturations of pulmonary venous and systemic venous blood flows that have mixed and reached the aorta. This is summarized in the following equation:

$$\text{Aortic } O_2 \text{ saturation} = \frac{\begin{array}{c}[(\text{systemic venous saturation})(\text{total systemic venous blood flow}) \\ +\ (\text{pulmonary venous saturation})(\text{total pulmonary venous blood flow})]\end{array}}{(\text{total systemic blood flow} + \text{total pulmonary venous blood flow})}$$

The primary goal in the management of patients with single ventricle physiology is optimization of systemic oxygen delivery and perfusion pressure. This is necessary if end-organ (myocardial, renal, hepatic, splanchnic) dysfunction and failure are to be prevented. This goal is achieved by balancing the systemic and pulmonary circulations. The term *balanced circulation* is used because both laboratory and clinical evaluations have demonstrated that maximal systemic oxygen delivery (the product of systemic oxygen content and systemic blood flow) is achieved for single ventricle lesions when Q_P:Q_S is at or just below 1:1. Increases in Q_P:Q_S in excess of 1:1 are associated with a progressive decrease in systemic oxygen delivery because the subsequent increase in systemic oxygen content is more than offset by the progressive decrease in systemic blood flow and by diastolic hypotension due to runoff into the pulmonary circulation. Decreases in Q_P:Q_S below 0.7 to 0.8:1 are associated with a precipitous decrease in systemic oxygen delivery because the subsequent increase in systemic blood flow is more than offset by the dramatic decrease in systemic oxygen content.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:45-65.

A.6. What is a “pink Tet”?

The term *pink Tet* refers to any noncyanotic patient with TOF/PS or TOF with pulmonary atresia. In these patients, Q_P:Q_S is sufficiently high (Q_P:Q_S generally greater than 0.8:1 in the presence of a normal mixed venous saturation and pulmonary vein saturation) to maintain a deoxyhemoglobin concentration less than 5 g per dL (SaO_2 generally >80%). The designation

of “pink Tet” would apply to TOF/PS patients with minimal valvular and subvalvular PS and to all patients with TOF with pulmonary atresia where pulmonary blood flow is supplied from a large PDA and/or MAPCAs.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

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A.7. What are hypercyanotic spells? How are they treated?

The occurrence of hypoxic spells in TOF patients may be life-threatening and should be anticipated in every patient with TOF/PS and any infundibular obstruction, even those who are not normally cyanotic. The peak frequency of spells is between 2 and 3 months of age; spells occur more frequently in severely cyanotic patients. The onset of spells usually prompts urgent surgical intervention, so it is not unusual for the anesthesiologist to care for an infant who is at great risk for spells during the preoperative period. The etiology of spells is not completely understood, but infundibular spasm or constriction plays a role. Crying, defecation, feeding, fever, and awakening all can be precipitating events. Paroxysmal hyperpnea is the initial finding. There is an increase in rate and depth of respiration, leading to increasing cyanosis and potential syncope, convulsions, or death. During a spell, the infant will appear pale and limp secondary to poor cardiac output. Hyperpnea has several deleterious effects in maintaining and worsening a hypoxic spell. Hyperpnea increases oxygen consumption through the increased work of breathing. Hypoxia induces a decrease in SVR, which further increases the R-L shunt. Hyperpnea also lowers intrathoracic pressure and leads to an increase in systemic venous return. In the face of infundibular obstruction, this results in an increased RV pressure and an increase in the R-L shunt. Treatment of a “Tet spell” is focused on increasing the pulmonary circulation and decreasing the R-L shunt. It includes the following:

- Administration of 100% oxygen
- Compression of the femoral arteries or placing the patient in a knee-chest position to transiently increase SVR and reduce the R-L shunt
- Manual compression of the abdominal aorta will increase SVR; this maneuver is particularly effective for the anesthetized patient. After the chest is open, the surgeon can manually compress the ascending aorta to increase impedance to LV ejection.
- Administration of IV morphine sulfate (0.05 to 0.1 mg per kg), which sedates the patient and may have a depressant effect on respiratory drive and hyperpnea
- Administration of 15 to 30 mL per kg of a crystalloid solution IV. Enhancing preload will increase heart size, which may increase the diameter of the RVOT.
- Administration of sodium bicarbonate to treat the severe metabolic acidosis that can be seen during a spell. Correction of the metabolic acidosis will help normalize SVR and reduce hyperpnea. Bicarbonate administration (1 to 2 mEq per kg IV) in the absence of a blood gas determination is warranted during a spell.
- Phenylephrine (dose 5 to 10 µg per kg IV or 2 to 5 µg/kg/min as an infusion) can be used to increase SVR and reduce R-L shunting. In the presence of severe RV outflow obstruction, phenylephrine-induced increases of PVR will have little or no effect in increasing the RV outflow resistance further. It is important to point out that treatment with α-adrenergic agents to increase SVR does nothing to treat the underlying cause of the spell, although the decrease in unstressed venous volume induced by these agents may augment preload.
- β-Adrenergic agonists are absolutely contraindicated. By increasing contractility, they will cause further narrowing of the stenotic infundibulum.
- Administration of propranolol (0.1 mg per kg IV) or esmolol (0.5 mg per kg IV followed by an infusion of 50 to 300 µg/kg/min) may reduce infundibular spasm by depressing contractility. In addition, slowing of heart rate may allow for improved diastolic filling (increased preload), increased heart size, and an increase in the diameter of the RVOT.
- Extracorporeal membrane oxygenation resuscitation is another alternative in refractory episodes when immediate operative intervention is not possible.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

A.8. What palliative surgical procedures are available for treating this patient with TOF/PS?

Palliative shunt procedures to increase pulmonary blood flow can be used for patients with TOF/PS in whom complicated surgical anatomy precludes definitive repair at the time of presentation. In addition, some institutions delay elective complete repair until 12 to 18 months of age with placement of a palliative shunt if cyanosis occurs before that time

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interval. The palliative shunt procedures involve creation of a systemic-to-pulmonary arterial shunt analogous to a PDA. Ideally, these surgical shunts should be mildly restrictive simple shunts. In the presence of a proximal obstruction to pulmonary blood flow, these shunts produce an L-R shunt and an increase in pulmonary blood flow. The volume load imposed on the LV by these shunts parallels the increases in pulmonary flow that they produce. There will be progressive hypertrophy of the body and infundibulum of the RV during the interval from shunt placement to definitive repair as RVOT obstruction will not be relieved. The shunts can be summarized as follows:

Waterston shunt—a side-to-side anastomosis between the ascending aorta and the right PA. This procedure is performed through a right thoracotomy without CPB.

Potts shunt—a side-to-side anastomosis between the descending aorta and the left PA. This procedure is performed through a left thoracotomy without CPB.

Waterston and Potts shunts are of historic interest only. It is difficult to size the orifice of this shunt correctly. Too small an orifice will limit pulmonary blood flow, whereas too large an orifice will create pulmonary overperfusion and congestion and predispose to development of unilateral pulmonary vascular obstructive disease. These shunts may produce distortion of the PA, making subsequent definitive repair difficult. In addition, they are difficult to take down at the time of the definitive procedure.

Central shunt—Placing a synthetic tube graft between the ascending aorta and the main or branch PA. This shunt can be performed with or without CPB through a thoracotomy or median sternotomy. It often is used when prior shunt procedures have failed.

Blalock-Taussig shunt (BTS)—an end-to-side anastomosis of the right or left subclavian artery to the ipsilateral branch PA. Currently, a modification of this procedure known as the *modified Blalock-Taussig shunt* (*MBTS*) is used. It involves interposing a length of Gore-Tex tube graft (3.5 to 4.0 mm in infants) between the subclavian or innominate artery and the branch PA. These shunts usually are performed on the side opposite the aortic arch through a thoracotomy without CPB (Fig. 38.5).

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

A.9. What definitive surgical procedures are available for treating this patient with TOF/PS?

Currently, most patients with TOF/PS have an elective full correction between the ages of 2 and 10 months. In some centers, surgery is delayed as long as possible within this time interval, with the precise timing of repair dictated by the onset of cyanotic episodes. Definitive repair for TOF/PS is being accomplished in neonates in some centers if favorable anatomy is present. Surgery is aimed at relieving the RV outflow obstruction by resection of hypertrophied, obstructing muscle bundles and augmentation and enlargement of the RVOT with a pericardial patch. Unless the pulmonic annulus is near normal size and the pulmonary valve is only mildly stenotic, enlargement of the outflow tract involves extension of the patch across the pulmonary valve annulus and into the main PA. Because a transannular patch creates pulmonic insufficiency, it is avoided when possible. If stenosis of the PA extends to the bifurcation, the pericardial patch can be extended beyond the bifurcation of the pulmonary arteries. Finally, the VSD is closed. In neonates, this is usually done through the right ventriculotomy created for resection of RVOT obstruction and placement of the transannular patch. In infants and older children, the VSD can be closed through a transtricuspid valve approach.

An important surgical consideration for patients with TOF/PS is the occurrence of coronary artery abnormalities. Approximately 8% of patients have either the left main coronary artery or the left anterior descending artery as a branch of the right coronary artery. In these

cases, a right ventriculotomy to enlarge the RVOT will endanger the left coronary artery. In such cases, an extracardiac conduit (RV to main PA) may be necessary to bypass the outflow tract obstruction and avoid injury to the coronary artery.

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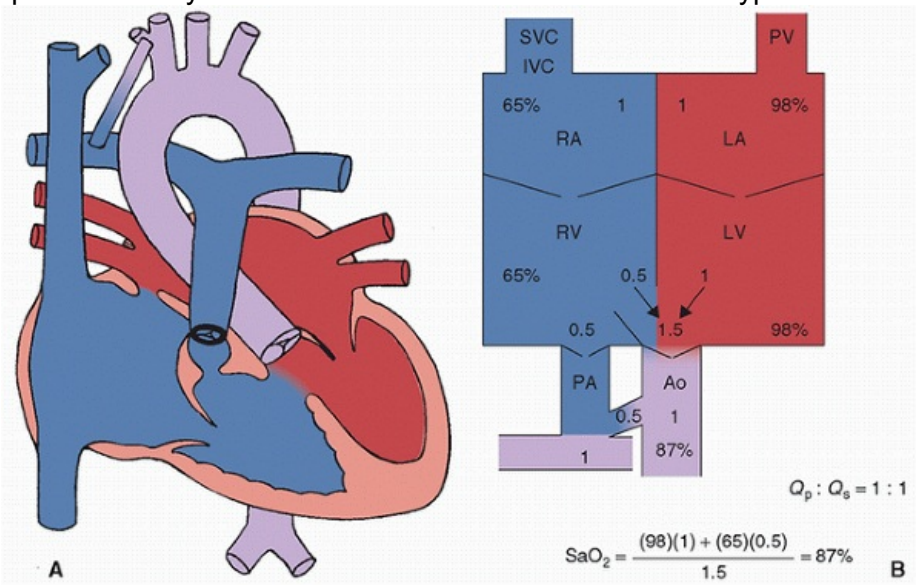


FIGURE 38.5 A. Palliative modified Blalock-Taussig shunt (MBTS) for tetralogy of Fallot with pulmonary stenosis (TOF/PS). Shunt is seen to connect the innominate artery to the right pulmonary artery (PA). This patient has a left aortic arch. **B.** Chamber oxygen saturations and relative flows for a patient with MBTS and TOF/PS. Arterial oxygen saturation (SaO_2) and Q_P:Q_S are illustrated. Ao, aorta; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; PV, pulmonary vein; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

Jonas RA, ed. Tetralogy of Fallot with pulmonary stenosis. In: *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:279-300.

A.10. What palliative and definitive surgical procedures are available for treating a patient with TOF with pulmonary atresia?

Surgery in groups 1 and 2 TOF with pulmonary atresia patients is aimed at establishing a reliable source of pulmonary blood flow in the neonatal period, as these patients are dependent on prostaglandin E_1 (PGE_1) to maintain a PDA and pulmonary blood flow. These patients may undergo a palliative shunt procedure or a definitive procedure. The definite procedure would be creation of continuity between the RV and the main PA through placement of an RV to PA conduit, with VSD closure generally performed through the ventriculotomy used for the proximal attachment of the conduit. Patients in groups 3 and 4 present difficult management problems. As a rule, these patients presenting with single ventricle physiology have a tendency for pulmonary blood flow to become excessive (Q_P:Q_S >2 to 3:1) as the PVR drops following birth. In group 3 patients, neonatal repair with placement of an RV to PA conduit is undertaken to place the PAs in continuity with the RV in an effort to promote native PA growth. In this circumstance, the VSD is left open as a source of R-L shunting and delivery of desaturated blood to the systemic circulation because it would be impossible for the RV to deliver an adequate cardiac output to the left atrium across the hypoplastic pulmonary vascular bed. These infants then undergo multiple cardiac catheterization procedures in

order to (1) dilate and stent the hypoplastic native PAs and (2) to embolize with coil the MAP-CAs, which provide pulmonary blood flow that is competitive to the blood flow supplied by native PAs. MAPCAs that provide pulmonary blood flow to segments of lung not supplied by native PAs must be unifocalized to the proximal pulmonary circulation.

Unifocalization may have to be performed and involves removal of the collateral vessel from the aorta with subsequent reanastomosis to the RV to PA conduit or a proximal PA branch. Although the traditional approach has been through a thoracotomy, more recently, most groups have favored a central approach working through a median sternotomy. It is only when 80% to 90% of the pulmonary vascular bed is in direct continuity with the RV that closure or fenestrated closure of the VSD can be considered. Usually, this will mean that at least 10 to 12 bronchopulmonary segments are now in direct

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continuity with the RV.

In group 4 patients, it may be necessary to unifocalize several large collaterals to the distal end of conduit from the RV as the initial intervention. Alternatively, several large collaterals could be unifocalized to an MBTS or central shunt. These procedures serve to promote pulmonary vascular growth, prevent the development of pulmonary vascular obstructive disease, and control the Q_P:Q_S.

Jonas RA, ed. Tetralogy of Fallot with pulmonary atresia. In: *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:440-456.

B. Preoperative Evaluation and Preparation

B.1. What preoperative history and physical examination information do you want?

Clinical history should include medications, allergies, past hospitalizations and operations (including prior anesthetic experiences), and a thorough review of systems. Performance of age-appropriate activities will aid in the evaluation of cardiac function and reserve. The neonate and infant in cardiac failure will manifest symptoms of low cardiac reserve during feeding, which is a strenuous activity, even for a normal newborn. A parent might report that sweating, tiring, dyspnea, and circumoral cyanosis occur during feeding. The observation by a parent that the patient cannot keep the same pace as siblings is often a reliable clinical sign that cyanosis or congestive heart failure is worsening.

Interpretation of vital signs must be age-specific. Growth curves also are useful, as congestive heart failure will inhibit age-appropriate gains in weight, height, and head circumference. It is not unusual for patients with severe congestive heart failure to weigh less at 3 or 4 months of age than at birth. Interestingly, cyanotic children often do not manifest this failure to thrive. Physical examination will reveal cyanosis, clubbing, or signs of congestive heart failure similar to those seen in adults, such as hepatomegaly, ascites, edema, or tachypnea. Rales may not be heard in infants and children with congestive heart failure, and the degree of heart failure may be determined more reliably by some of the signs and symptoms outlined previously. The degree of cyanosis is related to the percentage of desaturated hemoglobin. A markedly hypoxemic child with baseline arterial saturations in the 70% range may be anemic and clinically appear less cyanotic than another child with similar arterial saturation and a more appropriate hematocrit of 65%.

Physical examination should include an evaluation of the limitations to vascular access and monitoring sites imposed by previous surgery. A child who has undergone a palliative shunt procedure may have a diminished pulse or unobtainable blood pressure in the arm in which the subclavian artery has been incorporated into the shunt. This obviously has implications for arterial catheter placement, sphygmomanometric blood pressure monitoring, and use of pulse oximetry perioperatively. Finally, the child who has undergone multiple palliative procedures may have poor venous access, which may influence the mode of induction.

It is often difficult to differentiate clearly between signs and symptoms of congestive heart failure and a mild upper respiratory tract infection. Because increased pulmonary blood flow seems to predispose multiple respiratory tract infections, the physical examination may show mild tachypnea, wheezing, or upper airway congestion and, in the absence of abnormal laboratory findings or fever, may be impossible to distinguish from congestive heart failure. However, the decision to proceed to surgery may be necessary even when the differentiation

between worsening congestive heart failure and a respiratory tract infection cannot be made with certainty.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

B.2. Which other abnormalities need to be considered in this patient?

Because approximately 8% of children with congenital heart disease have other congenital abnormalities, it is prudent to consider and define these defects. For example, patients with TOF/PS or TOF with pulmonary atresia have a higher incidence of 22q11.2 deletion syndrome. Phenotypes of this syndrome include DiGeorge syndrome, velocardiofacial syndrome, and conotruncal anomaly face syndrome leading to hypocalcemia, immunodeficiency, facial dysmorphia, palate anomalies, velopharyngeal dysfunction, renal anomalies, and speech, feeding as well as neurocognitive, behavioral, and psychiatric disorders. Tracheal stenosis and bronchomalacia may be a serious problem for TOF with pulmonary atresia

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patients who have undergone tracheoesophageal fistula repair. Needless to say, many of these defects may seriously complicate airway management.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

Kobrynski LJ, Sullivan KE. Velocardiofacial syndrome, DiGeorge syndrome: the chromosome 22q11.2 deletion syndromes. *Lancet.* 2007;370:1443-1452.

B.3. In general, what nothing by mouth (NPO) guidelines will you follow and what premedication will you give to a child with congenital heart disease?

Generally speaking, the rule of 2, 4, 6, 8 can be used as the NPO interval for neonates, infants, and children with congenital heart disease:

- 2 hours for clear liquids
- 4 hours for breast milk
- 6 hours for formula
- 8 hours for solid food

Premedication before induction can be used to facilitate a number of objectives. In older children, it can be used to alleviate anxiety before an IV or inhalation induction. In younger children, premedication eases separation of the child from the parents. In infants, judicious premedication alone or in combination with inhaled nitrous oxide can greatly simplify placement of an IV catheter in an otherwise struggling infant. Midazolam 1.0 mg per kg orally in infants and younger children who have not had prior cardiac surgery is useful. In children older than 1 year who have undergone prior operative procedures, oral ketamine 7 to 10 mg per kg in combination with midazolam 1.0 mg per kg works well. These children are remarkably tolerant to midazolam as the result of either heightened anxiety or previous intraoperative and postoperative exposure to benzodiazepines. In circumstances where premedication is deemed important and the child will not take oral medication, the intramuscular route can be used. Ketamine 2 to 3 mg per kg and glycopyrrolate (10 µg per kg) alone or in combination with midazolam 0.1 mg per kg work well.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:45-65.

Ferrari LR, Rooney FM, Rockoff MA. Preoperative fasting practices in pediatrics. *Anesthesiology.* 1999;90:978-980.

C. Intraoperative Management

C.1. How will you induce anesthesia in this patient if intravenous (IV) access cannot be obtained?

An alternative to IV induction in infants and neonates with difficult peripheral IV access is intramuscular induction with ketamine (3 to 5 mg per kg), succinylcholine (5 mg per kg), and glycopyrrolate (10 µg per kg). Glycopyrrolate is recommended to reduce the airway secretions associated

with ketamine administration and to prevent the bradycardia, which may accompany succinylcholine administration. This technique provides prompt induction and immediate control of the airway with tracheal intubation and is useful in circumstances where it is anticipated that initial IV access will have to be obtained through the external jugular vein, femoral vein, or internal jugular vein. This technique is hampered by the fact that the short duration of action of succinylcholine limits the period of patient immobility. An alternative technique combines intramuscular ketamine (4 to 5 mg per kg), glycopyrrolate (10 µg per kg), and rocuronium (1.0 mg per kg). This technique is hampered by the longer time interval until attainment of adequate intubating conditions and the longer duration of action of rocuronium as compared to succinylcholine.

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DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:45-65.

C.2. Why would end-tidal carbon dioxide ($ETCO_2$) monitoring be of particular use in a patient with TOF/PS?

$ETCO_2$ monitoring is routinely employed in patients with congenital heart disease, with the caveat that the difference between $PaCO_2$ and $ETCO_2$ will vary as physiologic dead space varies and that, in some circumstances, the difference may be large (>10 to 15 mm Hg). Any acute reduction in pulmonary blood flow (decreased cardiac output, pulmonary embolus, increased intracardiac R-L shunting) will increase this gradient. In a patient with TOF/PS, a gradual reduction in $ETCO_2$ will often precede a decrease in SaO_2 as the first manifestation of the increased R-L intracardiac shunting associated with a “Tet spell.”

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:45-65.

C.3. What is near-infrared spectroscopy (NIRS) and what does it measure?

NIRS is a real-time, online monitor of cerebral tissue oxygenation. This technology is based on the physical principle that light of an appropriate wavelength passing through a solution of a colored compound (chromophore) will be absorbed by the compound. As a result of this absorption, the intensity of the light emerging from the solution will be lower than the intensity of the light projected into the solution. This principle through application of the Beer-Lambert equation “$\log [I_O/I] = c \alpha d$” allows quantification of the concentration (c) of a chromophore if the emergent light intensity (I) is measured and the following are known:

- Extinction coefficient (α), a constant that describes the absorption characteristics of a particular chromophore at a given wavelength of light
- Thickness of the solution (d)
- Incident light intensity (I_O)

NIRS technology is particularly suited to use in neonates and infants because the thin skull and small head allow light to be transmitted through one side of the head and detected on the other side, a technique known as *transmission spectrometry.*

Cerebral oxygen saturation (ScO_2) as measured by all NIRS technology is the combined oxygen saturation of an uncertain mix of arterioles, capillaries, and venules. Traditional pulse oximetry differs in this respect from NIRS because it is capable of isolating and measuring the arteriole component by gating measurements to pulsatility. It has been previously assumed that ScO_2 represented contributions of cerebral arterial and venous blood in a ratio of 25:75, with the contribution of capillary blood felt to be negligible. More recent data suggest that in children, the average ratio is 15:85. The issue is further complicated by the fact that there is significant variability in the ratio (from 0:100 to 40:60) between patients.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:45-65.

C.4. What are the important management issues during creation of a palliative shunt?

- When a thoracotomy approach is used, unilateral lung retraction will be required for surgical exposure. The resulting atelectasis may severely compromise oxygenation and

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CO_2 removal. Intermittent reinflation of the lung may be necessary during the operative procedure. These reinflations should be coordinated with the surgeon. For all the shunts described, the main or branch PA will have to be partially occluded by a clamp to allow creation of the distal anastomosis. The resulting increase in physiologic dead space may compromise oxygenation and CO_2 removal and will increase the arterial $ETCO_2$ gradient.

- Efforts to increase pulmonary blood flow by reducing PVR with ventilatory interventions and by increasing L-R shunting should be initiated before PA occlusion.
- Partial occlusion of the aorta with a clamp will be necessary during creation of Waterston, Potts, and central shunts. The resulting increase in LV afterload may compromise systolic function.
- All of the palliative shunts impose a volume load on the LV. Inotropic support may be necessary to ensure systemic and shunt perfusion after shunt creation.
- Palliative shunts are mildly restrictive simple shunts. It is important to maintain SVR and reduce PVR to maintain pulmonary blood flow in these patients.
- Be prepared to treat an episode of hypercyanosis.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

C.5. What is the effect of inhalation anesthetics on airway reflexes, myocardial contractility, systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR) in children?

Sevoflurane, isoflurane, and desflurane induce dose-related myocardial depression and SVR reduction with mild depression of contractility at 1 and 1.5 minimal alveolar concentration (MAC). Halothane induces a greater degree of myocardial depression at 1 and 1.5 MAC than sevoflurane, isoflurane, or desflurane. At these concentrations, neither sevoflurane, isoflurane, nor halothane alters the ratio of PVR to SVR substantially enough to induce any change in Q_P:Q_S.

Isoflurane and, particularly, desflurane are not good choices for inhalational induction because their pungency is responsible for a high incidence of airway complications in children. Desflurane has hemodynamic effects similar to isoflurane and may be useful as an adjuvant to narcotic anesthesia or as a primary maintenance agent after the airway has been secured. Sevoflurane has cardiovascular effects similar to isoflurane and is a good agent for inhalational induction in children; the incidence of airway complications is similar to that of halothane. Perhaps more important is the fact that inhalational induction with sevoflurane causes less myocardial depression than halothane in children.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

Laird TH, Stayer SA, Rivenes SM, et al. Pulmonary-to-systemic blood flow ratio effects of sevoflurane, isoflurane, halothane, and fentanyl/midazolam with 100% oxygen in children with congenital heart disease. *Anesth Analg.* 2002;95:1200-1206.

C.6. What are the pre-cardiopulmonary bypass (CPB) anesthetic goals for a patient undergoing definitive surgical correction of TOF/PS?

- Maintain heart rate, contractility, and preload to maintain cardiac output. Euvolemia is important to prevent exacerbation of dynamic RVOT obstruction from hypovolemia and reflex increases in heart rate and contractility.
- Avoid increases in the PVR:SVR ratio. The less severe the RV outflow obstructive lesions, the more important this becomes. Increases in PVR relative to SVR, and decreases in SVR relative to PVR, will increase R-L shunting, reduce pulmonary blood flow, and produce or worsen cyanosis.
- Adjust ventilatory parameters to reduce PVR.
- Maintain or increase SVR. This is particularly important when RV outflow obstruction is severe and changes in PVR will have little or no effect on shunt magnitude and direction.

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- Aggressively treat episodes of hypercyanosis.

- Maintain contractility. Depression of contractility, particularly in the face of severe RV outflow obstruction, may produce RV afterload mismatch and drastically reduce pulmonary blood flow. The exception to this is a patient in whom the dynamic component of infundibular obstruction is active. Reducing contractility in these patients may reduce RV outflow obstruction through relaxation of the infundibulum.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

C.7. What interventions will reliably reduce PVR?

PO_2. Both alveolar hypoxia and arterial hypoxemia induce pulmonary vasoconstriction. An arterial O_2 tension lower than 50 mm Hg increases PVR over a wide range of arterial pH; however, this effect is enhanced when pH is lower than 7.40. Conversely, high levels of inspired O_2 can reduce an elevated PVR.

PCO_2. Hypercarbia increases PVR, independent of changes in arterial pH. Hypocarbia, on the other hand, reduces PVR only through production of an alkalosis. In fact, reliable reductions in PVR and increases in pulmonary blood flow and PO_2 are seen in children with R-L shunts when hyperventilation to a PCO_2 near 30 mm Hg and a pH near 7.50 is instituted. Similarly, postbypass hyperventilation to a PCO_2 of 30 to 35 mm Hg and a pH of 7.50 to 7.56 in patients with preoperative pulmonary hypertension results in a reduction in PVR when compared with ventilation that produces normocarbia or hypercarbia.

pH. Both respiratory and metabolic alkalosis reduce PVR, whereas both respiratory and metabolic acidosis increase PVR.

Variation in lung volumes. At small lung volumes, atelectasis results in compression of extra-alveolar vessels, whereas at high lung volumes, hyperinflation of alveoli results in compression of intra-alveolar vessels. Therefore, PVR is normally lowest at lung volumes at or near the functional residual capacity. Positive end-expiratory pressure (PEEP) may cause an increase in PVR by increasing alveolar pressure through hyperinflation. However, in situations in which PEEP works to recruit atelectatic alveoli and increase arterial PO_2, a decrease in PVR generally is seen.

Vasodilator agents. There is no IV drug that selectively acts as a pulmonary vasodilator. In general, IV drugs intended to induce pulmonary vasodilation (PGE_1, prostaglandin I_2 [PGI_2], nitroglycerin, sodium nitroprusside, and tolazoline) induce systemic vasodilation as well. Inhaled nitric oxide, PGE_1, and PGI_2 are the only specific pulmonary vasodilators available.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

C.8. How does heparin administration and activated coagulation time (ACT) monitoring differ in children as compared with adults?

Before use of cardiotomy suction, cannulation, and commencing bypass, it is essential that adequate anticoagulation be obtained. Unfractionated heparin is currently the anticoagulant used for CPB. It generally is acknowledged that an ACT in excess of 400 seconds is necessary to ensure adequate anticoagulation for the safe conduct of CPB.

While there is a large heparin anticoagulation monitoring literature in adults, there is a very small literature in children. The ACT, commonly used to assess CPB anticoagulation, is also prolonged by hypothermia, hemodilution, platelet dysfunction, and low coagulation factor levels. As a result, in children, the ACT will overestimate the antifactor IIa and Xa effects of heparin.

Most institutions use an age- or weight-based protocol to administer the initial pre-CPB dose of heparin such as patients less than 30 kg—300 IU per kg; or patients greater than 30 kg—400 IU per kg. The large circuit prime volume to blood volume ratio would be expected to decrease plasma heparin levels with initiation of CPB unless an appropriate quantity of heparin is added to the CPB prime. Most institutions add heparin to the CPB prime as follows: patients less than 30 kg —2.5 IU per mL of CPB prime; or patients greater than 30 kg—3.0 IU per mL of CPB prime.

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Heparin should always be given into a central line through which venous return can be demonstrated easily or as is more common in infants/neonates directly into the heart (usually the right atrium) by the surgeon. This is necessary to ensure that the heparin dose has reached the central circulation. An ACT can be drawn within minutes of heparin administration as peak arterial ACT prolongation occurs within 30 seconds and peak venous ACT prolongation within 60 seconds.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia.* 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:228-252.

C.9. How is heparin reversed?

Protamine is a polyvalent cation derived from salmon sperm that is currently used to neutralize systemic heparinization. Protamine normally is given once stable hemodynamics are maintained after termination of CPB. It should not be administered until the likelihood that having to reinstitute CPB is small. After protamine neutralization of heparin begins, the cardiotomy suction should not be used and removal of the arterial and venous cannulas should proceed. This prevents contamination of the heparinized CPB circuit with protamine should prompt reinstitution of CPB be necessary and prevents thrombus formation on the cannulas.

There are several approaches to the neutralization of heparin with protamine, all with reportedly good clinical results. Some centers use 1.0 to 1.3 mg of protamine for each 100 units of heparin determined to exist at the termination of CPB. This ratio is based on the in vitro protamine-heparin neutralization ratio of 1.3:1.0. The amount of heparin present is determined by obtaining an ACT when CPB terminates and using reverse extrapolation of the patient's heparin dose-response curve to correlate ACT and heparin dose. This method has been criticized because the ACT obtained at the termination of CPB is prolonged by factors other than heparin, such as CPB-induced platelet dysfunction and hemodilution. This may result in an overestimation of the heparin present at the termination of CPB and a larger than necessary protamine dose.

Some centers simply administer a fixed dose of protamine based on the patient's weight (3 to 4 mg per kg) regardless of the heparin dose administered, whereas others administer 1.0 to 1.3 mg of protamine for each 100 units of heparin administered. Obviously, these methods do not rely on any post-CPB assessment of residual heparin effect (ACT) to determine the protamine dose. Nonetheless, these methods have been shown to result in adequate heparin reversal. In the case of the fixed dose regimen, heparin reversal is obtained at much lower protamine doses than predicted by the reverse extrapolation method.

The Hepcon (Medtronic, Minneapolis, MN) automated heparin protamine titration method measures clotting times enhanced by addition of thromboplastin in several channels that contain varying quantities of protamine. The first channel to clot is the channel in which the protamine-to-heparin ratio is closest to neutralization. The absolute clotting time is not important, only the determination of the channel with the appropriate ratio. Therefore, the determination should be independent of nonheparin factors that prolong the ACT.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia.* 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:228-252.

C.10. What is the incidence of protamine reactions in children?

The incidence of protamine reactions in children following cardiac surgery is generally believed to be substantially lower than that in adults. A recent retrospective analysis of 1,249 children revealed the incidence of hypotension (at least 25% decrease in mean arterial pressure) following protamine administration to be 1.76% to 2.88%, depending on the stringency of criteria linking the episode to protamine administration. In this series, no episodes of pulmonary hypertension or RV dysfunction were noted. There is a report of pulmonary hypertension and cardiovascular collapse in 6-week-old infant following protamine administration.

Clinical experience indicates that pulmonary hypertensive episodes in children following protamine administration are very rare.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia.* 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:228-252.

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C.11. What is the role of transesophageal echocardiography (TEE) in this patient?

It has been demonstrated that intraoperative TEE has a major impact on post-CPB decision making (such as return to CPB to repair residual lesions) in approximately 15% of cases when it is used nonselectively. In the subset of patients undergoing valve repair and outflow tract reconstruction, TEE provides the best immediate assessment of the adequacy of the operative procedure and, if necessary, directs its revision. While detection of retained intracardiac air is certainly facilitated by the use of intraoperative TEE, it remains to be determined what role the technology will play in improving cardiac de-airing algorithms particularly in neonates/infants.

The role of TEE in the detection of residual VSDs following repair of both simple and complex defects deserves some discussion. Residual defects less than 3 mm are detectable by TEE but generally do not require immediate reoperation because they are hemodynamically insignificant. The majority (75%) of these small defects are not present at the time of hospital discharge as determined by transthoracic echocardiography. Residual defects greater than 3 mm detected by TEE require immediate reoperation only if they are associated with intraoperative hemodynamic (elevated left atrial pressure and/or pulmonary artery pressure in the presence of good ventricular function) and oximetric (Q_P:Q_S >1.5:1 or right atrium to PA oxygen saturation step-up with FIO_2 ≤0.50) evidence that they are significant.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart disease.* London: Arnold; 2004:45-65.

Yang SG, Novello R, Nicolson S, et al. Evaluation of ventricular septal defect repair using intraoperative transesophageal echocardiography: frequency and significance of residual defects in infants and children. *Echocardiography.* 2000;17:681-684.

C.12. What effect would a residual ventricular septal defect (VSD) have in this patient following separation from CPB?

A residual VSD is likely to be very poorly tolerated in the patient with TOF/PS. The most likely manifestation is low cardiac output syndrome associated with elevated heart rate, left atrial pressure, and pulmonary artery pressure. RVOT obstruction will be completely or near completely eliminated postrepair. PVR is likely to be low and the pulmonary vasculature is likely to be very compliant. As a result, there will be potential for a large L-R intracardiac shunt with a residual VSD. This will place an acute, large volume load on both the LV and RV. This is likely to be particularly poorly tolerated by the RV that is concentrically hypertrophied and poorly compliant in response to the chronic pressure overload that existed preoperatively.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

D. Postoperative Management

D.1. How should postoperative ventilation be managed in this patient following placement of a transannular patch for TOF/PS?

The inspiratory phase of mechanical positive pressure ventilation increases impedance to RV ejection by increasing RV afterload by elevating alveolar pressure and creating more West Zone I and II lung segments. As a result, the extent of this afterload elevation is directly related to the duration of inspiration (respiratory rate and inspiratory-to-expiratory [I:E] ratio) and to mean airway pressure. Increasing RV afterload will impede antegrade pulmonary blood flow and exacerbate the extent of pulmonary insufficiency induced by the transannular patch. RV afterload will also be increased by elevations in PVR.

As discussed in section C.7, ventilation and gas mixture should be adjusted to minimize PVR. This should be accomplished with a tidal volume of 10 to 15 mL per kg, 3 to 5 mm Hg of PEEP, and a respiratory rate and I:E ratio adjusted to minimize mean airway pressure.

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DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

D.2. Following complete repair of TOF/PS in an infant, what arterial oxygen saturation (SaO_2) is acceptable?

Following complete repair of TOF/PS with no residual lesions and minimal intrapulmonary shunt, the SaO_2 should be 100%. In infants and small children, particularly those left with pulmonary insufficiency as the result of a transannular patch and those expected to have restrictive RV function as a result of a ventriculotomy and/or extensive RV hypertrophy, the surgeon may choose to leave a small (3 to 4 mm) atrial level communication or patent foramen ovale. This will allow intracardiac R-L shunting, with the ability to augment systemic cardiac output at the expense of systemic oxygen saturation in the setting of RV dysfunction by allowing direct delivery of desaturated venous blood to the left atrium. In these patients, a PaO_2 of 40 to 50 mm Hg and a SaO_2 of 70% to 80% are acceptable until RV function improves over the course of days.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

D.3. Following placement of a modified Blalock-Taussig shunt (MBTS) for TOF/PS in an infant, what SaO_2 is acceptable?

As illustrated in Figure 38.5B, in the presence of some antegrade pulmonary blood flow, an appropriate SaO_2 would be 80% to 90%. In the absence of any antegrade pulmonary blood flow, single ventricle physiology would exist and an SaO_2 of 70% to 80% would be more appropriate. SaO_2 is determined by the relative volumes and saturations of recirculated systemic venous blood and effective systemic blood flows that have mixed and reached the aorta. This is summarized in the following equation:

$$\text{Aortic } Sao_2 = \frac{[(\text{pulmonary venous saturation} \times \text{effective systemic blood flow}) + (\text{systemic venous saturation} \times \text{recirculated systemic venous blood flow})]}{(\text{total systemic blood flow})}$$

This is demonstrated in Figure 38.5B where the $SaO_2 = [(98 \times 1) + (65 \times 0.5)] / 1.5 = 87$. Three variables will ultimately affect SaO_2:

1. *The ratio of total pulmonary to total systemic blood flow (Q_P:Q_S).* A greater proportion of the arterial blood will consist of saturated blood (pulmonary venous blood) than of desaturated blood (systemic venous blood) when Q_P:$Q_S \geq 1{:}1$. Q_P:Q_S will be increased when systemic arterial blood pressure is high and PVR is low.
2. *Systemic venous saturation.* For a given Q_P:Q_S and pulmonary venous saturation, a decrease in systemic venous saturation will result in a decreased arterial saturation. Decreases in systemic venous saturation occur as the result of decreases in systemic oxygen delivery or increases in systemic oxygen consumption. Recall that systemic oxygen delivery is the product of systemic blood flow and arterial oxygen content. Arterial oxygen content, in turn, is dependent on the hemoglobin concentration and the arterial saturation. Efforts should be made to increase hematocrit into the range of 35% to 45%, cardiac output should be enhanced with inotropes (dopamine, 5 to 10 µg/kg/min), and systemic O_2 consumption reduced by appropriate levels of sedation/anesthesia and muscle relaxation if necessary.
3. *Pulmonary venous saturation.* In the absence of large intrapulmonary shunts and/or ventilation/perfusion ([V with dot above]/[Q with dot above]) mismatch, pulmonary venous saturation should be close to 100% when breathing room air. In the presence of pulmonary parenchymal disease, pulmonary venous saturation may be reduced. The [V with dot above]/[Q with dot above] mismatch component of pulmonary

venous desaturation will be largely eliminated with an FIO_2 of 1.0, while the intrapulmonary shunt contribution will not be eliminated. For any given systemic venous saturation and Q_P:Q_S, a reduction in pulmonary venous saturation will result in a decreased arterial saturation.

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DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167-251.

D.4. What is junctional ectopic tachycardia (JET)?

Postoperative JET is a transient tachyarrhythmia that occurs immediately following congenital heart surgery. A much rare form of congenital JET exists as well. JET is due to enhanced automaticity in the area of the atrioventricular (AV) node or proximal His bundle. Associated with JET is a higher than average incidence of AV block. The incidence of JET following TOF/PS repair may be as high as 20% and is felt to be secondary to surgical trauma in the area of the AV node secondary to the retraction necessary to expose the VSD and RVOT from across the tricuspid valve.

JET typically manifests with a junctional rate only slightly faster than the sinus node rate and is the only narrow complex tachycardia in which the atrial rate is less than the ventricular rate (A:V ratio <1:1). Much less commonly (10%), there may be retrograde activation of the atrium with inverted P waves noted and A:V ratio = 1:1. In either case, there is loss of AV synchrony (loss of atrial kick). In many instances, this arrhythmia is well tolerated. However, JET with heart rate greater than 170 beats per minute is associated with hemodynamic instability and increased postoperative mortality.

Cardioversion is ineffective as is adenosine. The most effective therapy for treatment of JET is atrial pacing at a rate slightly faster than the junctional rate such that AV synchrony is reinitiated. This therapy is effective unless the junctional rate is very fast (>160 to 170 beats per minute), at which point atrial pacing at a faster rate is unlikely to improve hemodynamics because the reinitiation of AV synchrony is offset by the dramatic reduction in diastolic filling time present at these rates. In this circumstance, the most effective therapy is multimodal. JET requiring aggressive treatment prolongs postoperative ventilation times and intensive care unit stay. The goal of aggressive therapy is to terminate JET or reduce the rate to the point where atrial pacing can be reinitiated. The following modalities are applied in this order:

- Fever is aggressively treated with antipyretics.
- Sedation and hemodynamics are optimized.
- Reduction of inotrope doses is useful because most agents have positive chronotrophic activity. This may be difficult in the setting of hemodynamic instability and low cardiac output syndrome.
- Mild systemic hypothermia is introduced. A cooling blanket and icepacks are used to reduce patient temperature to 32°C (89.6°F) to 35°C (95°F). This usually requires sedation and paralysis to prevent shivering.
- Procainamide or amiodarone therapy is initiated.

Walsh EP. Automatic atrial and junctional tachycardias. In: Walsh EP, Saul JP, Triedman JK, eds. *Cardiac Arrhythmias in Children and Young Adults with Congenital Heart Disease.* Philadelphia, PA: Lippincott Williams & Wilkins; 2001:115-135.

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Chapter 39
Transposition of the Great Arteries

James A. DiNardo

A 3-day-old, full-term, 3.4-kg newborn is scheduled for an arterial switch operation (ASO). Shortly after birth, he demonstrated reverse differential cyanosis with a right arm arterial saturation of 40% and a lower extremity saturation of 60%, despite prostaglandin E_1. A bedside balloon atrial septostomy was performed with resolution of reverse differential cyanosis and improvement of arterial saturation to 75%. Prostaglandin E_1 was discontinued 4 hours after the septostomy. Now, he is extubated, receiving 0.5 L per minute supplemental O_2 through nasal cannula. His arterial oxygen saturation is 75%; blood pressure, 63/37 mm Hg; pulse, 145 beats per minute; and respiration, 46 breaths per minute.

A. Medical Disease and Differential Diagnosis

1. What defines the cardiac situs?
2. What is transposition of the great arteries (D-TGA)?
3. What additional cardiac lesions are associated with D-TGA?
4. What is the natural history of D-TGA?
5. What is the pathophysiology of D-TGA?
6. What determines the oxygen saturation in patients with D-TGA?
7. Why did this infant have reverse differential cyanosis?
8. What are the preoperative issues pertaining to the coronary arteries in D-TGA?
9. What are the clinical subsets of D-TGA?
10. What is the differential diagnosis of D-TGA and how is the diagnosis made?
11. What preoperative interventions can help stabilize a patient with D-TGA?
12. What are the surgical options for repair? Why is one chosen over the others?

B. Preoperative Evaluation and Preparation

1. What information is important to prepare for this case?
2. What are the anesthetic goals before cardiopulmonary bypass (CPB)?
3. What is the plan for glucose management in this patient?

C. Intraoperative Management

1. How would you monitor this infant?
2. What would be the best method of induction?
3. Is CPB in infants and children different from adults?
4. What is modified ultrafiltration (MUF)?
5. Briefly describe the surgical techniques of the Mustard/Senning, ASO, and Rastelli procedures.

6. What is hypothermia and how is it classified? What is low-flow cardiopulmonary bypass (LFCPB)? What is deep hypothermic circulatory arrest (DHCA)?
7. Why is hypothermia beneficial to the brain during LFCPB and DHCA?

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8. Explain the difference between *α*-stat and pH-stat blood gas management.
9. What are the immediate post-CPB issues following ASO?

D. Postoperative Management

1. How is myocardial ischemia addressed in the intensive care unit (ICU) following the ASO?
2. What immediate postoperative problems would be anticipated following the Rastelli procedure?
3. What intermediate and long-term surgical problems are seen after ASO?
4. What are the long-term outcomes after ASO?
5. What are the long-term outcomes after Rastelli repair for D-TGA with left ventricular outflow tract (LVOT) obstruction?
6. What is long-term neurologic outcome like after ASO?

A. Medical Disease and Differential Diagnosis

A.1. What defines the cardiac situs?

Cardiac situs refers to the orientation of the right atrium; if the right atrium is on its normal position, that is, to the right, the cardiac situs is “solitus” (or normal); otherwise, the cardiac situs is “inversus” (mirror). With the use of echocardiography, the atria, atrioventricular valves (tricuspid and mitral), ventricles, ventriculoarterial valves (pulmonary and aortic), and great arteries (pulmonary artery and aorta) can be identified, thus diagnosing the various cardiac congenital malformations. There are three “axioms,” which help to identify the atria and the ventricles: (1) The right atrium receives the vena cava and coronary sinus; (2) there is always concordance (agreement) between the atrioventricular valve and ventricle, that is, the tricuspid valve is always the inflow valve for the right ventricle and the mitral valve the inflow valve for the left ventricle; and (3) the inflow/atrioventricular (tricuspid) and ventriculoarterial valve of the right ventricle are separated by a muscular part, the conus or infundibulum, but the mitral and ventriculoarterial valve of the left ventricle are in fibrous continuity.

Baum VC, Duncan PN. When right is right and when it's not: laterality in cardiac structures. *Anesth Analg*. 2011;113:1334-1336.

Gologorsky E, Gologorsky A, Giquel J, et al. An adult patient with congenitally corrected transposition of the great arteries. *Anesth Analg*. 2010;111:1122-1124.

A.2. What is transposition of the great arteries (D-TGA)?

D-TGA refers specifically to the anatomic circumstance wherein there is concordance of the atrioventricular (AV) connections associated with discordance of the ventriculoarterial connections. By far the most common manifestation of this anatomy occurs in patients with [S,D,D] segmental anatomy, also known as *D-TGA* (there is atrial situs *S*olitus, *D*-loop ventricles, and *D*-loop great arteries). A right-sided right atrium (RA) connects through a right-sided tricuspid valve and right ventricle (RV) to a right-sided and anterior aorta. A left-sided left atrium (LA) connects through a left-sided mitral valve and left ventricle (LV) to a left-sided and posterior pulmonary artery (PA). As a result, there is fibrous continuity between the mitral and pulmonic valves with a lack of fibrous continuity (conus) between the tricuspid and aortic valves. In D-TGA, the combination of AV concordance (RA to RV; LA to LV) and ventriculoarterial discordance (RV to aorta; LV to PA) produces a parallel rather than a normal series circulation.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45-65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

A.3. What additional cardiac lesions are associated with D-TGA?

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The most commonly associated cardiac anomalies are a persistent patent foramen ovale (PFO), patent ductus arteriosus (PDA), ventricular septal defect (VSD), and subpulmonic stenosis or LVOT obstruction. Approximately 50% of patients with D-TGA will present with a PDA before prostaglandin E_1 administration. The foramen ovale is almost always patent, but a true secundum atrial septal defect (ASD) exists in only approximately 5% of patients. Although angiographically detectable VSDs may occur in 30% to 40% of patients, only approximately one-third of these defects are hemodynamically significant. Therefore, for practical purposes, 75% of patients have an intact interventricular septum (IVS). LVOT obstruction is present in approximately 30% of patients with VSD and is most often due to an extensive subpulmonic fibromuscular ring or posterior malposition of the outlet portion of the ventricular septum.

Wernovsky G. Transposition of the great arteries. In: Allen HD, Clark EB, Gutgesell HP, et al, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adult*. 6th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2001:1027-1086.

A.4. What is the natural history of D-TGA?

D-TGA is a common congenital heart lesion accounting for 5% to 7% of all congenital cardiac defects, second in frequency only to isolated VSDs. Without intervention, D-TGA has a high mortality rate: Forty-five percent will die within the first month, and 90% will die within the first year of life. This is particularly unfortunate because infants with D-TGA rarely have extracardiac defects. Advancements in medical and surgical therapy in the last 20 years have greatly improved the outlook for these infants. In fact, following stabilization with prostaglandin E_1 and the Rashkind-Miller balloon septostomy, many of these infants can be offered a definite surgical procedure (arterial switch), giving them a quality of life similar to that of normal children.

Hypoxia and intractable congestive heart failure (CHF) are the two primary causes of death. The early onset and progression of pulmonary artery hypertension (PAH) plays a major role in the dismal outlook in these patients. Compared with other forms of congenital heart disease, infants with transposition of great arteries (TGA) are at particular risk for accelerated development of PAH. Systemic hypoxemia, the presence of bronchopulmonary collaterals (which deliver deoxygenated blood to the precapillary pulmonary arterioles), platelet aggregation in the lung, and polycythemia have all been implicated. Infants with TGA and large VSD without LVOT obstruction are at an even higher risk for the early development of PAH due to exposure of the pulmonary vascular bed to increased blood flow and systemic pressures. Advanced, nonreversible pulmonary hypertension reduces the corrective surgical options available to the patient.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker, PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

A.5. What is the pathophysiology of D-TGA?

In the parallel arrangement of D-TGA, deoxygenated systemic venous blood recirculates through the systemic circulation without reaching the lungs to be oxygenated. This recirculated systemic venous blood represents a *physiologic right-to-left shunt*. Likewise, oxygenated pulmonary venous blood recirculates uselessly through the pulmonary circulation. This recirculated pulmonary venous blood represents a *physiologic left-to-right shunt*. Therefore, in a parallel circulation, the physiologic shunt or the percentage of venous blood from one system that recirculates in the arterial outflow of the same system is 100% for both circuits. Unless there are one or more communications between the parallel circuits to allow intercirculatory mixing, this arrangement is not compatible with life.

The sites available for intercirculatory mixing in D-TGA can be intracardiac (PFO, ASD, VSD) or extracardiac (PDA, bronchopulmonary collaterals). Several factors affect the amount of intercirculatory mixing. The number, size, and position of anatomic communications are important. One large, nonrestrictive communication will provide better mixing than two or three restrictive communications. Reduced ventricular compliance and elevated

systemic and pulmonary vascular resistance (PVR) tend to reduce intercirculatory mixing by impeding flow across the anatomic communications.

The position of the communication is also important. Poor mixing occurs even with large anterior muscular VSDs due to their unfavorable position. Finally, in the presence of adequate intercirculatory mixing sites, the extent of intercirculatory mixing is directly related to the total pulmonary blood flow. Patients with reduced pulmonary blood flow secondary to subpulmonic stenosis or PAH will have reduced intercirculatory mixing.

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DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45-65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

A.6. What determines the oxygen saturation in patients with D-TGA?

In D-TGA, intercirculatory mixing is the result of anatomic right-to-left and anatomic left-to-right shunts that are equal in magnitude. The anatomic right-to-left shunt produces effective pulmonary blood flow, which is the volume of systemic venous blood reaching the pulmonary circulation. The anatomic left-to-right shunt produces an effective systemic blood flow, which is the volume of pulmonary venous blood reaching the systemic circulation. Effective pulmonary blood flow, effective systemic blood flow, and the volume of intercirculatory mixing are always equal. The systemic blood flow is the sum of recirculated systemic venous blood plus effective systemic blood flow. Likewise, total pulmonary blood flow is the sum of recirculated pulmonary venous blood plus effective pulmonary blood flow. Recirculated blood makes up the largest portion of total pulmonary and systemic blood flow, with effective blood flows contributing only a small portion of the total flows. This is particularly true in the pulmonary circuit where the total pulmonary blood flow (Q_P) and the volume of the pulmonary circuit (LA, LV, PA) is three to four times larger than the total systemic blood flow (Q_S) and the volume of the systemic circuit (RA, RV, aorta). The net result is production of a transposition physiology, where the PA oxygen saturation is greater than the aortic oxygen saturation. Figure 39.1 further elucidates these concepts.

Arterial saturation (SaO_2) is determined by the relative volumes and saturations of the recirculated systemic and effective systemic blood flows reaching the aorta. This is summarized in the following equation:

$$\text{Arterial saturation} = \frac{[(\text{systematic venous saturation})\,(\text{recirculated systemic blood flow})] + [(\text{pulmonary venous saturation})\,(\text{effective systemic blood flow})]}{(\text{total systemic blood flow})}$$

This is illustrated in Figure 39.1 where:

$SaO_2 = [(50)(1.2)] + [(99)(1.1)] / 2.3 = 73\%$

Obviously, the greater the effective systemic blood flow (intercirculatory mixing) relative to the recirculated systemic blood flow, the greater the SaO_2. For a given amount of intercirculatory mixing and total systemic blood flow, a decrease in systemic venous or pulmonary venous saturation will result in a decrease in SaO_2.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45-65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

A.7. Why did this infant have reverse differential cyanosis?

In D-TGA with intact IVS, the anatomic mixing sites are usually a PDA and a PFO. The dynamics of intercirculatory mixing in D-TGA with intact IVS are complex. Anatomic shunting at the atrial level is ultimately determined by the size of the atrial communication and the cyclic pressure variations between the left and right atria. The volume and compliance of

the atria, ventricles, and vascular beds in each circuit as well as heart rate (HR) and phase of respiration influence this relationship. Shunting is from the RA to the LA during diastole as the result of the reduced ventricular and vascular compliance of the systemic circuit (RV and systemic arterial circuit). In systole, shunt is from the LA to the RA primarily because of the large volume of blood returning to the LA as a result of the high volume of recirculated pulmonary blood flow.

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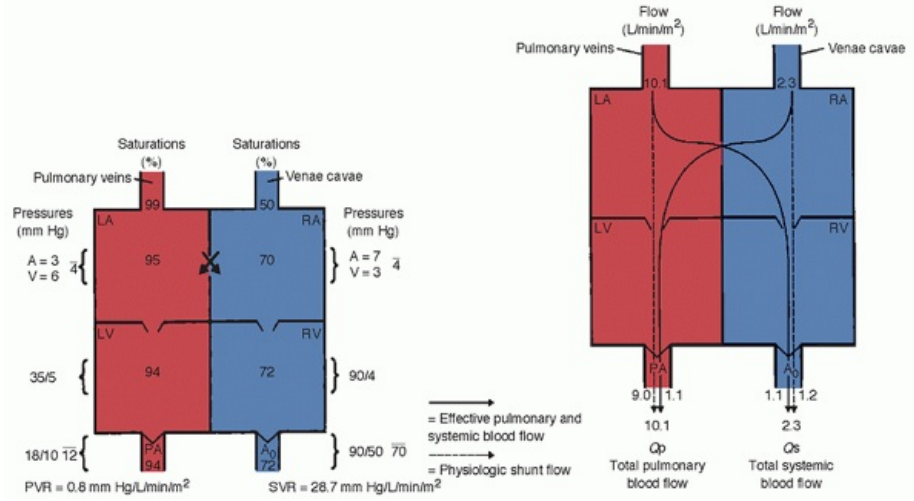


FIGURE 39.1 Depiction of saturations, pressures, and blood flows in complete transposition of the great vessels with intercirculatory mixing at the atrial level and a small left ventricular outflow tract gradient. It is apparent that total pulmonary blood flow (10.1 L/min/m^2) is almost five times the total systemic blood flow (2.3 L/min/m^2). Effective (EFF) pulmonary and effective systemic blood flow are equal (1.1 L/min/m^2) and are the result of an anatomic shunt at the atrial level. The physiologic left-to-right shunt is 9 L/min/m^2; this represents blood recirculated from the pulmonary veins to the pulmonary artery. The physiologic right-to-left shunt is 1.2 L/min/m^2; this represents blood recirculated from the systemic veins to the aorta. In this depiction, pulmonary vascular resistance is low (approximately 1/35 of systemic vascular resistance), and there is a small (17 mm peak to peak) gradient from the left ventricle to the pulmonary artery. These findings are compatible with the high pulmonary blood flow depicted. LA, left atrium; LV, left ventricle; PA, pulmonary artery; PVR, pulmonary vascular resistance; *Q*p, total pulmonary blood flow; *Q*s, total systemic blood flow; RA, right atrium; RV, right ventricle; SVR, systemic vascular resistance. (Modified from Freed MO, Keane JF. Profiles in congenital heart disease. In: Grossman W, ed. *Cardiac Catheterization and Angiography*. Philadelphia, PA: Lea & Febiger; 1986:463.)

The direction of shunting across the PDA largely depends on the PVR and the size of the intra-atrial communication. When the PVR is low and the intra-atrial communication is nonrestrictive, shunting is predominantly from the aorta to the PA through the PDA (effective pulmonary blood flow) and predominantly from the LA to RA across the atrial septum (effective systemic blood flow). When PVR is elevated, shunting across the PDA is likely to be bidirectional that in turn encourages bidirectional shunting across the atrial septum. When PVR is high and PA pressure exceeds aortic pressure, shunting at the PDA will be predominantly from the PA to the aorta. This will create reverse differential cyanosis —physiology wherein the preductal arterial saturation (right arm) is lower than the postductal arterial saturation (legs). This physiology is usually the result of a restrictive atrial communication producing left atrial hypertension and is associated with low effective blood flows (poor mixing) and hypoxemia. A balloon atrial septostomy can be lifesaving in this setting. Decompression of the LA promotes mixing at the atrial level and also reduces PVR and PA pressure promoting mixing at the PDA. Other causes of reverse differential cyanosis

to be considered in D-TGA are the presence of an interrupted aortic arch or severe aortic coarctation.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45-65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

A.8. What are the preoperative issues pertaining to the coronary arteries in D-TGA?

As in normally related great vessels, the coronary arteries in D-TGA arise from the aortic sinuses that face the PA. In

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normally related vessels, these sinuses are located on the anterior portion of the aorta, whereas in D-TGA, they are located posteriorly. In most D-TGA patients (70%), the right sinus is the origin of the right coronary artery, whereas the left sinus is the origin of the left main coronary artery. In the remainder of cases, there is considerable variability, with the most common variations being shown in Figure 39.2.

Most patients with D-TGA have a coronary anatomy that is suitable for the coronary reimplantation necessary in the ASO. Patients with certain types of coronary anatomy (intramural coronaries, single coronary artery) are at risk for postoperative myocardial ischemia and early mortality because reimplantation can result in the distortion of the coronary ostia or the narrowing of the artery itself. Patients with intramural coronaries generally require resuspension of the posterior leaflet of neopulmonary valve once the coronaries and a surrounding tissue cuff are excised.

The presence of a single coronary artery or intramural coronary arteries is a risk factor for mortality, and this risk has persisted over the last two decades.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

A.9. What are the clinical subsets of D-TGA?

Four clinical subsets based on anatomy, pulmonary blood flow, and intercirculatory mixing can be used to characterize patients with D-TGA. These are summarized in Table 39.1.

A.10. What is the differential diagnosis of D-TGA and how is the diagnosis made?

Figure 39.3 delineates the differential diagnosis for D-TGA in the cyanotic newborn.

D-TGA may be associated with either cyanosis or CHF. In patients in whom intercirculatory mixing is limited, cyanosis is severe with little evidence of CHF. CHF is the more common finding in patients with increased pulmonary blood flow, a large quantity of intercirculatory mixing, and mild cyanosis.

Chest radiographs may appear normal in the first few weeks of life in infants with D-TGA and intact IVS. Eventually, the triad of an enlarged egg-shaped heart (large RA and RV), narrow superior mediastinum, and increased pulmonary vascular markings evolve. In patients with D-TGA and VSD without LVOT obstruction, a large cardiac silhouette and prominent pulmonary vascular markings are seen at birth. Right axis deviation and right ventricular hypertrophy are the electrocardiographic (ECG) findings in D-TGA with intact IVS, whereas right axis deviation, LV hypertrophy, and RV hypertrophy are seen with D-TGA and VSD.

Two-dimensional echocardiography is the diagnostic modality of choice in the diagnosis and assessment of infants with D-TGA. It accurately establishes the diagnosis of D-TGA and reliably identifies associated abnormalities such as VSD, mitral and tricuspid valve abnormalities, and LVOT obstruction. It also reliably delineates coronary artery anatomy. Echocardiographic analysis of the IVS position or LV geometry is also used to noninvasively assess the LV to RV pressure ratio and IV mass in neonates with D-TGA and IVS who are being evaluated as candidates for an ASO.

In institutions with high-level echocardiography, a comprehensive cardiac catheterization is no longer routinely performed in neonates with D-TGA. A limited catheterization may be performed in conjunction with a balloon atrial septostomy. In the rare instance where coronary anatomy cannot be clearly delineated by echocardiography, coronary angiography may be indicated. During catheterization of infants with PAH, a trial of ventilation at an FIO_2 of

1.0 may be used to determine whether PVR is fixed or remains responsive to oxygen-induced pulmonary vasodilatation.

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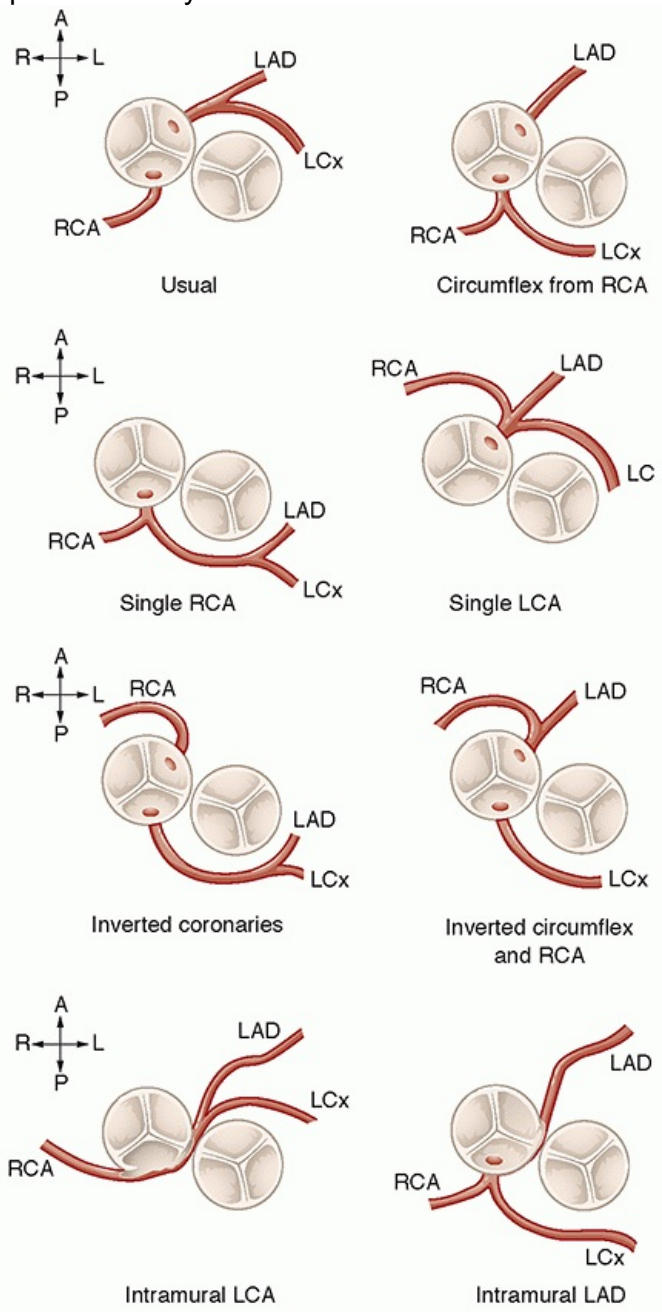


FIGURE 39.2 Depiction of the most common coronary artery patterns in transposition of the great vessels. The aorta is depicted anterior and to the right of the pulmonary artery. LAD, left anterior descending coronary artery; LCA, left coronary artery; LCx, left circumflex coronary artery; RCA, right coronary artery. (Adapted from Mayer JE Jr, Sanders SP, Jonas RA, et al. Coronary artery pattern and outcome of arterial switch operation for transposition of the great arteries. *Circulation*. 1990:82[5 suppl]:144.)

TABLE 39.1 Clinical Subsets of Transposition of Great Arteries

ANATOMY	PULMONARY BLOOD FLOW	INTERCIRCULATORY MIXING
D-TGA with IVS	Increased	Small
D-TGA with IVS; nonrestrictive atrial septum or PDA	Increased	Large

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D-TGA with VSD	Increased	Large
D-TGA with VSD and LVOT obstruction	Reduced	Small
D-TGA with PAH	Reduced	Small

D-TGA, transposition of great arteries; IVS, intact ventricular septum; PDA, patent ductus arteriosus; VSD, ventricular septal defect; LVOT, left ventricular outflow tract; PAH, pulmonary artery hypertension.

From DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45-65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

A.11. What preoperative interventions can help stabilize a patient with D-TGA?

Intact Ventricular Septum

Most neonates with D-TGA and intact IVS will be hypoxemic (arterial saturation ≤60%) within the first day of life. A proportion of these patients will have severely reduced effective pulmonary and systemic blood flow resulting in a PaO_2 less than 20 mm Hg, hypercarbia, and an evolving metabolic acidosis secondary to the poor tissue oxygen delivery. Prostaglandin E_1 (0.01 to 0.05 μg/kg/min) is administered to dilate and maintain the patency of the ductus arteriosus. This will be effective in increasing effective pulmonary and systemic blood flow and in improving PaO_2 and tissue oxygen delivery *if* (1) PVR is less than systemic vascular resistance (SVR) and (2) there is a nonrestrictive or minimally restrictive atrial septal communication. In some centers, all neonates stabilized on prostaglandin E_1 alone have a balloon atrial septostomy to enlarge the atrial septal communication so that prostaglandin E_1 can be stopped and surgery scheduled on a semi-elective basis. Prostaglandin E_1 infusion is associated with apnea, pyrexia, fluid retention, and platelet dysfunction.

If prostaglandin E_1 does not improve tissue oxygen delivery, then an emergent balloon atrial septostomy is performed in the catheterization laboratory utilizing angiography or in the ICU utilizing echocardiography. These patients also require tracheal intubation and mechanical ventilation. This allows reduction of PVR through induction of a respiratory alkalosis and elimination of pulmonary ventilation/perfusion ([V with dot above]/[Q with dot above]) mismatch. Sedation and muscle relaxation reduce oxygen consumption, thereby increasing mixed venous O_2 saturation. Recall that for a given amount of intercirculatory mixing and total systemic blood flow, an increase in systemic venous or pulmonary venous saturation will result in an increase in arterial saturation.

In rare instances, the combination of prostaglandin E_1, an atrial septostomy, and mechanical ventilation with sedation/muscle relaxation may be ineffective. In this circumstance, extracorporeal membrane oxygenation (either venoarterial or venovenous) support to improve tissue oxygenation and to reverse end-organ insult and lactic acidosis before surgery is an alternative approach to emergent surgery in a critically ill neonate.

Ventricular Septal Defect

Infants in this subset are mildly cyanotic with symptoms of CHF. Pulmonary blood flow is increased, and there is extensive intercirculatory mixing. Reducing PVR to further augment

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pulmonary blood flow and intercirculatory mixing will not greatly influence the systemic oxygenation. Reducing PVR in these patients may increase the recirculated volume in the pulmonary circuit by increasing circuit compliance. Maintaining systemic blood flow will then necessitate an increase in cardiac output from a failing heart. These patients are commonly stable enough not to require immediate surgical or catheterization laboratory intervention. They are, however, candidates for an ASO before intractable CHF or advanced PAH occurs.

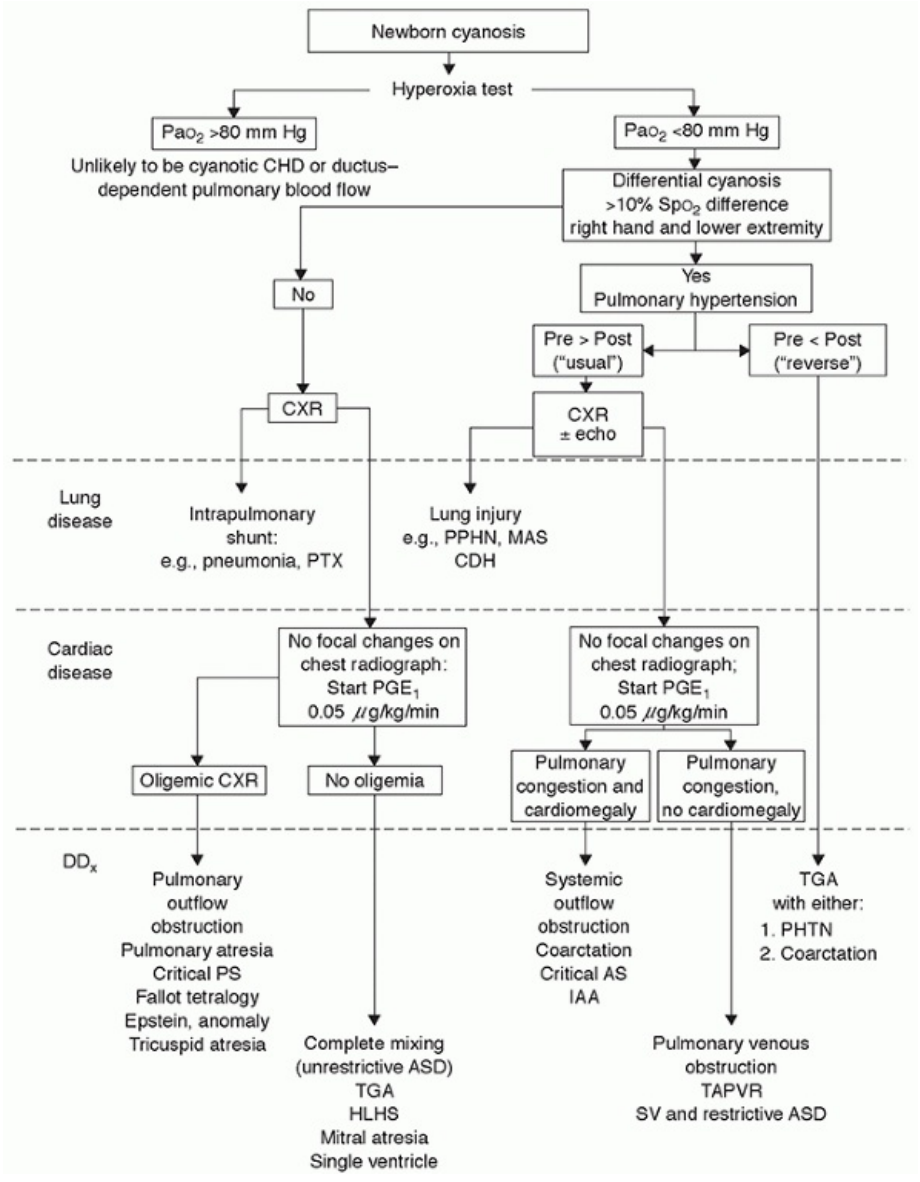


FIGURE 39.3 The differential diagnosis of transposition of the great arteries. AS, aortic stenosis; ASD, atrial septal defect; CDH, congenital diaphragmatic hernia; CHD, congenital heart disease; CXR, chest radiograph; DD_X, differential diagnosis; HLHS, hypoplastic left heart syndrome; IAA, interrupted aortic arch; MAS, meconium aspiration syndrome; PGE_1, prostaglandin E_1; PHTN, pulmonary hypertension; PPHN, persistent pulmonary hypertension of the newborn; PS, pulmonary stenosis; PTX, pneumothorax; SV, single ventricle; TAPVR, total anomalous pulmonary venous return; TGA, transposition of great arteries.

Ventricular Septal Defect and Left Ventricular Outflow Tract Obstruction

The degree of cyanosis in these infants will depend on the extent of LVOT obstruction. LVOT obstruction reduces pulmonary blood flow and intercirculatory mixing, and it protects the pulmonary vasculature from the increased pressures and volumes that accelerate the development of PAH. The more severe the LVOT obstruction, the less effective will be the efforts to increase pulmonary blood flow by decreasing PVR. When LVOT obstruction is severe, the infant is severely cyanotic and progressively develops erythrocytosis. These infants may require a palliative aortopulmonary shunt to increase pulmonary blood flow. Ideally, a definitive repair in the form of a Rastelli, LeCompte, or Nikaidoh procedure is

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performed in the neonatal period.

Pulmonary Artery Hypertension

The goal of diagnosis and treatment of infants with D-TGA is to intervene surgically before the development of PAH. As PAH advances, the child becomes progressively cyanotic and polycythemic. Efforts to reduce PVR will increase pulmonary blood flow and intercirculatory mixing in infants where PVR is not fixed. Infants with advanced PAH (PVR >10 Wood units; histologic grade 4) are generally candidates only for palliative therapy. In particular, closure of a VSD in the presence of advanced pulmonary hypertension carries a high mortality rate owing to the afterload mismatch and the resultant pulmonary ventricular (LV) dysfunction. These patients are candidates for a palliative intra-atrial physiologic repair (Mustard or Senning procedure) without closure or with fenestrated closure (4- to 5-mm hole in the center of the VSD patch) of the VSD.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45-65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

A.12. What are the surgical options for repair? Why is one chosen over the others?

Arterial Anatomic Repair: Arterial Switch (Jatene) Operation

The ASO anatomically corrects the discordant ventriculoarterial connections and is the procedure of choice for patients with D-TGA. Following repair, the RV is connected to the PA and the LV to the aorta. Clinical success with the ASO, summarized in Figure 39.4, was achieved in 1975. In order for the ASO to be successful, the original pulmonary ventricle (LV) must have sufficient mass to be capable of functioning as the systemic ventricle following the switch. Patient selection and the timing of the surgical procedure are, therefore, important variables in determining the success of this procedure. The ASO was originally described in patients with D-TGA and a large VSD or a large PDA. In these patients, the pulmonary ventricle (LV) remains exposed to systemic pressures, and the LV mass remains sufficient to support the systemic circulation. For this subset of patients, the ASO is generally performed within the first 2 to 3 months of life, before intractable CHF or irreversible PAH intervene.

In patients with D-TGA and IVS, there is a progressive reduction in LV mass as the physiologic pulmonary hypertension present at birth resolves progressively over the first weeks following birth. Adequate LV mass to support the systemic circulation reliably exists in these patients for only the first 3 or 4 weeks following birth. In patients with D-TGA and IVS, the ASO can be performed primarily or as the second phase of a staged procedure. A successful primary ASO must generally be performed within the first 4 weeks of life; most are performed in the first few days of life. Previously, favorable candidates for the procedure in the neonatal period were shown to have an LV to RV pressure ratio of at least 0.6 by catheterization.

Currently, two-dimensional echocardiography is used to noninvasively assess the LV to RV pressure ratio. Three types of ventricular septal geometry have been described. Patients in whom the ventricular septum bulges to the left (type 3), indicating a low pressure in the pulmonary ventricle (LV), are not candidates for a neonatal ASO. Patients with septal bulging to the right (type 1), indicating a high pressure in the pulmonary ventricle (LV), and those patients with an intermediate septal position (type 2) are considered good candidates. Most neonates with D-TGA and intact IVS who are suitable candidates for an ASO have type 2 septal geometry.

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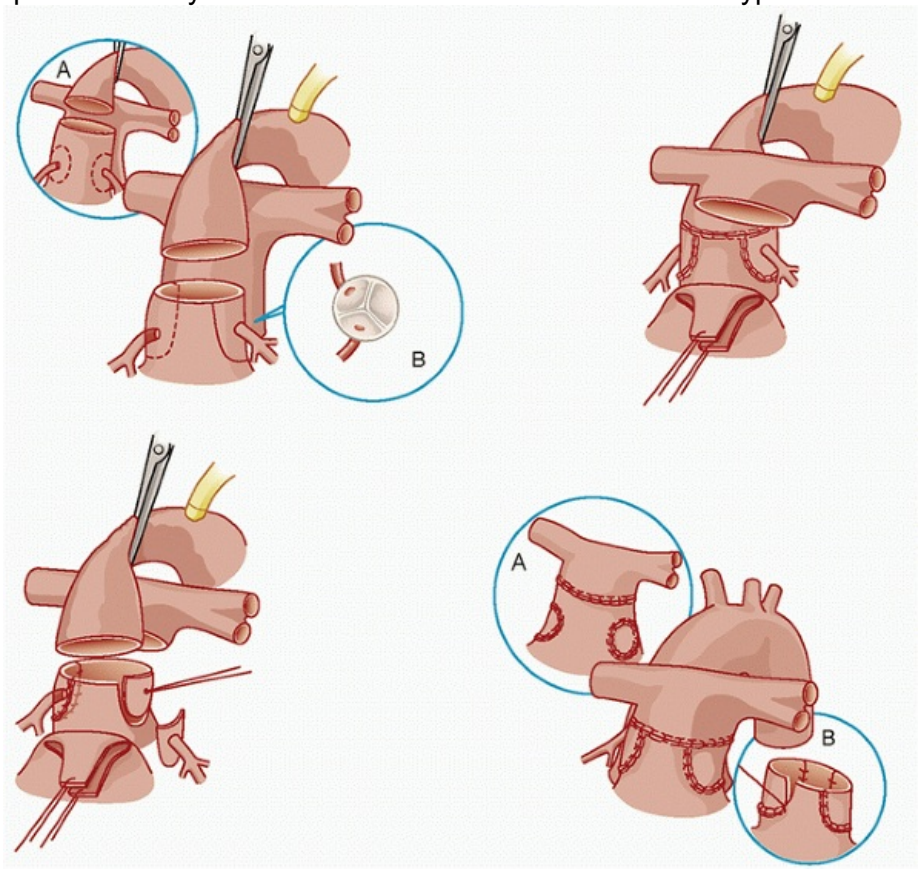


FIGURE 39.4 Details of the arterial switch procedure. **Upper left.** Aorta is transected and left and right main coronary arteries are excised using **(A)** either button of aortic wall or **(B)** segment of aortic wall extending from rim of aorta. **Lower left.** Equivalent segment of pulmonary arterial wall is excised, and coronary arteries are sutured to pulmonary artery. **Upper right.** Distal pulmonary artery is brought anterior to ascending aorta (LeCompte maneuver), and proximal pulmonary artery is anastomosed to distal aorta. **Lower right.** Sites of coronary explantation are repaired using either **(A)** patch of prosthetic material or **(B)** segment of pericardium. Finally, proximal aorta is sutured to distal pulmonary artery. (Adapted from Castaneda AR, Norwood WI, Jonas RA, et al. Transposition of the great arteries and intact ventricular septum: anatomical repair in the neonate. *Ann Thorac Surg*. 1984;38:438-443.)

The staged ASO for D-TGA with intact IVS is used for those neonates in whom surgery cannot be performed in the first month of life secondary to events such as prematurity, sepsis, low birth weight (<1.0 kg), or late referral. The staged procedure retrains the LV to accept the systemic workload. The preparatory surgery involves creation of a nonrestrictive atrial septum (if it does not already exist), placement of a PA band, and creation of an aortopulmonary shunt with entry to the PA distal to the band. The band must be tight enough to increase pressure in the pulmonary ventricle (LV) to approximately one-half to

two-thirds of that in the systemic ventricle (RV). This will increase the afterload sufficiently to stimulate an increase in LV mass. Historically, after 3 to 6 months, the PA was debanded, the shunt taken down, and an ASO performed. Currently a rapid two-stage repair is undertaken in which the ASO is performed as early as 1 week after preparatory PA banding, often during the same hospitalization. This approach is based on the fact that a doubling of LV mass is seen after 1 week of PA banding. The staged procedure is complicated by the fact that the adjustment of the PA band to the proper tightness is not an easy task and that the PA band and systemic to PA shunt may result in a distortion of the PA, making the definite ASO difficult. Intraoperative transesophageal echocardiography (TEE) is useful in guiding placement of the PA band. The band is tightened enough to flatten the IVS by shifting it toward the RV.

Intra-atrial Physiologic Repairs: Mustard and Senning Procedures

Both the Mustard and the Senning procedures are atrial switch procedures that surgically create discordant AV connections in D-TGA. Systemic venous blood is routed to the LV and the PA, whereas pulmonary venous blood is routed to the RV and the aorta. This arrangement results in physiologic but not anatomic correction of D-TGA as the morphologic RV becomes the systemic ventricle. Given the current success with and the almost universal application of the more

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definitive ASO, these intra-atrial switch procedures are primarily of historic interest in patients with D-TGA.

Rastelli, LeCompte, and Nikaidoh Procedures

These procedures are used as a method of anatomically correcting D-TGA with VSD and LVOT obstruction when LVOT obstruction in the form of subpulmonic and/or pulmonic stenosis is surgically uncorrectable. Performance of an ASO under these circumstances would leave the infant with residual LVOT obstruction (aortic or subaortic stenosis).

DiNardo JA. Transposition of the great arteries. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:256-278.

Honjo O, Kotani Y, Bharucha T, et al. Anatomical factors determining surgical decision-making in patients with transposition of the great arteries with left ventricular outflow tract obstruction. *Eur J Cardiothorac Surg*. 2013;44:1085-1094.

Martins P, Castela E. Transposition of the great arteries. *Orphanet J Rare Dis*. 2008;3:27-36.

B. Preoperative Evaluation and Preparation

B.1. What information is important to prepare for this case?

The preoperative evaluation should begin with a careful history and physical examination. Gestational age, birth complications, family history, and any other medical problems should be noted. A comprehensive airway evaluation should be performed and the previous endotracheal tube size and leak pressure noted. Arterial and intravenous access should be assessed. A type and cross must be sent to the blood bank to ensure adequate red blood cells and blood component therapies are available in the operating room (OR).

The preoperative ECG and chest radiograph should be reviewed. The preoperative echocardiograms should be reviewed. Particular attention should be paid to septal geometry, biventricular function, coronary anatomy, and adequacy of mixing at the atrial septal and ductal levels. Prostaglandin E_1 was discontinued in the patient, but the ductus arteriosus may remain patent.

Laboratory data should include a complete blood count, electrolytes, platelet count, arterial blood gas, calcium, blood urea nitrogen, creatinine, liver function tests, and glucose. Given that this infant presented with severe hypoxemia, end-organ dysfunction must be ruled out. The liver function tests and creatinine should be normal; if they are elevated, consideration should be given to further medical optimization. A head ultrasonographic examination should be performed to rule out intraventricular hemorrhage.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45-65.

B.2. What are the anesthetic goals before cardiopulmonary bypass (CPB)?

- Maintain HR, contractility, and preload to maintain cardiac output; decreases in cardiac output decrease systemic venous saturation with a resultant fall in arterial saturation.
- Maintain ductal patency with prostaglandin E_1 (0.01 to 0.05 μg/kg/min) in ductal-dependent patients.
- Avoid increases in PVR relative to SVR; increases in PVR will decrease pulmonary blood flow and reduce intercirculatory mixing; in patients with PAH, ventilatory interventions should be used to reduce PVR; in patients with LVOT obstruction that is not severe, ventilatory interventions to reduce PVR increase pulmonary blood flow and intercirculatory mixing.
- Reductions in SVR relative to PVR should be avoided; decreased SVR increases recirculation of systemic venous blood and decreases arterial saturation.
- In patients with D-TGA and VSD with symptoms of CHF, ventilatory interventions to reduce PVR are not warranted

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because they will produce small improvements in arterial saturation at the expense of systemic perfusion.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

B.3. What is the plan for glucose management in this patient?

Maintenance for caloric requirements in the awake neonate/infant are 100 kcal/kg/day or 4 kcal/kg/hr. This caloric requirement can be met with glucose 25 g/kg/day or 1 g/kg/hr. From a practical point of view, this glucose requirement can be met with 10% dextrose (100 mg per mL) run at the maintenance volume replacement rate of 4 mL/kg/hr. Ten percent dextrose run at half this rate (2 mL/kg/hr) is usually sufficient to meet the caloric requirements of an anesthetized infant while avoiding both the hyperglycemia and hypoglycemia that can be detrimental to neurologic outcome particularly following DHCA. Dextrose infusions should be discontinued before commencement of CPB because the associated neuroendocrine response to CPB generally produces mild hyperglycemia. Some infants receive nutritional support as part of medical stabilization before surgery. High-calorie total parenteral nutrition and intralipid therapy should be discontinued and replaced with a 10% dextrose infusion several hours before transport to the OR. Continued administration of these high-calorie infusions makes intraoperative serum glucose management problematic. In these patients, higher dextrose infusion rates may be necessary pre-CPB to avoid rebound hypoglycemia.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45-65.

C. Intraoperative Management

C.1. How would you monitor this infant?

Ideally, preinduction monitoring should include a blood pressure cuff, ECG, pulse oximeter, and an end-tidal carbon dioxide monitor. In reality, a pulse oximeter and an ECG may be all that is practical in the early stages of induction. The other monitors are then quickly added as induction progresses. Pulse oximeter probes should be placed on an upper and lower extremity (preductal and postductal if relevant). An intra-arterial catheter (radial or femoral) is placed immediately after induction. Many infants transferred from the ICU will have an umbilical artery or femoral artery catheter in place. A central venous pressure and drug infusion catheter is placed after intubation and stabilization. Double-lumen central venous catheters inserted through the femoral or internal jugular vein are preferred. Nasopharyngeal, tympanic, and rectal temperature probes are also placed following induction. A bladder catheter should be placed. A TEE probe can be inserted following induction and intubation.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45-65.

C.2. What would be the best method of induction?

This infant would have an IV catheter in place on transfer to the OR. Anesthesia is generally induced and maintained using a synthetic opioid-based (fentanyl or sufentanil) technique. These opioids may be used alone in high doses (25 to 100 μg per kg fentanyl or 2.5 to 10 μg per kg sufentanil) or in low to moderate doses (5 to 25 μg per kg fentanyl or 0.5 to 2.5 μg per kg sufentanil) in combination with an inhalation agent (generally isoflurane or sevoflurane) or a benzodiazepine (generally midazolam). The high-dose technique is particularly useful in neonates and infants. High-dose opioids provide hemodynamic stability, do not depress the myocardium, and blunt reactive pulmonary hypertension.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45-65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

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C.3. Is CPB in infants and children different from adults?

The major differences between adult and pediatric CPB are summarized in Table 39.2.

Flows of 2.0 to 2.5 L/min/m^2 are commonly used for infants, children, and adults during mild to moderate systemic hypothermia. Owing to age-related differences in the relationship of surface area to weight, these flow rates expressed in mL/kg/min will be substantially higher in the neonate than in the adult. The recommended full flow rates for pediatric CPB are summarized in Table 39.3.

The vast majority of operative procedures in children require the use of either total CPB or DHCA. Venous cannulation for DHCA is usually accomplished with a single large venous cannula in the RA. Once cooling is complete and circulatory arrest is established, the cannula is removed to allow for maximum surgical exposure. For total CPB, once the cavae (and other sources of systemic venous return) are cannulated, surgical tourniquets or tapes are passed around the external circumference of the vessels. When these tapes are tightened around the cannulae, the right heart can be isolated completely and subsequently opened without entrainment of air into the venous circuit or obscuration of the surgical field by venous blood. During delivery of antegrade cardioplegia, it is essential that at least one tape be left untightened to allow egress of cardioplegia solution from the coronary sinus without

distention of the RA. In older children, a larger cannula is used in the inferior vena cava (IVC) as compared with the superior vena cava (SVC) because a larger portion of systemic venous return (two-thirds) is from the IVC.

TABLE 39.2 Major Differences between Adult and Pediatric Cardiopulmonary Bypass

PARAMETER	ADULT	PEDIATRICS
Hypothermic temperature	Rarely below 25°C-32°C	Commonly 15°C-20°C
Use of total circulatory arrest	Rare	Common
Pump prime		
Dilution effects on blood volume	25%-33%	200%-300%
Additional additives in pediatric primes		Blood, albumin
Perfusion pressures	50-80 mm Hg (some centers accept 30 mm Hg)	20-50 mm Hg
Influence of pH management strategy	Minimal at moderate hypothermia	Marked at deep hypothermia
Measured $PaCO_2$ differences	30-45 mm Hg	20-80 mm Hg
Glucose regulation		
Hypoglycemia	Rare—requires significant hepatic injury	Common—reduced hepatic glycogen stores

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Hyperglycemia	Frequent—generally easily controlled with insulin	Less common—rebound hypoglycemia may occur

TABLE 39.3 Recommended Full Flow Rates for Pediatric Cardiopulmonary Bypass

PATIENT WEIGHT (kg)	FULL CPB FLOW RATES (mL/kg/min)
<3	150-200
3-10	125-175
10-15	120-150
15-30	100-120
30-50	75-100
>50	50-75

CPB, cardiopulmonary bypass.

As with venous cannulation, arterial cannulation in children, particularly infants/neonates, can be technically challenging. It may be necessary in circumstances where the ascending aorta and aortic arch are hypoplastic and systemic blood flow is ductal-dependent (as in hypoplastic left heart syndrome) to obtain systemic perfusion through the ductus arteriosus by cannulating the PA. When the aortic arch is interrupted, cannulation of the aorta both proximal and distal to the interruption is necessary. Because the arterial cannula is relatively large as compared to the aorta in infants/neonates, complete or partial obstruction of the aorta by the cannula itself is possible. Constant vigilance is necessary to avoid this problem. If dampening of the arterial trace, distention of the systemic ventricle, or an increase in CPB line pressure occurs with placement or manipulation of the arterial cannula, the surgeon should immediately be made aware of the situation so the cannula can be repositioned. Some centers utilize near-infrared spectroscopy and transcranial Doppler ultrasonographic technology as adjunctive methods to assess cerebral blood flow during CPB.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:228-252.

DiNardo JA. Profound hypothermia and circulatory arrest. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:253-265.

C.4. What is modified ultrafiltration (MUF)?

Ultrafiltrators are devices commonly added to the CPB circuit to remove excess fluid and produce hemoconcentration. When used in conjunction with CPB, these devices produce an ultrafiltrate that occurs as the result of a hydrostatic pressure gradient across a semipermeable membrane. These are the same devices that can be used for hemodialysis when they are used in conjunction with a dialysate. When used in conjunction with CPB, they are commonly called *hemoconcentrators* because they produce an increase in hematocrit by removing excess fluid.

These devices consist of a core of microporous hollow fibers made of polysulfone, polyamide, or polyacrylonitrile material arranged in a bundle. The pore size is generally 0.30 to 0.40 μm. Owing to the pressure drop across the device, blood

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inflow must be obtained from the arterial side of the CPB circuit while blood outflow is diverted to the cardiotomy reservoir or venous reservoir. The ultrafiltrate is collected in a container connected to a vacuum source.

The ultrafiltrate is discarded and has the composition of glomerular filtrate. The rate at which ultrafiltrate is produced is dependent on the transmembrane pressure (TMP) gradient. TMP is determined by the arterial inlet pressure (P_a), the venous outlet pressure (P_v), the absolute value of applied suction at the outlet (P_n), the oncotic pressure at the inlet (P_i), and the oncotic pressure at the outlet (P_o):

$$\mathrm{TMP} = \frac{P_a + P_v}{2} + P_n - \frac{P_i + P_o}{2}$$

P_n is increased by using the regulated vacuum source connected to the outlet of the device. TMP should not exceed 500 mm Hg.

Continuous ultrafiltration (CUF) refers to ultrafiltration occurring throughout CPB or during those intervals when venous reservoir volume is sufficient to allow it. MUF is a technique that allows ultrafiltration to continue after weaning from CPB. MUF may be performed utilizing either an arteriovenous or venovenous system. In the arteriovenous system, inflow to the ultrafiltrator during MUF is directly from the aortic cannula. Outflow from the ultrafiltrator is to the RA. Blood volume is kept constant as ultrafiltrate is lost by replacing it with blood from the CPB circuit, which passes through the ultrafiltrator before being delivered to the RA. In this way, the CPB circuit can remain primed and the patient's blood, as well as the CPB blood, can be hemoconcentrated. In the venovenous system, the IVC cannula provides inflow to the ultrafiltrator with the aid of a roller pump, whereas outflow from the ultrafiltrator is returned to the SVC cannula. Blood volume is kept constant as ultrafiltrate is lost by replacing it with blood from the CPB circuit, which passes through the ultrafiltrator before being delivered to the SVC. The end point for termination of MUF following CPB varies from institution to institution, with institutions terminating MUF after a set time interval (15 to 20 minutes), a set hematocrit (40%), or a set volume removed (750 mL per m^2). Heparin anticoagulation must be maintained during MUF, with protamine reversal of heparin initiated after termination of MUF.

MUF may be an effective method of attenuating the deleterious consequences of a CPB strategy that involves large asanguinous primes, particularly in neonates and infants. In the studies comparing MUF to no ultrafiltration, a CPB technique consisting of a very large asanguinous pump prime (400 to 900 mL) with packed cells added to reach a hematocrit of 15% to 20% has generally been used. This is precisely the group of patients who would need and who would benefit from aggressive removal of excess fluid to reduce total body water and increase hematocrit and coagulation factors. Furthermore, it has been demonstrated that MUF and continuous ultrafiltration during CPB are indistinguishable in their effect on hematocrit, mean arterial pressure, HR, and LV shortening fraction when equal volumes of fluid are removed.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:228-252.

Wang S, Palanzo D, Ündar A. Current ultrafiltration techniques before, during and after pediatric cardiopulmonary bypass procedures. *Perfusion*. 2012;27:438-446.

C.5. Briefly describe the surgical techniques of the Mustard/Senning, ASO, and Rastelli procedures.

Intra-atrial Physiologic Repairs: Mustard and Senning Procedures

In both procedures, the interatrial septum is excised, creating a large ASD. In the Mustard procedure, a baffle made of native pericardium or synthetic material is then used to redirect pulmonary and systemic venous blood. In the Senning procedure, autologous tissue from the right atrial wall and interatrial septum is used in place of the pericardium or synthetic material. In either case, pulmonary venous blood flows over the baffle and is directed across the tricuspid valve into the RV and out the aorta. Systemic venous blood flows on the underside of the baffle to be directed across the mitral valve into the LV and out of the PA. This arrangement results in physiologic but not anatomic correction of D-TGA, as the morphologic RV becomes the systemic ventricle. These procedures are performed with hypothermic CPB, bicaval cannulation, and aortic cross-clamping during cardioplegic arrest. Intervals of LFCPB are customarily used.

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Arterial Anatomic Repair: Arterial Switch (Jatene) Operation

The PA and the aorta are transected distal to their respective valves. The coronary arteries are initially explanted from the ascending aorta with 3 to 4 mm of surrounding tissue. The explant sites are repaired either with pericardium or synthetic material. The coronary arteries are reimplanted into the proximal PA (neoaorta). The distal PA is brought anterior to the

aorta (LeCompte maneuver) to be reanastomosed to the old proximal aorta (right ventricular outflow) and the distal aorta reanastomosed to the old proximal PA (left ventricular outflow). As a result, the great arteries are switched to create ventriculoarterial concordance with both an anatomic and physiologic repair achieved. The ASO is done using hypothermic CPB with aortic cross-clamping and cardioplegic arrest. Intervals of LFCPB are customarily used. A short interval of DHCA may be employed to close the atrial septum or VSD if a single venous cannula rather than bicaval venous cannulation is used. Closure of a VSD is preferentially done transatrially through the tricuspid valve. It is desirable to avoid approaching a VSD through the RV because an incision in the RV may contribute substantially to postoperative RV dysfunction.

DiNardo JA. Transposition of the great arteries. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:256-278.

Jatene AD, Fontes VF, Paulista PP, et al. Anatomic correction of transposition of the great vessels. *J Thorac Cardiovasc Surg*. 1976;72:364-370.

Rastelli Procedure

The PA is transected and ligated just distal to or at the level of the pulmonary valve. A right ventriculotomy is performed, and the VSD is closed with a patch tunnel such that the LV is in continuity with the aorta. The VSD may have to be enlarged, in some cases, to prevent subaortic stenosis. RV to PA continuity is achieved by placement of valved conduit or valved homograft between the right ventriculotomy site and the proximal main PA. The result is LV to aortic continuity and RV to PA continuity with bypass of the subpulmonic and pulmonic stenosis. This procedure is performed with hypothermic CPB, bicaval cannulation, and aortic cross-clamping during cardioplegic arrest. Intervals of LFCPB are customarily used.

Historically, most of these patients had a palliative systemic to PA shunt placed in the newborn period and then returned for the Rastelli procedure and takedown of the shunt at 2 to 3 years of age. The delay was felt necessary to avoid performing a right ventriculotomy in infants with immature myocardium and limited contractile elements and to allow adequate growth of the RV and pulmonary arteries to permit placement of an RV to PA conduit. In the current era with improvements in myocardial protection, CPB technology, and surgical technique, this procedure can be performed as a primary procedure in the neonatal period.

DiNardo JA. Transposition of the great arteries. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:256-278.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

C.6. What is hypothermia and how is it classified? What is low-flow cardiopulmonary bypass (LFCPB)? What is deep hypothermic circulatory arrest (DHCA)?

The levels of systemic hypothermia employed during CPB are generally defined as follows: mild (35°C [95.0°F] to 32°C [89.6°F]), moderate (31°C [87.8°F] to 26°C [78.8°F]), deep (25°C [77°F] to 20°C [68°F]), and profound (<20°C [68°F]). Unfortunately, it is not uncommon for temperatures less than 20°C (68°F) used in conjunction with pediatric cardiac surgery to be called *deep hypothermia*. LFCPB in neonates/infants conducted in conjunction with temperatures of 18°C (64.4°F) to 25°C (77°F) is generally defined as 50 to 70 mL/kg/min or approximately 1.0 to 1.5 L/min/m^2.

Profound hypothermic circulatory arrest, commonly referred to as *DHCA*, is a technique employed to improve exposure of intracardiac defects and to facilitate aortic arch reconstruction in infants and children. DHCA is conducted in conjunction with temperatures of 18°C (64.4°F) to 20°C (68°F) and allows cessation of CPB, venous and arterial cannula removal,

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and exsanguination of the patient into the venous reservoir of the CPB circuit. There has been substantial refinement of the technique of DHCA since its successful inception in the 1970s. In the current era, DHCA is used selectively and for short intervals. It is utilized primarily for the aortic arch reconstruction component of the Norwood procedure, repair of interrupted aortic arch, neonatal repair of total anomalous pulmonary venous connection,

and complicated intracardiac repairs such as complete AV canal defects in small (<2.0 kg) neonates and infants.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:228-252.

DiNardo JA. Profound hypothermia and circulatory arrest. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:253-265.

C.7. Why is hypothermia beneficial to the brain during LFCPB and DHCA?

Hypothermia is arguably the most important component of LFCPB and DHCA. Hypothermiainduced reduction in cerebral metabolic rate for oxygen ($CMRO_2$) slows the rate of depletion of high-energy phosphates and the development of intracellular acidosis. This in turn delays or prevents the neuronal energy failure that leads to terminal membrane depolarization and subsequent neuronal injury or death during an ischemic episode. Q_{10} defines the ratio of organ O_2 consumption at a defined temperature to the O_2 consumption at a temperature 10°C (18°F) lower. The cerebral Q_{10} is approximately 3.65 in children and 2.3 in adults. Despite this, the cerebral metabolic rate will still be approximately 10% to 15% of its normothermic baseline at 15°C (59°F). If it is assumed that 3 to 5 minutes of cerebral ischemia can be tolerated at 37°C (98.6°F) and the Q_{10} is 3.0, 9 to 15 minutes of ischemia can be tolerated at 27°C (80.6°F) and 27 to 45 minutes can be tolerated at 17°C (62.6°F).

In addition to reducing $CMRO_2$, hypothermia also serves to ameliorate some of the sequelae of neuronal ischemia when instituted *before* the ischemia insult. Specifically, hypothermia markedly reduces release of the excitatory neurotransmitters glutamate, aspartate, and glycine that accompany cerebral ischemia and subsequent reperfusion. In energy-deprived cells, glutamate in particular is neurotoxic in part due to the role it plays in inducing massive calcium influx through *N*-methyl-D-aspartic acid receptors. Hypothermia also blunts the inhibitory effect of hypoxia on nitroxidergic (postganglionic parasympathetic nerve where nitric oxide is the neurotransmitter)-induced cerebral vasodilatation. In addition, there is evidence that hypothermia may attenuate neutrophil migration into ischemic tissue.

DiNardo JA. Profound hypothermia and circulatory arrest. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:253-265.

McCullough JN, Zhang N, Reich DL, et al. Cerebral metabolic suppression during hypothermic circulatory arrest in humans. *Ann Thorac Surg*. 1999;67:1895-1899.

C.8. Explain the difference between α-stat and pH-stat blood gas management.

pH-stat and *α*-stat acid-base management are commonly discussed in association with management of CPB. pH-stat and *α*-stat regulation are acid-base management methods that directly influence blood flow to the brain and other organs. Although pH-stat and *α*-stat acid-base management are commonly mentioned in association with temperature-corrected and temperature-uncorrected blood gases, it must be emphasized that these are entirely different concepts. The method of blood gas interpretation (corrected or uncorrected) does not dictate the method of acid-base management (pH-stat or *α*-stat). *α*-Stat or pH-stat management is possible with use of both temperature-corrected and temperature-uncorrected blood gases. In addition, it is important to point out that at a patient temperature of 37°C (98.6°F), there is no difference between pH-stat and *α*-stat management. The difference between these two strategies becomes more marked as patient temperature progressively decreases below 37°C (98.6°F) and is not clinically relevant until patient temperature is less than 30°C (86°F).

When a blood gas sample is drawn from a patient at 25°C (77°F) and sent to the blood gas laboratory, the sample is

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warmed to 37°C (98.6°F) before measurement. The values obtained at 37°C (98.6°F) are called the *temperature-uncorrected values*. These values are converted to temperature-corrected values using a nomogram. The nomogram accounts for temperatureinduced changes in pH, O_2 solubility, and CO_2 solubility in a closed-blood system. When blood in a closed system is cooled to a lower temperature, the electrochemically neutral pH is higher and the associated PCO_2 is lower than in a closed blood system at 37°C (98.6°F). Therefore, electrochemical neutrality is maintained by keeping pH alkalotic in temperature-corrected blood gases and normal in temperature-uncorrected gases. This is known as *α-stat*

regulation. For practical purposes, it is easier to use uncorrected gases and keep pH and PCO_2 in the range considered normal at 37°C (98.6°F). It has been demonstrated clinically that cerebral blood flow and oxygen consumption are appropriately coupled when *α*-stat regulation is used. Deep hypothermia in the presence of *α*-stat regulation produces loss of cerebral autoregulation such that cerebral blood flow varies directly with arterial pressure.

pH-stat regulation refers to maintaining pH and PCO_2 at normal values for blood at 37°C (98.6°F) regardless of actual blood temperature. With this strategy, a blood sample will have a normal pH and PCO_2 when temperature-corrected gases are used, and acidotic pH and PCO_2 values when temperature-uncorrected gases are used. For practical purposes, pH-stat is maintained by adding CO_2 to the ventilating gas during hypothermic CPB to increase PCO_2 and decrease the pH. In contrast to *α*-stat regulation, in which total CO_2 content is kept constant, pH-stat regulation results in an increase in total CO_2 content. The cerebral vasculature maintains vasomotor responses to varying PCO_2 during hypothermic CPB. This response is maintained during both moderate and deep hypothermia despite the fact that deep hypothermia induces loss of cerebral blood flow autoregulation. It has been demonstrated clinically that when pH-stat regulation is used with moderate hypothermic CPB, there is uncoupling of cerebral blood flow and metabolism and loss of cerebral autoregulation. As a result, cerebral blood flow varies linearly with arterial blood pressure, and cerebral hyperperfusion exists with cerebral blood flow far in excess of that dictated by cerebral metabolic rate. This hyperperfusion state is the result of (1) reduced cerebral oxygen consumption induced by hypothermia and (2) cerebral vasodilation resulting from a disproportionately high PCO_2 for the degree of hypothermia present. The potential danger of the hyperperfused state is that it may result in increased delivery of microemboli into the cerebral circulation.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:228-252.

DiNardo JA. Profound hypothermia and circulatory arrest. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:253-265.

C.9. What are the immediate post-CPB issues following ASO?

Bleeding from the extensive suture lines in the post-CPB period may be problematic. Efforts to reduce aortic blood pressure combined with aggressive blood component therapy are often required. In neonates, it may require 1 to 2 units of platelets (0.25 to 0.5 units per kg) to obtain a therapeutic platelet count increase. Because platelets are suspended in fresh frozen plasma, a platelet transfusion of this size usually results in a fresh frozen plasma transfusion of 10 to 15 mL per kg.

Myocardial ischemia following reimplantation of the coronary arteries is a potential problem following the ASO. In some circumstances, the ischemia is transient secondary to coronary air emboli. TEE is very useful to ensure adequate removal of air from the LA and LV before the termination of CPB. It is also useful in assessing the potency of the reimplanted coronary arteries. Maintenance of high perfusion pressures on CPB after aortic cross-clamp removal will facilitate the distal migration of air emboli. In other instances, kinking of the reimplanted artery or compromise of the implanted coronary ostia may require immediate surgical intervention. Pharmacologic intervention with traditional therapies to improve the balance of myocardial oxygen demand and delivery such as nitroglycerin and *β*-blockade are never a long-term alternative to prompt surgical revision of the appropriate anastomosis.

Despite comprehensive preoperative evaluation, the LV of patients undergoing an ASO may be marginal in its ability to support the systemic circulation in the post-CPB period. This may occur as the result of myocardial ischemia, inadequate LV mass, poor protection of the LV during aortic cross-clamping, or a combination of these variables. TEE is useful in identifying and continuously evaluating both global and regional LV systolic dysfunction. It also detects mitral regurgitation, which may occur secondary to papillary muscle dysfunction or to dilation of the mitral valve annulus. Inotropic support of the

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LV and afterload reduction may be necessary to terminate CPB.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

D. Postoperative Management

D.1. How is myocardial ischemia addressed in the intensive care unit (ICU) following the ASO?

Myocardial ischemia in the ICU following an ASO as heralded by ST-segment/T-wave changes or the development of atrial or ventricular arrhythmias requires immediate attention. Myocardial ischemia should be considered to be mechanical in nature until proved otherwise. Compression of the coronary ostia by swelling of thrombin gelfoam pads or thrombus formation around the coronary anastomoses must be considered. In this setting, surgical reex-ploration is likely to be immediately therapeutic.

Another source of mechanically induced myocardial ischemia in the ASO patient occurs as the result of LV dilation. A unique cycle of LV dilation initiating and exacerbating myocardial ischemia exists in patients having undergone the ASO. Myocardial ischemia, afterload mismatch, or overzealous volume infusion can result in LV distension and LA hypertension. This will be particularly likely if there is mitral insufficiency from either papillary muscle dysfunction or dilation of the mitral valve annulus. LV distention may result in tension on and kinking of the coronary reanastomosis sites. LA hypertension produces elevations in PA pressure and distention of the PA. As the LeCompte maneuver brings the distal PA anterior to the ascending aorta, distention of the PA may actually compress or place tension on the coronary ostia. The resulting myocardial ischemia produces further LV dilation, progressive elevations in LA and PA pressures, and continuing compromise of coronary blood flow. Attempts to induce coronary vasodilatation with nitroglycerin are unlikely to be beneficial in this setting, although its preload and afterload reducing may be beneficial. A more rational approach would be initiation of milrinone therapy.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

DiNardo JA. Transposition of the great arteries. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:256-278.

D.2. What immediate postoperative problems would be anticipated following the Rastelli procedure?

Right (pulmonary) ventricular dysfunction may occur in the post-CPB period. These patients are at risk because a right ventriculotomy is used to close the VSD and to create the new pulmonary outflow tract. Heart block may also occur given the proximity of the VSD to the intraventricular conduction pathways. A residual VSD may be present. Because the VSD closure to create LV to aortic continuity is more of a tunnel than a patch closure, LV outflow tract obstruction is also possible.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

D.3. What intermediate and long-term surgical problems are seen after ASO?

Supravalvular pulmonary stenosis is probably the most common complication of ASO. This stenosis is due to retraction of the tissue used to replace the tissue excised with the explanted coronaries and, in most patients, is not extensive enough to result in valvular pulmonary stenosis. Series with long-term follow-up (15 years) confirms that the incidence of supravalvular stenosis severe enough to require reoperation (generally a gradient >50 to 60 mm Hg) is approximately 4% to 8%. Aortic insufficiency occurs in approximately 10% to 15% of patients at long-term follow-up, with the majority (96%) graded as trivial or mild. Time has shown aortic insufficiency to be a rare source of morbidity or indication for reoperation

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following the ASO.

Early concerns existed regarding the long-term patency and growth potential of the reimplanted coronary arteries. Fortunately these problems have not materialized on a large scale.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357-380.

Villafañe J, Lantin-Hermoso MR, Bhatt AB, et al. D-transposition of the great arteries: the current era of the arterial switch operation. *J Am Coll Cardiol*. 2014;64:498-511.

D.4. What are the long-term outcomes after ASO?

The initial result for the arterial switch in experienced institutions is excellent, with an actuarial survival at 1 year of 90% for patients with D-TGA and IVS, and 83% for patients with D-TGA and VSD. Other experienced groups have reported similar results. A recent review of 470 patients from one institution experienced in the ASO, however, revealed a 1-year survival rate of 92% and an 8-year survival rate of 91% for patients with both D-TGA and intact IVS and D-TGA and VSD. A similar review of 1,200 patients from another experienced institution revealed a 1- and 15-year survival rate of 92% for patients with D-TGA and intact IVS, and 1- and 15-year survival of 81% and 80% for D-TGA and VSD, respectively. A recent multi-institution review of 631 patients with D-TGA and 167 patients with D-TGA and VSD revealed similar initial and long-term (15 years) outcomes. Freedom from adverse cardiovascular events has recently been shown to be 93% at 25 years.

The overwhelming majority (90% to 97%) of patients have normal-sized, patent coronary arteries as assessed by coronary angiography. A recent study of a large cohort demonstrated that survival without coronary events (death from myocardial infarction, sudden death, and reoperation for coronary stenoses) is 92.7% at 1 year and 88.2% at 15 years. The incidence of coronary events is bimodal with a high early and low late event rate. Eighty-nine percent of all coronary events occurred in the first 3 months after ASO. The event rate did not increase again until 6 years after ASO. Two types of coronary anatomy (a single coronary artery origin or two coronaries originating close to each other at a facing commissure) were risk factors for a coronary event.

One of the potential advantages of the ASO over the atrial switch procedure is the use of the native LV as the systemic ventricle. Long-term follow-up indicates that patients who have undergone an ASO have higher systemic ventricular ejection fractions than do patients who have undergone atrial switch procedures. In fact, patients who had D-TGA and intact IVS repaired in infancy and patients who had D-TGA and VSD repaired later have LV end diastolic dimensions and contractile indices similar to normal patients. Myocardial contractility in patients having undergone a rapid or traditional two-stage arterial switch is mildly depressed as compared to patients having undergone a primary arterial switch. No progression of this ventricular dysfunction has been noted at either intermediate or long-term follow-up.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357-380.

Khairy P, Clair M, Fernandes SM, et al. Cardiovascular outcomes after the arterial switch operation for D-transposition of the great arteries. *Circulation*. 2013;127:331-339.

Villafañe J, Lantin-Hermoso MR, Bhatt AB, et al. D-transposition of the great arteries: the current era of the arterial switch operation. *J Am Coll Cardiol*. 2014;64:498-511.

D.5. What are the long-term outcomes after Rastelli repair for D-TGA with left ventricular outflow tract (LVOT) obstruction?

Outcome following the Rastelli procedure for TGV with VSD and LVOT obstruction is good, with a near 100% early survival rate. A recent series reports survival to be 93% at 5, 10, and 20 years. The need for reintervention (either surgical or catheterization) increases over time. Intervention to relieve right ventricular outflow tract (RVOT) (RV to PA conduit) obstruction accounts for 75% of all interventions, with pacemaker insertion and relief of LVOT obstruction (aortic outflow)

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accounting for most of the remaining interventions. In an effort to reduce the need to reintervene for LVOT obstruction associated with the Rastelli procedure, some institutions are making greater use of the LeCompte and Nikaidoh procedures.

Brown JW, Ruzmetov M, Huynh D, et al. Rastelli operation for transposition of the great arteries with ventricular septal defect and pulmonary stenosis. *Ann Thorac Surg*. 2011;91:188-194.

Emani SM, Beroukhim R, Zurakowski D, et al. Outcomes after anatomic repair for d-transposition of the great arteries with left ventricular outflow tract obstruction. *Circulation*. 2009;120:S53-S58.

Hazekamp MG, Gomez AA, Koolbergen DR, et al. Surgery for transposition of the great arteries, ventricular septal defect and left ventricular outflow tract obstruction: European Congenital Heart Surgeons Association multicentre study. *Eur J Cardiothorac Surg*. 2010;38:699-706.

D.6. What is long-term neurologic outcome like after ASO?

The best assessment of neurologic outcome following ASO is data from the Boston Circulatory Arrest Trial. In this trial, infants undergoing ASO for D-TGA with IVS or VSD randomized 171 infants to a strategy of either DHCA or LFCPB using *α*-stat pH management. Infants in the DHCA group underwent an average of 52 minutes of DHCA, whereas those in the LFCPB group underwent 14 minutes of DHCA.

At age 8 years, parents of children in the trial reported more problems with attention, learning, speech, and the frequency of developmental delay than parents of children in a normative sample. Despite this, children in the cohort had overall physical and psychosocial health status similar to the general population. Furthermore, there was no association between physical and psychosocial scores and the presence or absence of a VSD or the use of LFCPB versus DHCA. Neurodevelopmental outcome in this cohort was generally not adversely affected unless the duration of DHCA exceeded 41 minutes. Beyond 41 minutes, there was a nonlinear (steadily worsening) outcome with increasing duration of DHCA.

Eight-year and 16-year data from the trial also demonstrated that neurologic status, IQ, academic achievement, memory, problem solving, and visual-motor integration did not differ between the DHCA and LFCPB groups. Nonetheless, DHCA was associated with greater functional deficiencies (motor function, speech apraxia, visual-motor tracking, phonic awareness) than LFCPB (impulsive behavior, worse behavior as rated by teachers).

Bellinger DC, Wypij D, duPlessis AJ, et al. Neurodevelopmental status at eight years in children with dextro-transposition of the great arteries: the Boston Circulatory Arrest Trial. *J Thorac Cardiovasc Surg*. 2003;126:1385-1396.

Bellinger DC, Wypij D, Rivkin MJ, et al. Adolescents with d-transposition of the great arteries corrected with the arterial switch procedure: neuropsychological assessment and structural brain imaging. *Circulation*. 2011;124:1361-1369.

Dunbar-Masterson C, Wypij D, Bellinger DC, et al. General health status of children with D-transposition of the great arteries after the arterial switch operation. *Circulation*. 2001;104:I138-I142.

Wypij D, Newburger JW, Rappaport LA, et al. The effect of duration of deep hypothermic circulatory arrest in infant heart surgery on late neurodevelopment: the Boston Circulatory Arrest Trial. *J Thorac Cardiovasc Surg*. 2003;126:1397-1403.

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Chapter 40
Pyloric Stenosis

Aarti Sharma

Vinod Malhotra

A 3-week-old first-born male infant had projectile vomiting, which contained the ingested formula but no bile. His body weight was 2.5 kg; serum electrolytes: K^+ 2.2 mEq per L, Cl^- 86 mEq per L; and blood pH 7.68. This infant was also noted to have a systolic murmur heard best at the second intercostal space along the left sternal border, which was assessed by a cardiologist and diagnosed as a ventricular septal defect (VSD).

A. Medical Disease and Differential Diagnosis

1. What is the diagnosis in this patient?
2. What is the differential diagnosis of pyloric stenosis?
3. What are the metabolic problems in this newborn secondary to his disease?
4. What are the adverse effects of metabolic alkalosis?
5. How would you treat this infant?
6. How would you determine fluid replacement in a newborn, and what fluids would you use?
7. How would you correct the metabolic alkalosis in this patient?
8. What causes a cardiac murmur?

B. Preoperative Evaluation and Preparation

1. How would you evaluate this patient preoperatively?
2. How would you evaluate a heart murmur?
3. How would you differentiate between functional versus organic murmur?
4. What are the types of VSD? What type of shunt do they cause?
5. What are the risks of surgery and anesthesia in a patient with VSD?
6. How would you prepare this patient rapidly for emergency surgery? Is surgical intervention an acute emergency in this case?
7. How would you prepare this patient for anesthesia?

C. Intraoperative Management

1. What induction-intubation sequence would you use?
2. What are the anatomic characteristics of the airway in the newborn and how do they differ from those in the adult?
3. How do you determine the size of an endotracheal tube in a pediatric patient?
4. What anesthesia system would you use and why?
5. What are the advantages and the disadvantages of commonly employed nonrebreathing systems?
6. How would you monitor this patient intraoperatively?

7. How does the pulse oximeter function?
8. What factors affect the measurement of oxygen saturation by the pulse oximeter?

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D. Postoperative Management

1. What are the complications that can occur in the postanesthesia recovery period?
2. How would you treat postextubation “croup” in this infant?

A. Medical Disease and Differential Diagnosis

A.1. What is the diagnosis in this patient?

The most likely diagnosis in this patient is pyloric stenosis. The factors that favor the diagnosis are as follows:

- Age—3 weeks (average age at onset; range 5 days to 5 months)
- Boy child (boy-to-girl ratio = 4:1)
- Projectile vomiting (characteristic)
- Contents—ingested formula, no bile

The resultant biochemical abnormality in this patient is a hypokalemic, hypochloremic, metabolic alkalosis.

Pyloric stenosis occurs in 3 of 1,000 infants born in the United States; its incidence may be increasing. It is more common in Whites of Northern European ancestry, less common in Blacks, and rare in Asians. Reduced nitric oxide in pyloric tissue may contribute to the pathogenesis of pyloric stenosis.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2015.

A.2. What is the differential diagnosis of pyloric stenosis?

Pyloric stenosis can be distinguished from other congenital anomalies that cause obstruction of the alimentary tract in the newborn. These other anomalies include chalasia of the esophagus, hiatus hernia, duodenal atresia, jejunal atresia, ileal atresia, pancreatic annulus, malrotation of the gut, intra-abdominal hernias, and Meckel's diverticulum. Pathognomonic features of pyloric stenosis include absence of bile staining of the vomitus and visible gastric peristaltic waves on abdominal examination along with the palpable pyloric mass. The diagnosis is commonly made clinically. An “olive” is sometimes palpated in the epigastrium just to the right of the midline. The diagnosis can be confirmed by abdominal ultrasound. Occasionally, an upper gastrointestinal (GI) series with barium may be necessary.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2015.

A.3. What are the metabolic problems in this newborn secondary to his disease?

Metabolic changes occur secondary to protracted vomiting and characteristically include a hypokalemic, hypochloremic alkalosis, as evident in this infant. Hyponatremia, although present, may not be manifested in serum value determinations because of severe dehydration. Compensatory respiratory acidosis is a frequent finding; it results from hypoventilation that may be marked and associated with periods of apnea. In severe dehydration leading to circulatory shock, the lack of adequate perfusion coupled with impaired renal and hepatic function may produce an entirely different picture of metabolic acidosis with hyperventilation, resulting in respiratory alkalosis. Therefore, depending on the severity and duration of vomiting and the type of fluid replenishment, one can encounter wide variations in arterial blood gas and electrolyte determinations. However, the most frequent findings are hypokalemia, hyponatremia, hypochloremia, and primary metabolic alkalosis with secondary respiratory acidosis. The renal response to vomiting is twofold. Initially, serum pH is maintained by the excretion of alkaline urine with sodium and potassium loss.

Then, after the depletion of these electrolytes, the kidneys secrete acidic urine (paradoxic acidosis), which exacerbates the metabolic alkalosis. These findings are summarized in Table 40.1.

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TABLE 40.1 Metabolic Findings in the Newborn Secondary to Pyloric Stenosis

	ARTERIAL BLOOD GASES				SERUM ELECTROLYTES			
SEVERITY OF DEHYDRATION	**pH**	**PCO_2**	**CO_2**	**PO_2**	**NA**	**K**	**CL**	**HCO_3**
Mild	↑	↑	↑	↔	↓↔	↓	↓↓	↑
Moderate	↑↑	↑↑	↑↑	↔	↓	↓↓	↓↓↓	↑↑
Severe	↓↓	↓	↓↓	↓	↓	↓↓	↓↓↓	↓↓

↔, no change; ↑/↓, slight change; ↑↑/↓↓, moderate change; ↑↑↑/↓↓↓, marked change.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:750-751.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2015.

A.4. What are the adverse effects of metabolic alkalosis?

- An increase in pH results in shifting of the oxygen-dissociation curve to the left, thereby binding more oxygen to the hemoglobin and unloading less oxygen at the tissue level. This phenomenon assumes even more importance in newborns because at 3 weeks they still have up to 70% fetal hemoglobin with an already low value of P50 (i.e., 20 to 22 mm Hg).
- Respiratory compensation is affected by hypoventilation with increased potential for atelectasis as well as periods of apnea
- Decrease in ionized calcium
- Increased potential for seizures

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2015.

A.5. How would you treat this infant?

Medical management of this infant with pyloric stenosis is acutely urgent. The principles of management can be grouped under the following three categories: supportive therapy, to stabilize the patient; diagnostic tests, to confirm the diagnosis and to monitor therapy; and surgery as the corrective therapy.

Supportive Therapy

- Circulatory support
- Correction of electrolyte imbalance
- Prevention of aspiration

Fluids

The infant with pyloric stenosis is hypovolemic and dehydrated secondary to persistent vomiting. Dehydration severity can

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vary from mild hypovolemia to circulatory shock. The following parameters are good indicators of dehydration severity:

- Physical appearance—skin turgor, parched mucous membranes, sunken fontanels, sunken eyeballs
- Blood pressure—decreased
- Pulse—increased
- Urine output—decreased
- Weight (birth and present) and weight loss

Quantitative assessment of these parameters gives a fair estimate of the amount of total body fluid depletion. A wide-bore intravenous cannula should be placed and an infusion started immediately to correct the deficits and provide maintenance fluids.

Electrolytes

The patient is alkalotic, hypokalemic, hypochloremic, and hyponatremic and must be provided with necessary ions to replenish the deficit. Albumin or Ringer's lactate may be used to treat the shock first. Next, the deficit should be corrected, 0.45% to 0.9% saline in 5% to 10% dextrose. Potassium (usually 40 mEq per L) must be added to this to correct hypokalemia and aid in the correction of alkalosis. However, potassium infusion should be withheld until satisfactory renal function is established. Fluid therapy should be continued until the infant is rehydrated and serum bicarbonate concentration is less than 30 mEq per dL, which implies that the alkalosis has been corrected.

Prevention of Aspiration

A nasogastric tube should be inserted to thoroughly empty the stomach, and the upper airway reflexes should be preserved.

Diagnostic Tests

- To assess the severity of fluid and electrolyte derangement and to monitor therapy, the following should be evaluated: complete blood count, serum electrolytes, blood gases, blood urea nitrogen (BUN), electrocardiogram (ECG) (for marked hypokalemia).
- To confirm the diagnosis: barium swallow, ultrasound imaging

Surgery

Pyloromyotomy is the definitive treatment for these infants. Ramstedt pyloromyotomy through a right upper quadrant transverse incision has been the traditional treatment for hypertrophic pyloric stenosis. Recently, laparoscopic and circumumbilical approaches have been introduced as alternative methods to improve cosmesis, but concerns about greater operative times, costs, and complications remain. Surgery should be carried out early but only after the patient has been stabilized satisfactorily.

Blatnik JA, Ponsky TA. Advances in minimally invasive surgery in pediatrics. *Curr Gastroenterol Rep*. 2010;12(3):211-214.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2015.

A.6. How would you determine fluid replacement in a newborn, and what fluids would you use?

The general principles of fluid therapy are based on fluid maintenance, correction of deficits, and replacement of losses.

Maintenance Fluids

In the newborn, maintenance fluids are as follows:

- First 48 hours of life—75 mL/kg/day or 3 mL/kg/hr

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- 2 days to 1 month—150 mL/kg/day or 6 mL/kg/hr
- 1 month onward (up to 10 kg)—100 mL/kg/day or 4 mL/kg/hr

Estimation of the degree of dehydration in a newborn is shown in Table 40.2.

The maintenance fluids take into account the fluid losses occurring normally through the kidney, bowel, skin, and lungs. At birth, the kidney is still undergoing maturation, and what may be called “a glomerular imbalance” exists. What it implies is that some mature glomeruli may be connected to the immature tubules and vice versa. Hence, the kidney is functionally limited at birth but undergoes rapid maturation during the first week of life.

Electrolytes

The newborn is an obligate sodium loser as well as a poor tolerator of excessive sodium overload. The maintenance electrolytes are as follows:

- Sodium—3 to 5 mEq/kg/day
- Potassium—2 to 3 mEq/kg/day
- Chloride—1 to 3 mEq/kg/day

TABLE 40.2 Estimation of the Degree of Dehydration in a Newborn

	MILD	MODERATE	SEVERE
Percent fluid loss	5	10	15-20
Skin turgor	Poor	Very poor	Parched
Mucous membrane and tongue	Dry	Dry	Parched
Fontanel and eyes	Normal	Sunken fontanel	Sunken eyes
Urine	Concentrated oliguria	Oliguria	Oliguria, anuria
Pulse	Normal	Tachycardia	Marked tachycardia
Blood pressure	Normal	Hypotension	Marked hypotension, shock

Correction of Deficits

Deficits take into account the previous unreplaced losses because of a period of no intake by mouth and dehydration resulting from increased losses (e.g., from vomiting, diarrhea, and increased body temperature). The amount of deficit can be assessed by physical examination (see Table 40.2), body weight loss, and hematocrit.

Replacement of Losses

Replacing losses covers ongoing abnormal losses not covered by maintenance fluids. Intraoperatively, it covers evaporative losses from the operative site, third spacing, and losses from the lungs if dry gases are used in nonrebreathing circuits (Table 40.3).

The younger and more physically immature the patient, the higher the skin permeability, the ratio of body surface area to weight, and the metabolic demand. In addition, the use of radiant warmers and phototherapy increases insensible water loss.

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Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2782-2784.

A.7. How would you correct the metabolic alkalosis in this patient?

To correct the metabolic alkalosis in this patient, the underlying electrolyte derangements (hyponatremia, hypokalemia, and hypochloremia) must be corrected. We correct the deficits by using calculated volumes of 5% dextrose in normal saline or Ringer's lactate solution, which helps to restore sodium and chloride mainly. Dextrose, 5%, with one-fourth strength normal saline may be used to provide maintenance fluids. Once renal function is established, potassium supplements are added to the infusion. Depending on the deficit, this therapy can require anywhere from 12 to 72 hours. In severely alkalotic patients, HCl (hydrochloric acid) and NH_4Cl (ammonium chloride) have been used to correct the derangement. However, we have rarely found it necessary.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1210-1211.

TABLE 40.3 Fluid Requirement to Replace Intraoperative Fluid Losses (Except Blood Loss) in the Newborn

	FLUID REPLACEMENT (mL/kg/hr)
Minor surgery (e.g., herniorrhaphy)	1-3
Moderate surgery (e.g., pyloromyotomy)	3-5
Major surgery (e.g., intestinal)	5-7
Respiratory water loss due to dry gases	2

A.8. What causes a cardiac murmur?

Cardiac murmurs are caused by turbulent blood flow across cardiac valves or septal defects and are audible sound waves in the range of 20 to 2,000 Hz. Most murmurs in pediatric patients are normal or innocent, occurring in almost 50% of all school-aged children but must be distinguished from those murmurs associated with significant structural heart disease. Auscultation is critically important in diagnosing these murmurs; however, echocardiography remains the gold standard.

Allen HD, Driscoll DJ, Shaddy RE, et al, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adult*. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:89-91.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate this patient preoperatively?

The following information is necessary in evaluating this patient:

History

Onset of illness, frequency and amount of vomiting, last feeding, diarrhea, urine output, activity of the newborn (active or lethargic), and birth weight

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Physical Examination

Present body weight (to determine the weight loss), temperature, signs of dehydration (skin turgor, mucous membranes, fontanels, eyeballs, blood pressure, pulse, color, and volume of urine), muscle tone, and level of consciousness

Laboratory Findings

Complete blood count, electrolytes, BUN and blood sugar, urinalysis, and arterial blood gases

Based on the data available, we can determine the fluid and electrolyte status of the patient and correct these accordingly to stabilize the patient for surgery and anesthesia.

B.2. How would you evaluate a heart murmur?

Heart murmurs can be innocent or organic. By definition, innocent murmurs occur in the absence of structural or physiologic cardiac disease. The clinical diagnosis of a normal or innocent murmur should occur in the setting of an otherwise normal history, physical examination, and appearance. The presence of a family history of hypertrophic cardiomyopathy, congenital cardiac disease, or unexplained infant, childhood, or early adult death is particularly worrisome. The perinatal history of prematurity, maternal diabetes, drug or toxin ingestion, fetal distress, or clearly definable chromosomal disorders have particular cardiorespiratory relevance. The initial approach to the evaluation of the cardiovascular system should include an assessment of the cardiorespiratory system functionality as a pump and delivery system. An index of exercise or play capacity should be sought as a component of assessing growth and development. We would ask about exercise tolerance, shortness of breath, cyanotic episodes, growth (because congestive heart failure may manifest as failure to thrive), and symptoms of congestive heart failure.

Allen HD, Driscoll DJ, Shaddy RE, et al, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adult*. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:89-91.

B.3. How would you differentiate between functional versus organic murmur?

Normal murmurs of childhood are composed of five systolic and two continuous types but never solely diastolic (Table 40.4). A functional murmur is usually soft, 1/6 or 2/6 and never associated with palpable thrill. Pathologic murmurs are usually louder, 3/6 or greater and are associated with other cardiovascular pathologic features.

Park MK. *Park's Pediatric Cardiology for Practitioners*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2014:36-39.

TABLE 40.4 Innocent Murmurs of Childhood

SYSTOLIC MURMURS	CONTINUOUS MURMURS
Vibratory Still's murmur	Venous hum
Pulmonary flow murmur	Mammary arterial souffle
Peripheral pulmonary artery stenosis murmur	
Supraclavicular systolic murmur	
Aortic systolic murmur	

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B.4. What are the types of VSD? What type of shunt do they cause?

One common classification of VSD is based on anatomic location.

- Type I defects, or supracristal defects (5% of all VSDs), are outflow defects located above the crista supraventricularis just under the annulus of aorta.
- Type II defects, or infracristal defects (80% of all VSDs), are lower in membranous septum beneath the crista supraventricularis.
- Type III defects, or canal type (11% incidence), are inlet VSDs that accompany complete atrioventricular (AV) canal defects. They result from failure of the endocardial cushions to fuse.
- Type IV, or muscular, defects (2% to 7% incidence), probably results from excessive resorption of septal tissue during the muscular septal formation. They may be located anywhere in the muscular septum and may be multiple (also known as the Swiss cheese defect).

VSD is left-to-right shunt. Pathophysiologic effects of VSD include left-to-right shunting, pulmonary hypertension, and heart failure resulting from volume overload.

Allen HD, Driscoll DJ, Shaddy RE, et al, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adult*. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1471-1472.

B.5. What are the risks of surgery and anesthesia in a patient with VSD?

Infective endocarditis is a complication of most congenital cardiac anomalies, so the patient requires antibiotic prophylaxis. There is also risk of increasing the flow in the shunt or reversing the flow in the shunt, resulting from acute and persistent increases in systemic vascular resistance or decreases in pulmonary vascular resistance causing hypoxemia and congestive heart failure. Right ventricular infundibular hypertrophy may be present in the patients with a VSD. Normally, this is a beneficial change, because it increases the resistance to right ventricular ejection, leading to decrease in magnitude of the left-to-right shunt. Nevertheless, perioperative events that exaggerate this obstruction to right ventricular outflow, such as increased myocardial contractility or hypovolemia, must be minimized. Therefore, these patients are often anesthetized with a volatile anesthetic. In addition, intravascular fluid volume should be maintained by prompt replacement of blood loss. During the anesthetic, a normal end-tidal carbon dioxide should be maintained and routine air bubble precautions should be taken.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:51-52.

B.6. How would you prepare this patient rapidly for emergency surgery? Is surgical intervention an acute emergency in this case?

Hypertrophic pyloric stenosis is a medical emergency and not a surgical emergency. Therefore, no newborn should be subjected to the additional hazards of anesthesia and surgery until stabilized medically.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics* . 20th ed. Philadelphia, PA: Elsevier Saunders; 2015.

B.7. How would you prepare this patient for anesthesia?

Fluid and electrolyte replacement should be accomplished satisfactorily—this may take anywhere from 12 to 72 hours depending on the patient's status. The next step is to empty the stomach through a wide-bore nasogastric tube, lavaging out the gastric contents and any left-over barium. Alternatively, an oral-gastric approach allows for passage of a tube with wider lumen that ensures better stomach emptying. Premedication is usually atropine (0.01 to 0.02 mg per kg) intravenous or intramuscular if the patient does not have intravenous line.

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Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:750-751.

C. Intraoperative Management

C.1. What induction-intubation sequence would you use?

These children should arrive to the operating room with an intravenous access. Standard monitors are placed. The stomach is emptied by inserting an orogastric tube (atropine may be used as premedication) to reduce the chance of regurgitation during induction. Because the stomach may not be completely emptied, a rapid sequence induction and intubation with cricoid pressure is highly recommended to minimize the risk of aspiration. Awake intubation may be accomplished in skillful hands in a lethargic neonate or in a critically sick infant. In most cases, however, neonates presenting for this procedure are fit and do not require awake intubation, which can be more traumatic.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:750-751.

Jöhr M. Anesthesia for the child with full stomach. *Curr Opin Anaesthesiol*. 2007;20(3):201-203.

C.2. What are the anatomic characteristics of the airway in the newborn and how do they differ from those in the adult?

The special characteristics of the upper airway in the newborn are as follows:

- Nasopharynx—narrow nasal passages, obligate nasal breathers
- Oropharynx—large tongue, long and pendulous epiglottis
- Larynx—the distinctive features shown in Table 40.5

It is apparent, therefore, that the newborn who has low respiratory reserve can develop airway obstruction easily. The infant may present problems during intubation and tolerate airway trauma poorly.

Comparative anatomy of the larynx and trachea in the newborn and the adult is shown in Table 40.5.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:365-394.

TABLE 40.5 Comparative Anatomy of the Larynx and Trachea in the Newborn and the Adult

ANATOMIC FEATURES	NEWBORN	ADULT
Size	4 cm	10-13 cm
Shape	Funnel	Cylindrical
Position of the glottis	C3-C4	C6
Narrowest point	1 cm below vocal cords	At vocal cords
Vocal cords	Slanting anteriorly	Transverse or slightly

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		Slanting posteriorly
Mucous membrane	Loose (swells easily)	More firmly bound

C.3. How do you determine the size of an endotracheal tube in a pediatric patient?

The two parameters of endotracheal tube sizes are the tube length and diameter, depending on the age of the child, as shown in Table 40.6. However, these are approximate sizes and one must have one size bigger and one size smaller tube available when selecting any size tube. A simple way to remember these numbers is to know the sizes at newborn, 6 months, and 1 year. Between 2 and 12 years, the following guide may be used:

- Tube length from tip to incisor teeth (cm) = 11 + age in years
- Tube internal diameter (mm) = 4 + age / 4
- French size (French) = 18 + age
- External circumference (French) = ID (mm) × 4 + 2

(French size means external circumference in millimeters, which equals π times external diameter; $\pi = 3.1416$)

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:365-394.

C.4. What anesthesia system would you use and why?

We employ the circle system with a light circuit. The circle system is more advantageous because it maintains heat and humidification better and offers the freedom of choosing varying gas flows. The controversy about the increased resistance in the adult system is discounted by the fact that the respiration is assisted or controlled intraoperatively. Newer anesthesia machines use valves with much less resistance than older models. Dead space in these systems is no more than that of the Mapleson circuits.

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment.* 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:209-218.

C.5. What are the advantages and the disadvantages of commonly employed nonrebreathing systems?

Commonly used nonrebreathing systems include Bain Breathing circuit (Mapleson D system) and Jackson-Rees modification of Ayre's T-piece. They offer the following advantages and disadvantages:

Advantages

- Minimal dead space
- No valves, low resistance
- Lightweight
- Reservoir bag to assist ventilation
- Good appreciation of patient's respiratory exchange

TABLE 40.6 Endotracheal Tube Size for Pediatric Patient

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AGE	LENGTH	INTERNAL DIAMETER (mm)	FRENCH SIZES
Newborn	10	3.0	14
6 mo	12	3.5	16
1 y	14	4.0	18
2 y	15	4.5	20
4 y	16	5.0	22
6 y	17	5.5	24
8 y	18	6.0	26
10 y	19	6.5	28
12 y	20	7.0	30

Disadvantages

- High flow of fresh gases required
- Low flows may allow rebreathing of gases without CO_2 absorption
- Loss of heat and humidity because of high flow of cold, dry gases (Bain's circuit allows some heating of inspired gases by surrounding fresh gas flow tubing with expired gas tubing)
- Scavenging problems of waste gases

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment.* 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:191-208.

C.6. How would you monitor this patient intraoperatively?

Monitoring should include blood pressure, ECG, rectal temperature, precordial stethoscope, pulse oximeter, and an end-tidal CO_2 monitor.

C.7. How does the pulse oximeter function?

The commonly used pulse oximeter (Nellcor pulse oximeter Model 100) combines the scientific principles of spectrophotometric oximetry and plethysmography. Light of two wavelengths, 660 nm (red) and 925 nm (infrared), is emitted by a pair of light-emitting diodes (LED) and is passed through the tissue being measured to a photodetector. Because the saturated hemoglobin absorbs more blue light than unsaturated hemoglobin, the absorption of light for each color is an indication of the ratio of oxygen saturated blood to unsaturated blood. The pulsating vascular bed, by expanding and relaxing, creates a change in light-path length that modifies the amount of light detected. The microprocessor-controlled circuitry in the unit senses the pulsatile waveform, which is solely produced by the arterial blood, thereby allowing measurement of pulse rate and arterial saturation. The oximeter is reliably accurate in 50% to 100% saturation range.

Nellcor Pulse Oximeter Model N-100, Instruction Manual. Hayward, CA: Nellcor Inc; 1984.

Tremper KK, Barker SJ. Pulse oximetry. *Anesthesiology*. 1989;70:98-108.

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C.8. What factors affect the measurement of oxygen saturation by the pulse oximeter?

Dysfunctional hemoglobin, as with carboxyhemoglobin, sulfhemoglobin, and methemoglobin, can affect the accuracy of the oximeter. Intravascular dyes such as indocyanine green and methylene blue can also interfere with the accuracy of the instrument. Skin color, tissue thickness, venous blood, light intensity, and ambient light do not affect the accuracy of the instrument because they do not pulse.

Nellcor Pulse Oximeter Model N-100, Instruction Manual. Hayward, CA: Nellcor Inc; 1984.

Tremper KK, Barker SJ. Pulse oximetry. *Anesthesiology*. 1989;70:98-108.

D. Postoperative Management

D.1. What are the complications that can occur in the postanesthesia recovery period?

The patient should be carefully observed for signs of respiratory depression and periods of apnea secondary to combination of metabolic alkalosis, general anesthesia, and decreased body temperature. However, these infants do not appear to be at increased risk of postoperative apnea. Hypoventilation predisposes to atelectasis. Patient should be awake and responsive to avoid aspiration. Severe hypoglycemia resulting from depletion of liver glycogen stores has been reported 2 to 3 hours after surgery. Postextubation “croup” is a potentially dangerous complication in this age group.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:1282-1288.

D.2. How would you treat postextubation “croup” in this infant?

Treatment of the potentially catastrophic postextubation laryngeal edema should be immediate, vigorous, and carried out under direct observation of the anesthesiologists. It consists of the following:

- Increasing inspired oxygen concentration (50% to 60%)
- Humidification of inspired gases
- Adequate hydration using parenteral fluids
- Light sedation to calm the patient and allow for cooperation in therapy
- Avoidance of any significant respiratory depression
- Epinephrine through handheld nebulizer and mask, 50 μg/kg/min of active isomer
  - Racemic epinephrine (2.25%) 0.05 mL per kg diluted in 5-mL saline solution delivered in 10 minutes

Treatment should be given over 10 minutes and may be repeated every 30 minutes, as necessary. Rebound phenomenon may be expected approximately 2 hours after cessation of this therapy.

- Steroids—dexamethasone, 0.5 to 1 mg per kg IV
- Reintubation—if signs of deterioration or hypoxia appear
- Tracheostomy, if necessary—rarely, subglottic edema may be so rapid and so severe that tracheostomy is the only choice

The age group most likely to manifest this complication is 1 to 4 years. Infants younger than 1 year are at most risk, mainly because of the size of their airway. Fortunately, an infant of this age is most amenable to early and vigorous intervention and should always be treated as an emergency requiring the continued presence of and evaluation by a physician who is adept at securing an airway for the child.

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Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:365-394.

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Chapter 41

Inflammatory Airway Disease in Childhood: Laryngotracheobronchitis

Miles Dinner

Michelle Carley

A 3-year-old boy was brought to the emergency room because of respiratory distress. He was noted to have stridor with substernal retractions and excessive drooling. He complained of a sore throat and had a fever of 39.5°C (103.1°F).

A. Medical Disease and Differential Diagnosis

1. What portion of the airway is affected in the croup syndrome and why?
2. What is stridor?
3. How does stridor correlate with anatomic location?
4. Define croup. What is the clinical presentation of laryngotracheitis?
5. What is the differential diagnosis of acute upper airway obstruction in children?
6. What is bacterial tracheitis?
7. What congenital problems can mimic features of croup?
8. How is the severity of croup assessed?
9. What is the medical management of croup? Does this have implications for the anesthesiologist?
10. What is epiglottitis? What are its common causes? What is the incidence?
11. What are the clinical manifestations of epiglottitis?
12. How is the diagnosis of epiglottitis made?
13. What is postextubation croup? How is it managed?
14. What are the nonacute causes of partial airway obstruction in children?

B. Preoperative Evaluation and Preparation

1. Is intubation always required in children with epiglottitis?
2. Why is general anesthesia administered to a child with epiglottitis?
3. How would you prepare the patient for anesthesia?

C. Intraoperative Management

1. How is the airway of the child with epiglottitis best secured?
2. How would you induce anesthesia?
3. Should a child with epiglottitis undergo a rapid sequence induction?
4. Is awake intubation a practical alternative to secure the patient's airway?
5. What would you do if the airway cannot be secured with intubation?
6. Should this patient have a nasotracheal or orotracheal tube placed?
7. Shortly after intubation, frothy secretions were obtained on suctioning the endotracheal tube. What is the reason for this? How can this be treated?

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D. Postoperative Management

1. How long should this patient remain intubated? What criteria determine extubation time?
2. How would you make this patient comfortable during the course of intubation?
3. What outcome can one expect for the child with acute epiglottitis?

A. Medical Disease and Differential Diagnosis

A.1. What portion of the airway is affected in the croup syndrome and why?

The subglottis is typically involved in infants and children presenting with classic croup. The *subglottis* is defined as the segment of the upper airway directly below the vocal cords fusing with the upper trachea. It contains pseudostratified columnar respiratory epithelium, which is loosely adherent and prone to swelling. Because this area is fully cartilagenized in childhood, it lacks the ability to expand and thus can produce early symptoms due to even small degrees of inflammation.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's a Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:653-682.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2473, 2890-2891.

Sobol SE, Zapata S. Epiglottitis and croup. *Otolaryngol Clin North Am*. 2008;41:551-566.

A.2. What is stridor?

Stridor is the high-pitched adventitious sound produced in the respiratory cycle by the turbulent flow of respiratory gases through a segmental narrowing in the airway. It can be biphasic, inspiratory, or expiratory, depending on the anatomic location.

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Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2473, 2890-2891.

A.3. How does stridor correlate with anatomic location?

Inspiratory stridor is characteristic of laryngeal or supraglottic obstruction. Such conditions as laryngeal papillomatosis, laryngeal web, laryngomalacia, and vocal cord paresis produce inspiratory stridor. Expiratory stridor is usually typical of intrathoracic processes such as extrinsic tracheal compression by a vascular ring or mass, tracheomalacia, or bronchotracheitis. Biphasic stridor is indicative of lesions or infections involving both the larynx and subglottis such as the croup syndrome, subglottic stenosis, or intralaryngeal masses.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's a Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:653-682.

A.4. Define croup. What is the clinical presentation of laryngotracheitis?

Croup is a generalized term referring to infections of the upper respiratory tract with a characteristic cough, inspiratory stridor, and possible respiratory distress. Other terms, namely, *laryngotracheobronchitis*, *spasmodic croup*, and *bacterial tracheitis*, are interwoven within the croup syndrome but have specialized meanings. For instance, spasmodic croup

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suggests a noninfectious inflammatory process as opposed to the viral etiology of laryngotracheobronchitis. Most cases occur during the colder months. There is a 1:1 male-to-female prevalence. Also known as *laryngotracheobronchitis* because of the structures involved, croup is caused by a number of viruses, including human rhinovirus; *Haemophilus parainfluenzae* virus type 1, 2, and 3; respiratory syncytial virus; influenza virus; or human corona virus. It commonly affects children between 6 months and 3 years of age, with a median age of 18 months. It manifests subacutely as an exacerbation of cold symptoms with low fever, barking cough, noisy breathing, and hoarseness. Exudative inflammation of the upper airway may cause

dyspnea and in extreme cases can lead to exhaustion and frank hypoxia. In most cases, it is self-limited and benign.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's a Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:653-682.

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van der Hoek L, Sure K, Ihorst G, et al. Human coronavirus NL63 infection is associated with croup. *Adv Exp Med Biol*. 2006;581:485-491.

A.5. What is the differential diagnosis of acute upper airway obstruction in children?

A full differential for this condition involves a host of infectious causes. Among the most important are bacterial tracheitis, diphtheria, retropharyngeal abscess, peritonsillar abscess, measles, and Epstein-Barr viral infection. Other causes to be considered are thermal burns, foreign body aspiration, laryngeal fractures, angioneurotic edema, vocal cord paralysis, and uvulitis.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's a Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:653-682.

Mandal A, Kabra SK, Lodha R. Upper airway obstruction in children. *Indian J Pediatr*. 2015;82(8):737-744.

Wald EL. Croup: common syndromes and therapy. *Pediatr Ann*. 2010;39:15-21.

A.6. What is bacterial tracheitis?

This is a severe and potentially fatal disease of an infectious nature occurring as a consequence of infection with *Staphylococcus aureus*, various streptococcal species, and *Haemophilus influenzae*. It occurs in colder weather in young children as a secondary complication of viral laryngotracheitis. Although presenting the same symptoms as epiglottitis, it tends not to evolve as rapidly and generally does not have odynophagia and drooling, two characteristic signs of epiglottitis. Most of these children require intubation for thick and difficult-to-clear secretions, and during endoscopy, subglottic edema with mucosal ulceration is seen.

Mandal A, Kabra SK, Lodha R. Upper airway obstruction in children. *Indian J Pediatr*. 2015;82(8):737-744.

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Wald EL. Croup: common syndromes and therapy. *Pediatr Ann*. 2010;39:15-21.

A.7. What congenital problems can mimic features of croup?

A host of anatomic problems can share similar signs and symptoms with the infectious agents causing airway compromise. It is only by the absence of fever and the chronicity of the situation that these are distinguishable. Vocal cord paralysis, laryngeal webs, laryngomalacia, subglottic masses (hemangiomas), and stenosis as well as vascular anomalies are to be included.

Johnson DW. Croup [published online ahead of print September 29, 2014]. *BMJ Clin Evid*.

Wald EL. Croup: common syndromes and therapy. *Pediatr Ann*. 2010;39:15-21.

A.8. How is the severity of croup assessed?

One evaluates the following parameters in assessing severity of the illness: (1) Work of breathing: Is there tachypnea and/or retractions? (2) Chest wall motion: Is the tidal volume adequate with inspiration? (3) Overall appearance: Is the child cyanotic, obtunded, or comfortable? (4) Vocal quality: Is there stridor, diminished voice, or cry? Severe croup unresponsive to the medical therapy may require tracheal intubation. Once the diagnosis of croup has been established, the child is given a croup score, which helps determine therapy (Table 41.1).

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Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's a Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:653-682.

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Westley CR, Cotton EK, Brooks JG. Nebulized racemic epinephrine by IPPB for the treatment of croup: a double-blind study. *Am J Dis Child*. 1978;132:484-487.

TABLE 41.1 The Westley Croup Score

	0	1	2	3	4	5
Cyanosis	None	—	—	—	With agitation	At rest
Level of consciousness	Normal, including sleep	—	—	—	—	Disoriented
Stridor	None	With agitation	At rest	—	—	—
Air entry	Normal	Decreased	Markedly decreased	—	—	—

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Retractions	None	Mild	Moderate	Severe	—	—

Mild croup has a score <2, moderate is between 3 and 7, and severe has a score >8.

A.9. What is the medical management of croup? Does this have implications for the anesthesiologist?

Mild croup is treated with inspired gas humidification, hydration, and oxygen to improve the attendant hypoxemia. Croup tents, croupettes, and blow-by oxygen are helpful. Steroids and racemic epinephrine are the prime modalities of therapy. If the patient has moderate retractions and appears dyspneic, 0.5 mL of a 2.25% racemic epinephrine solution in 2.5 mL of normal saline can be administered via nebulizer.

Airway resistance can be high with the reactive transudation and intraluminal narrowing. By vasoconstricting the arterioles of the mucosal vasculature, racemic epinephrine relieves edema. Racemic epinephrine is a 1:1 mixture of the levo (L) and dextro (D) isomers to limit cardiac stimulation because only the L form is an active component. Patients improve markedly within 30 minutes, but the clinician should be cautioned that the relief may only last a few hours, although patients tend not to be in worse condition when it wears off. The *Beta* 2 activity will cause bronchial smooth muscle relaxation. Avoid racemic epinephrine in children with glaucoma and ventricular outflow obstruction.

Dexamethasone and budesonide when given early in viral croup can be beneficial in reducing inflammation and alleviating symptoms. This takes time to work, however, requiring hours for effective onset. The pediatric dose of dexamethasone is 0.6 mg per kg orally or intramuscularly. Clinical evaluation of topical steroids such as budesonide has shown effective improvement, especially with laryngeal edema. Nebulized budesonide has been shown to be as effective as dexamethasone in treatment. The role of heliox (helium-oxygen mixture) has yet to be defined but may be helpful in severe croup.

Bjornson C, Russell K, Vandermeer B, et al. Nebulized epinephrine for croup in children. *Cochrane Database Syst Rev*. 2013;(10):CD006619.

Eboriadov M, Chryssanthopoulou D, Stamodis P, et al. The effectiveness of local corticosteroid therapy in the management of mild to moderate croup. *Minerva Pediatr*. 2010;62:23-28.

Kliegman RM, Stanton BF, St Geme J, et al, eds. *Nelson Textbook of Pediatrics* . 19th ed. Philadelphia, PA: WB Saunders; 2011:1445-1450.

Terregino CA, Nairn SJ, Chansky ME, et al. The effect of heliox on croup: a pilot study. *Acad Emerg Med*. 1998;5:1130-1133.

A.10. What is epiglottitis? What are its common causes? What is the incidence?

Epiglottitis is an inflammation of the epiglottis usually secondary to an infectious process. It can involve other supraglottic structures such as the arytenoid, false cords, and posterior tongue leading to obstruction of the airway. Progression of swelling can rapidly lead to complete airway occlusion and death. Table 41.2 contrasts epiglottitis with croup. Epiglottitis is most often bacterial in origin. The causative agent used to be *H. influenzae* type B. The vaccine has resulted in a remarkable decline, although epiglottis may still occur even in vaccinated individuals. *Streptococcus pneumoniae* also has been infrequently associated with epiglottitis, and recently, group A *β*-hemolytic streptococci have been on the increase.

Burn injury, neoplastic infiltration, caustic ingestion, lymphoproliferative disease, and angioneurotic edema are other causes. The incidence has declined to 1.8 per 10,000 admissions at The Children's Hospital of Philadelphia after the *H. influenzae* type B vaccine. In one study, five cases of epiglottitis occurred among children who had been immunized.

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TABLE 41.2 Characteristics of Croup and Epiglottitis

	CROUP	EPIGLOTTITIS
Etiology	Parainfluenza virus	*Haemophilus influenzae*
Age	4 months to 2 years	2-5 years
Onset	Subacute exacerbation of preexistent URI	Acute
Temperature	Low-grade fever	High fever
Course	Usually mild, stridor may worsen at night	Rapid progress of symptoms
Symptoms	Barky cough, stridor	Dysphagia, sore throat Dysphonia, respiratory distress

URI, upper respiratory infection.

A recent retrospective review reaffirms that epiglottitis remains a significant problem in the United States, with nearly 4,000 admissions in 2006. The demographics of the disease have shifted away from that of predominantly pediatric nature to one of adulthood. The mean age in the study period from 1998 to 2006 surprisingly was 45 years old, and the mortality was 36%.

D'Agostino J. Pediatric airway nightmares. *Emerg Med Clin North Am*. 2010;28:119-126.

Shah RK, Roberson DW, Jones DT. Epiglottitis in the *Hemophilus influenzae* type B vaccine era: changing trends. *Laryngoscope*. 2004;114:557-560.

Shah RK, Stocks C. Epiglottitis in the United States: national trends, variances, prognosis, and management. *Laryngoscope*. 2010;120:1256-1262.

A.11. What are the clinical manifestations of epiglottitis?

This illness presents acutely in the otherwise healthy child between 2 and 5 years of age with fever as high as 40°C. Within a few hours, the epiglottic inflammation progresses and the child becomes dyspneic. The child sits forward to use the accessory muscles of respiration and complains of a fullness and pain in the throat. Speech sounds are muffled, known as a “hot potato voice.” Salivation often is characteristic and swallowing is difficult. The child appears anxious and concentrates only on breathing. The barking cough of croup usually is absent. The older child will assume a tripod posture with the neck extended to maximize air entry. As the child fatigues, cyanosis leading to complete asphyxia may ensue without intervention. Inspiratory effort is maximal with severe airway compromise, and thoracoabdominal asynchrony, otherwise known as paradoxical breathing, may be observed in the supine position; the abdomen protrudes and the chest wall retracts due to upper airway obstruction. Negative pressure pulmonary edema can occur. Chest auscultation may reveal decreased breath sounds.

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Kliegman RM, Stanton BF, St Geme J, et al, eds. *Nelson Textbook of Pediatrics* . 19th ed. Philadelphia, PA: WB

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Saunders; 2011:1445-1450.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1561.

A.12. How is the diagnosis of epiglottitis made?

Acute epiglottitis is a dire emergency and any child whose clinical presentation warrants the diagnosis of epiglottitis must be evaluated promptly in a hospital.

Although epiglottitis and croup have similar features, the presence of drooling and absence of coughing are sensitive and specific signs of epiglottitis, whereas the absence of drooling and the presence of coughing are sensitive and specific signs of croup.

Pharyngoscopy to visualize an inflamed epiglottis should not be attempted in an office setting because this can stimulate upper airway reflexes and lead to increasing dyspnea. All medical centers should have in place a management protocol that standardizes the approach to this rapidly progressive and fatal disease and that involves a team of physicians and nurses from the specialties of pediatrics, otolaryngology, and anesthesiology. A logical approach is as follows:

- The child is kept calm with a parent in attendance at all times. Supplementary oxygen, maintenance of a sitting position, and reassurance are essential.
- If the patient clinically conforms to a classical presentation of epiglottitis, the operating room is alerted and the child is taken there immediately for intubation.
- With other diagnostic considerations, such as a foreign body in the upper airway, retropharyngeal abscess, congenital anomalies, and croup, the child may be escorted to radiology. The time taken for the x-ray examination obviously should be avoided in the critically ill child. A physician skilled in airway management should accompany the child with all necessary resuscitation equipment available.
- The classic thumb sign on a lateral x-ray film is an aptly named shape seen with epiglottic enlargement. However, the absence of this sign does not eliminate the diagnosis of epiglottitis. Croup is distinguished by the steeple sign representing a uniform narrowing of the subglottic airway by inflammation. Recently, magnetic resonance imaging has demonstrated the standard measurements for the hypopharyngeal space in various age groups, and it has correlated this measurement with the change produced by epiglottic inflammation. This may be a useful tool in the future to assess the severity of airway involvement.
- Laboratory evidence is nonspecific, although a high white count with bands and polymorphonuclear leukocytes is more suggestive of epiglottitis than of croup.
- Fiberoptic pharyngoscopy can be most effective if performed gently by a skilled examiner; it immediately confirms or eliminates the diagnosis. Do not perform a laryngoscopy if anxiety is increased by the procedure and hence exacerbates airway obstruction.

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Tibballs J, Watson T. Symptoms and signs differentiating croup and epiglottitis. *J Paediatr Child Health*. 2011;47:77-82.

A.13. What is postextubation croup? How is it managed?

Anesthesiologists are often in the position of treating patients with postextubation airway edema, which resembles croup in its symptomatology.

Pediatric patients undergoing general endotracheal anesthesia may mimic many of the physical signs of the croup

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syndrome following extubation. The tracheal and subglottic mucosa have become irritated by the plastic tube, which initiates an inflammatory response, causing airway luminal narrowing. Because airway resistance is inversely proportional to the fourth power of the tracheal radius (with turbulent flow, this increases to the fifth power), the pediatric airway is especially compromised by edema. Halving the lumen will increase laminar airflow resistance 16 times.

Postextubation croup may manifest more frequently in a patient who has received large quantities of fluid or transfusions; maintained unusual or strained lateral head positioning; has a history of smoke inhalation, restrictive congenital anomalies such as a tracheoesophageal fistula, or acquired subglottic stenosis secondary to prolonged intubation as a neonate; has a coexistent upper respiratory infection, especially bronchitis; or has a cuffed or uncured endotracheal tube with a high (>25 cm H_2O) leak pressure. The air leak test, which gauges the pressure needed to generate an audible leak in the presence of an endotracheal tube, may be predictive of postextubation stridor in children over 7 years of age. Ensuring an adequate air leak may decrease the risk of postextubation croup.

Management involves reducing airway constriction by administering nebulized racemic epinephrine, steroids, and humidification of inspired gases. On occasion, reintubating with a soft endotracheal tube one-half to one size smaller than previously used is necessary until the inflammation subsides. Note that topical lidocaine ointment can have vasodilatory actions and should not be used in patients with postextubation croup.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's a Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:653-682.

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A.14. What are the nonacute causes of partial airway obstruction in children?

Several congenital anomalies are associated with respiratory difficulties. These can be subdivided into intrinsic and extrinsic pathologies as follows.

Extrinsic Pathologies

- Cystic hygroma—a proliferation or expansion of lymphatic channels, usually in the cervical region, which can compress the airway and lead to enlargement of the tongue
- Vascular anomalies—abnormalities of the aortic arch usually caused by aberrant vessels lead to compression of the airway. This is often position-dependent and may be responsible for coughing and wheezing when the patient is supine.
- Neoplastic compression of the trachea by lymphoma, hemangioma, neurofibromatosis, rhabdomyosarcoma, and other neural tumors in the mediastinum may occur and enlarge or compress airway structures.

Intrinsic Pathologies

- Subglottic stenosis—especially as acquired in previously intubated neonates. This form of airway narrowing occurs below the vocal cords, and it can lead to marked airway obstruction with respiratory infections. The congenital form may not be appreciated until an upper respiratory infection is present, when stridor may occur.
- Vocal cord paralysis—considered the second most common laryngeal anomaly in children, it is associated with the Arnold-Chiari malformation.
- Laryngeal structural anomalies—webs, laryngoceles, and cysts

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Fleisher GR, Ludwig S, eds. *Textbook of Pediatric Emergency Medicine* . 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:74-84.

B. Preoperative Evaluation and Preparation

B.1. Is intubation always required in children with epiglottitis?

Adult patients often can be managed under very vigilant observation provided that there is no impending obstructive danger. However, contemporary practice warrants the establishing of an airway with an endotracheal tube in the vast majority of infants and children. Nasotracheal intubation most often is used for ease of maintaining the child's comfort and safety. Endoscopic evaluation using appropriate fiberoptic airway endoscopy is a major advance in the management of epiglottitis.

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Fleisher GR, Ludwig S, eds. *Textbook of Pediatric Emergency Medicine* . 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:74-84.

B.2. Why is general anesthesia administered to a child with epiglottitis?

General anesthesia facilitates several activities. It gives the examiner a thorough look at the supraglottic area, which would be impossible and dangerous in the awake child. In addition, endotracheal intubation can be accomplished under controlled, relaxed conditions without trauma and laryngospasm. Intubation can be difficult because of the swelling and deformation of the paraepiglottic tissues. Clinicians who have no experience with this unusual appearance will find it easier to visualize landmarks and secure the airway when the patient is in a surgical plane of anesthesia.

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B.3. How would you prepare the patient for anesthesia?

Expedience is crucial. Once the diagnosis is made and the operating room alerted, the child is transported accompanied by parents and a physician with airway supportive equipment. An intravenous line can be placed more easily under anesthesia without upsetting the child. Anything that causes the child to cry will potentially worsen the obstruction and interfere with breathing. The child should, therefore, be kept calm and reassured. Nasal prong or face tent oxygen should be provided and portable pulse oximetry should be used.

Airway equipment including a suitable mask and endotracheal tubes up to two sizes smaller than normally expected should be available. Lidocaine, succinylcholine, atropine, and ketamine in appropriate dilutions should be ready. A cricothyrotomy tray should be available as a precaution.

The parent accompanies the child into the operating room. Before induction, the parent is instructed on his or her role in comforting the child, encouraging complicity with mask breathing, and gently holding the child when the inhalation induction commences. When parents can provide their assistance in an emotionally controlled, supportive way, a smooth, safe anesthetic induction via mask can be well facilitated.

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Tan GM. New way to mask induce a child. *Paediatric Anesth*. 2002;12:742-743.

C. Intraoperative Management

C.1. How is the airway of the child with epiglottitis best secured?

Little debate occurs over the safety and efficacy of endotracheal intubation provided that supportive staff is readily available. The endotracheal tube should be sized down 0.5 mm or 1.0 mm due to the inherent swelling and to protect against postextubation complications. Thick, copious secretions must be cleared frequently to prevent obstruction, and the child must be sedated to tolerate the endotracheal tube and to keep it secure in place.

Charles R, Fadden M, Brook J. Acute epiglottitis. *BMJ*. 2013;347:f5235.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's a Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:653-682.

Fleisher GR, Ludwig S, eds. *Textbook of Pediatric Emergency Medicine* . 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:74-84.

C.2. How would you induce anesthesia?

Verbal assurance is constantly given. The child is seated on the parent's lap in the operating room and is oxygenated. Sevoflurane is a good choice of induction agent because it is less pungent and irritant than desflurane and is usually well tolerated. The inhalation drug should be initiated in low concentration and slowly increased as tolerated. As the child gets sleepy, he or she is placed in the supine position. The patient may undergo a brief period of excitement during which care is taken not to be overzealous with ventilation. Spontaneous, unassisted

ventilation should continue as an intravenous line is placed. Glycopyrrolate 0.01 mg per kg is given intravenously as an antisialagogue. Ventilation may be assisted but not controlled. End-tidal gas is monitored continually, and the airway is adjusted to provide maximal tidal exchange. Sevoflurane concentration is increased as tolerated to 8%, provided cardiovascular stability is maintained to achieve adequate depth of anesthesia. Airway obstruction will decrease ventilation and anesthetic uptake, requiring longer induction time.

When the patient is in a deep plane of anesthesia (remember that the minimal alveolar concentration of sevoflurane in children is higher than in adults), a careful laryngoscopy is carried out. Paralysis is unnecessary in this deep plane of anesthesia. However, if several attempts are required with the possibility of the patient becoming light and reactive, a small dose of a neuromuscular blocker (e.g., rocuronium 0.4 mg per kg) will serve to maintain stable intubating conditions. This should be given only after it has been shown that the patient can be ventilated with a bag and mask.

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C.3. Should a child with epiglottitis undergo a rapid sequence induction?

In the child with a full stomach, a mask induction leaves the airway unprotected from aspiration of gastric contents. However, a rapid sequence induction may predispose the patient to severe hypoxia and hypoventilation should the clinician not be able to intubate expediently. Because the supraglottic landmarks are distorted by erythema and edema, recognition of the glottic inlet is obscured. In the spontaneously breathing patient, small air movements and the resultant

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secretional bubbling may highlight the glottic opening. In addition, paralysis in no way secures ventilatability.

If the patient must be manually ventilated, it is possible to meet with complete obstruction secondary to invagination of the swollen supraglottic tissues into the laryngeal introitus. In such a case, positive end-expiratory pressure or the jaw-thrust maneuver may fail to correct the airway obstruction.

Should the child be too agitated to cooperate with an inhalational induction, an intramuscular dose of ketamine (2 to 3 mg per kg) will accomplish sedation and preserve ventilation. However, it may accentuate airway reflexes, and the clinician should be wary of laryngospasm. Videolaryngoscopy with the various available modalities should be the choice whenever available.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's a Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:653-682.

Fleisher GR, Ludwig S, eds. *Textbook of Pediatric Emergency Medicine* . 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:74-84.

Nagler J, Bachur RG. Advanced airway management. *Curr Opin Pediatr*. 2009:299-305.

C.4. Is awake intubation a practical alternative to secure the patient's airway?

Awake intubation in these children is not generally recommended even though some authors have suggested awake intubation with topical anesthesia in the past. Risks of difficult visualization, agitation, trauma, worsening of epiglottic edema, and compromised ventilation far outweigh the benefits. Unless one has acquired great skill at awake pediatric intubation in the child with a normal airway, this technique should be avoided in these patients. In the adult, the awake GlideScope intubation has been reported with success.

Sinofsky AH, Milo SP, Scher C. The awake Glidescope intubation: an additional alternative to the difficult intubation. *Middle East J Anesthesiol*. 2010;20:743-746.

C.5. What would you do if the airway cannot be secured with intubation?

Preemptive preparation is critical, and an otorhinolaryngologist should be present. In the event that the airway is lost, percutaneous transtracheal ventilation can be performed. This involves

inserting a needle through the cricothyroid membrane as follows. Localize the cricothyroid membrane and topically cleanse the area with antiseptic. Anesthetize the skin with lidocaine (if time permitting) and then insert a 16-gauge catheter (attached to needle) in the midline in the inferior portion of the cricothyroid membrane and directed caudally. Attach a 3-mL syringe to the needle barrel applying negative pressure. If the syringe contains a few milliliters of saline, air bubbles will be apparent when the trachea is entered. Following entry, advance the catheter into the trachea. Depending on the hub size, a 3.0-mm or 3.5-mm endotracheal tube adapter can be inserted into the catheter to interface with an Ambu bag. Alternatively, a 6.5-mm or 7.0-mm endotracheal tube adapter can be inserted into a 3-mL syringe without the plunger to interface with an Ambu bag or anesthesia circuit (Fig. 41.1). Jet ventilation can also be applied with high-pressure tubing keeping careful observation of respiratory dynamics and saturation. A tracheotomy in skilled hands also can be performed.

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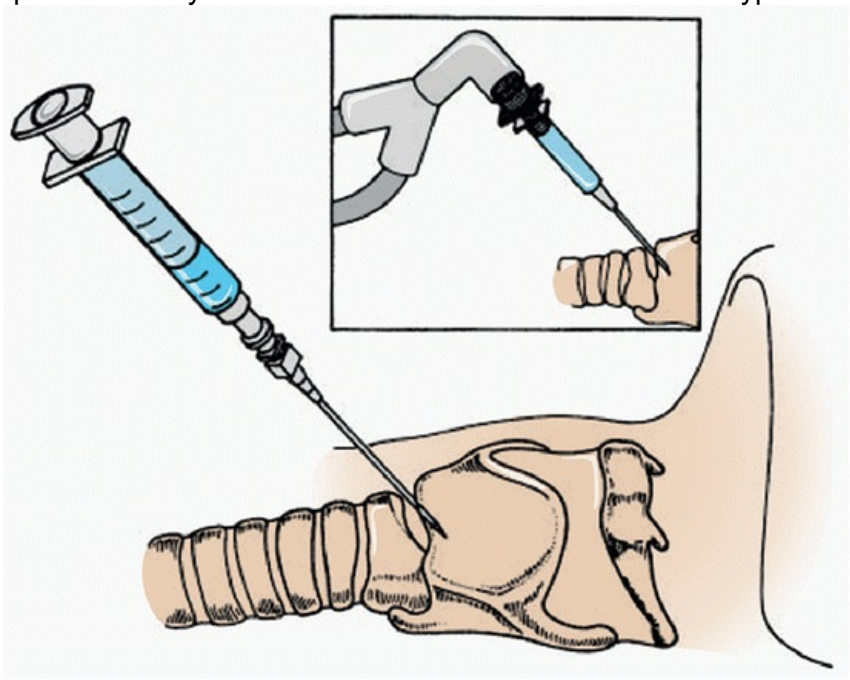


FIGURE 41.1 An emergency cricothyrotomy may be performed by passing a 14-gauge intravenous catheter through the cricothyroid membrane into the trachea. A 3-mL syringe with the plunger removed will accept a 15-mm endotracheal tube adapter that allows attachment of an oxygen-delivery system. (From Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:1035-1041, with permission.)

Delaney WA, Kaiser RE Jr. Percutaneous transtracheal jet ventilation made easy. *Anesthesiology*. 1991;74:952.

Deutsch ES. Tracheotomy: pediatric considerations. *Respir Care*. 2010;55:1082-1090.

C.6. Should this patient have a nasotracheal or orotracheal tube placed?

The patient will better tolerate a nasal endotracheal tube for prolonged intubation. Oropharyngeal toilet also will be easier. However, because the intubation can be difficult with epiglottitis and may predispose the patient to the problems listed in section C.4, the orotracheal route is easier and safer. Once the airway is secured orally, a nasotracheal tube can be inserted with laryngoscopic guidance.

C.7. Shortly after intubation, frothy secretions were obtained on suctioning the endotracheal tube. What is the reason for this? How can this be treated?

Davis et al. describe 7% of these patients as having pulmonary edema after intubation. This phenomenon relates to the transudation into the alveoli during periods of increased transpulmonary pressure. This occurs especially during obstructed inspiration. If the obstruction is complete, it is referred to as the “Müller” maneuver. The high negative pressures are buffered by the decreased venous return during exhalation. However, relief of the airway obstruction facilitates the extravasation of fluid for an increased venous return.

Treatment of this negative pressure pulmonary edema requires positive end-expiratory pressure. Diuretics and fluid restriction are not required because this condition generally is self-correcting. This can be administered by nasal bilevel means, mask continuous pressure, or intubation.

Davis HW, Gartner JC, Galvis AG, et al. Acute upper airway obstruction: croup and epiglottitis. *Pediatr Clin North Am*. 1981;28:859-880.

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Silva PS, Monteiro Neto H, Andrade MM, et al. Negative-pressure pulmonary edema: a rare complication of upper airway obstruction in children. *Pediatr Emerg Care*. 2005;21:751-754.

D. Postoperative Management

D.1. How long should this patient remain intubated? What criteria determine extubation time?

Earlier studies have shown a mean intubation duration of 36 hours in 23 patients with a range of 19 to 67 hours. These patients were treated with ampicillin or chloramphenicol, and the epiglottis was visualized before extubation. The current antibiotic regimen is cefazolin 75 to 100 mg/kg/day in three divided doses or clindamycin 30 to 40 mg/kg/day in three divided doses with the addition of a third-generation cephalosporin such as cefotaxime or ceftriaxone.

Criteria for extubation include an increased air leak around the endotracheal tube as well as decreased erythema and edema. Vernon and Sarnaik, however, feel that instrumentation and examination of the child is unnecessary and extubation at 36 to 48 hours can be accomplished easily in all patients. Hopkins recommended that the flexible fiberoptic laryngoscope be used to visualize the epiglottis and determine extubation time.

Charles R, Fadden M, Brook J. Acute epiglottitis. *BMJ*. 2013;347:f5235.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's a Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:653-682.

Damm M, Eckel HE, Jungehülsing M, et al. Airway endoscopy in the interdisciplinary management of acute epiglottitis. *Int J Pediatr Otorhinolaryngol*. 1996;38:41-51.

Hopkins RL. Extubation in epiglottitis. *Anesth Analg*. 1984;63:468.

Vernon DD, Sarnaik AP. Extubation in epiglottitis. *Anesth Analg*. 1984;63:469-470.

D.2. How would you make this patient comfortable during the course of intubation?

The child must be kept sedated to minimize movement, to prevent inadvertent extubation, and to provide anxiolysis. There are several options. Midazolam (0.075 mg per kg) as a starting dose titrated upward to effect followed by a continuous infusion of 0.04 to 0.1 mg/kg/hr will be effective, often in combination with a fentanyl infusion (1 to 3 μg/kg/hr). Alternatively, a short infusion of propofol can be given, taking care to monitor for propofol-related infusion syndrome. Dexmedetomidine is also a useful adjunct. A bilateral superior laryngeal nerve block in experienced hands may allow for better endotracheal tube toleration.

Of course, respiratory care, humidification, suctioning, and secretion mobilization must receive attention.

Charles R, Fadden M, Brook J. Acute epiglottitis. *BMJ*. 2013;347:f5235.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's a Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:653-682.

D.3. What outcome can one expect for the child with acute epiglottitis?

Residual airway problems are unusual in the vast majority of children. Most children who are diagnosed in time and intubated go on to a full recovery without sequelae. Complications are related to securing the airway and include associated pneumonia, respiratory failure, hypoxia, cardiac arrest, and death.

Charles R, Fadden M, Brook J. Acute epiglottitis. *BMJ*. 2013;347:f5235.

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Kliegman RM, Stanton BF, St Geme J, et al, eds. *Nelson Textbook of Pediatrics*. 19th ed. Philadelphia, PA: WB Saunders; 2011:1445-1450.

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Chapter 42
Cleft Palate

Aarti Sharma

A 3-month-old male infant was scheduled for repair of a cleft lip and a cleft palate. According to his pediatrician, the infant was born at full term and had no other medical problems.

A. Medical Disease and Differential Diagnosis

1. Describe the anatomic concept of a cleft palate and a cleft lip.
2. What is the cause of a cleft lip or a cleft palate?
3. What is the incidence of a cleft lip and a cleft palate?
4. Discuss the pathophysiology of a cleft lip and palate in the neonate and the older child (e.g., age >5 years).
5. What other conditions are associated with a cleft lip and a cleft palate?
6. What is Pierre Robin syndrome?
7. What is Treacher Collins syndrome?
8. What kind of specialized team care would these patients need?
9. Discuss indications and timing of closure of cleft lip and palate.
10. What is velopharyngeal incompetence, and how can it be diagnosed?
11. What is the relation of tonsillectomy and adenoidectomy to velopharyngeal incompetence?

B. Preoperative Evaluation and Preparation

1. What information do you need before closure of a cleft lip and palate?
2. What preoperative orders are needed?

C. Intraoperative Management

1. What monitors will you need for cheiloplasty and palatoplasty?
2. Discuss the induction and the anesthetic management for cleft lip and palate.
3. What positioning is recommended for cleft palate repair surgery?
4. What are the reported complications of this type of surgery and anesthesia?
5. Briefly describe the surgical techniques used to repair cleft defects.
6. How does a pharyngeal flap affect anesthetic management or any subsequent anesthetic administered to this patient?
7. What is an Abbe flap? What are its anesthetic implications?
8. What is the crucial problem of anesthesia for cleft palate? What are the unique considerations of this surgical repair?
9. What is laryngospasm? How would you make a diagnosis of laryngospasm?
10. How would you manage the patient with laryngospasm?

D. Postoperative Management

1. What complications of cleft lip and cleft palate surgery may be seen in the recovery room?
2. How do you protect the airway postoperatively?

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3. How would you control postoperative pain in patients following a cleft lip and cleft palate repair?

A. Medical Disease and Differential Diagnosis

A.1. Describe the anatomic concept of a cleft palate and a cleft lip.

Congenital clefts of upper lip occur because of failure of fusion of the maxillary, medial, and lateral nasal processes. They vary from a notch in the upper lip to a cleft through the lip and the floor of the nose involving the alveolar ridge, or they may be complete cleft of the lip and the palate.

The cleft palate is divided into prepalatal and postpalatal clefts. The incisive foramen marks the boundary between the two. They both have different embryologic development. A prepalatal cleft involves the anterior palate, alveolus, lip, nostril floor, and ala nasi. Postpalatal clefts may extend anywhere from soft and hard palate to the incisive foramen. The third type is a submucosal cleft in which a bone defect exists without a mucosal defect. The most common cleft of the palate is a left complete cleft of the prepalatal and palatal structures. The second most common is a midline cleft of all the soft palate and part of the hard palate without a cleft in the prepalatal area. Various degrees of the cleft palate and lip are shown in Figure 42.1.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. Chichester, United Kingdom: Wiley-Blackwell; 2012:832-834.

Thorne CH, Chung KC, Gosain AK, et al, eds. *Grabb and Smith's Plastic Surgery*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2014:173-175.

A.2. What is the cause of a cleft lip or a cleft palate?

Major components of face develop between 4 and 7 weeks of fetal life. There are three mesodermal islands, one central and two lateral. Prepalatal clefts are caused by the failure of these mesodermal elements to develop and fuse. Palatal clefts are caused when the palatal ridges fail to migrate medially, contact, and fuse (Fig. 42.1).

Thorne CH, Chung K, Gosain A, et al, eds. *Grabb and Smith's Plastic Surgery*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2014:173-175.

A.3. What is the incidence of a cleft lip and a cleft palate?

Cleft lip and cleft palate may occur together or separately. A cleft lip with or without a cleft palate occurs in 1:1,000 births. A cleft palate alone occurs in approximately 1:2,500 births. A cleft lip with or without a cleft palate is more common in boys, whereas isolated cleft palate is more common in girls.

The highest incidence of a cleft lip and a cleft palate occurs among Asians (1.61:1,000 births), whereas the lowest incidence is in African Americans (0.3:1,000 births). The incidence in Whites is intermediate (0.9:1,000 births).

Samanich J. Cleft palate. *Pediatr Rev*. 2009;30(6):230-232.

A.4. Discuss the pathophysiology of a cleft lip and palate in the neonate and the older child (e.g., age >5 years).

A cleft palate is responsible for some major physiologic disorders. The pharynx communicates more extensively with the nasal fossae and the oral cavity. The complex mechanisms of swallowing, breathing, hearing (through the eustachian tube), and speech are, therefore, impaired.

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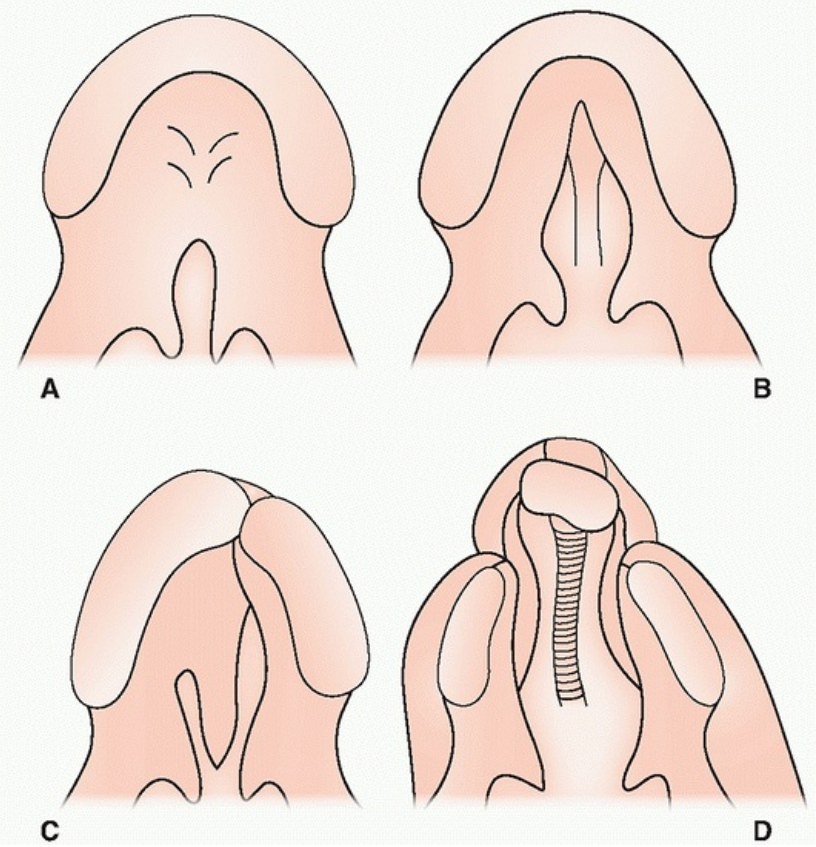


FIGURE 42.1 Various degrees of cleft palate and lip. **A.** Cleft of the soft palate only. **B.** Cleft of the soft and hard palate as far forward as the incisive foramen. **C.** Complete unilateral alveolar cleft, usually involving the lip. **D.** Complete bilateral alveolar cleft, usually associated with bilateral clefts of the lip. (Modified from McCarthy JG, ed. *Cleft Lip and Palate and Craniofacial Abnormalities*. Philadelphia, PA: WB Saunders; 1990. *Plastic Surgery*; vol 4.)

The presence of a cleft lip and palate in a neonate results in feeding difficulties. The neonate cannot suck because the cleft makes the creation of a negative pressure difficult. Breast-feeding is improbable and bottle-feeding is difficult.

Essentially, all children with a cleft palate have middle ear disease because abnormal anatomy of the nasopharynx adversely affects eustachian tube function. Chronic middle ear effusion produces varying degree of conductive hearing loss. Nasal septation between food and air is absent, creating a nonphysiologic mixing chamber in the nasopharynx. Not infrequently, this is associated with chronic rhinorrhea that must be distinguished preoperatively from infection.

Secondary defects of tooth development, growth of the ala nasi, and velopharyngeal function (contact between the soft palate and the posterior pharynx for speech and swallowing) can also occur.

Psychological problems may be considerable as this youngster approaches school age and peer association. The speech of these children is typically nasal with an inability to sound the so-called plosives (*p*/*k*/*d*/*t*) and fricatives (*s*/*f*).

Kosowski TR, Weathers WM, Wolfswinkel EM, et al. Cleft palate. *Semin Plast Surg*. 2012;26(4):164-169.

A.5. What other conditions are associated with a cleft lip and a cleft palate?

Associated anomalies occur 30 times more frequently in the patient with isolated cleft palate than in the noncleft population.

The most common non-syndrome-related abnormalities are umbilical hernias, clubfoot, and limb and ear deformities.

The most common syndromes associated with a cleft lip and a cleft palate are the following:

- Velocardiofacial (Shprintzen) syndrome

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- Van der Woude syndrome
- Stickler syndrome
- Pierre Robin syndrome
- Fetal alcohol syndrome
- Goldenhar syndrome (facio-auriculo-vertebral syndrome or hemifacial microsomia)
- Treacher Collins syndrome
- Nager syndrome
- Down syndrome

Calzolari E, Pierini A, Astolfi G, et al. Associated anomalies in multi-malformed infants with cleft lip and palate: an epidemiologic study of nearly 6 million births in 23 EUROCRAT registries. *Am J Med Genet A*. 2007;143A:528-537.

A.6. What is Pierre Robin syndrome?

This syndrome is characterized by retrognathia or micrognathia, glossoptosis, and airway obstruction. For facial cleft surgeons, Pierre Robin syndrome is defined by a triad of clinical criteria:

- Retrognathia
- Severe respiratory and/or digestive disorders in early infancy
- Cleft palate

An incomplete cleft of the palate is associated with the syndrome in approximately 50% of these patients. In patients with micrognathia (small jaw) or retrognathia, the chin is posteriorly displaced causing the tongue to fall backward toward the posterior pharyngeal wall. This results in obstruction of the airway on inspiration. Crying or straining by these children can often keep the airway open. However, when the child relaxes or sleeps, airway obstruction occurs. Because of these respiratory problems, feeding may become very difficult. This can lead to a sequence of events: glossoptosis, airway obstruction, crying or straining with increased energy expenditure, and decreased oral intake. This vicious cycle of events if untreated can led to exhaustion, cardiac failure, and ultimately death.

Jones KL, Jones MC, del Campo Casanelles M, eds. *Smith's Recognizable Patterns of Human Malformation*. 7th ed. Philadelphia, PA: WB Saunders; 2013:314.

A.7. What is Treacher Collins syndrome?

It is highly complex disease process consisting of the following:

- Hypoplastic cheeks, zygomatic arches, and mandible
- Microtia with possible hearing loss
- High-arched or cleft palate
- Macrostomia (abnormally large mouth)
- Antimongoloid slant to the eyes
- Colobomas (notching of the outer portion of the lower eyelid)
- Increased anterior facial height
- Malocclusion (anterior open bite)
- Small oral cavity and airway with normal-sized tongue
- Pointed nasal prominence

Jones KL, Jones MC, del Campo Casanelles M, eds. *Smith's Recognizable Patterns of Human Malformation*. 7th

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ed. Philadelphia, PA: WB Saunders; 2013:334-335.

A.8. What kind of specialized team care would these patients need?

These patients need a pediatrician to maintain their overall health and a surgeon and an anesthesiologist to accomplish the various surgeries. They need a speech therapist to prevent or

overcome the speech deficiencies and an orthodontist for early orthodontic intervention to develop and maintain relatively normal bite and dentition. The care team should also include a geneticist, pediatric dentist, prosthodontist, psychologist, medical social worker, and public health nurse.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2015.

A.9. Discuss indications and timing of closure of cleft lip and palate.

Functional goals of cleft palate surgery are normal speech, hearing, and maxillofacial growth. It is thought that speech and hearing are improved by early cleft palate repair (before 24 months of age) and that the delayed closure (after 4 years) is associated with less retardation of midfacial growth. An early two-stage palate repair is advocated in management of these patients. The recommended sequence involves closure of the soft palate at 3 to 6 months of age with secondary closure of the residual hard palate at 15 to 18 months of age. This sequence takes advantage of the early physiology and growth that occurs in the soft palate, which is vital in the development of speech. Furthermore, it avoids the potential pitfalls of the growth disturbance related to early periosteal undermining of palatal and vomerine tissue. This repair sequence also provides total palatal closure before speech evolves. If soft palate is repaired at the time of lip repair, an additional anesthetic is avoided.

Malek R, ed. *Cleft Lip and Palate: Lesions, Pathophysiology and Primary Treatment*. London: Martin Dunitz; 2001:197-205.

A.10. What is velopharyngeal incompetence, and how can it be diagnosed?

Velopharyngeal incompetence is the inability of the soft palate to fulfill its role in closing the nasopharynx, which seriously affects phonation.

To produce plosive sounds, *p*/*k*/*t*/*d*, or the sibilants, *s*/*sh*, the soft palate must touch the posterior pharyngeal wall to close the nose. Failure of closure results in the typical hypernasal speech. The most common cause of this is the cleft palate, but patients with congenitally short palates and no cleft can also have this typical speech pattern. Treatment consists of surgical lengthening of the palate by the pushback operation with or without pharyngeal flap. The diagnosis of velopharyngeal incompetence can be suggested by the child's speech. More objective diagnosis can be obtained by direct vision of the soft palate while the child is pronouncing certain keywords (*kah*, *kah*), by the fogging of the hand mirror placed under the nose during speech, and from cinefluorographic x-ray films.

In patients with velopharyngeal incompetence, videofluoroscopy and nasopharyngoscopy can provide information that will help select the appropriate procedure, either pharyngoplasty or posterior pharyngeal flap.

Dudas JR, Deleyiannis FW, Ford MD, et al. Diagnosis and treatment of velopharyngeal insufficiency: clinical utility of speech evaluation and videofluoroscopy. *Ann Plast Surg*. 2006;56(5):511-517.

A.11. What is the relation of tonsillectomy and adenoidectomy to velopharyngeal incompetence?

There is often a considerable mass of tonsillar and adenoidal tissue at the age when surgery is usually performed, and, in addition to the latent danger of infection, the flap used in pharyngoplasty creates an obstruction that seriously complicates their subsequent removal. Furthermore, bulky tonsils may hinder retrodisplacement of the soft palate or block the airflow by obstructing the cavum, which has already been reduced in volume by the retrodisplacement and the presence of the flap. It

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is, therefore, preferable to remove the tonsils and adenoids a few months before pharyngoplasty. The parents may wonder why this decision has been made because they have been repeatedly told that the adenoids should not be removed in the case of cleft palate because this might create or aggravate velar insufficiency. However, once velar inadequacy is confirmed, the parents are in a position to understand that these precautions are no longer justified and that the adenoids can represent a source of problems

if not treated with radical measures. During tonsillectomy, it is important to leave the tonsillar pillars absolutely intact because their muscle structure has a vital physiologic role.

Milczuk HA. Effects of oropharyngeal surgery on velopharyngeal competence. *Curr Opin Otolaryngol Head Neck Surg*. 2012;20(6):522-526.

B. Preoperative Evaluation and Preparation

B.1. What information do you need before closure of a cleft lip and palate?

Preoperative anesthetic evaluation is invaluable and includes the history and physical examination and suitable laboratory data. It gives a picture of the patient's general health. Hemoglobin level, which is often low in very young infants, should be obtained. If Treacher Collins or Pierre Robin syndrome is suspected, an x-ray film of the mandible may be helpful. Examination of the mouth may indicate potential intubation problems. The examination also offers a good opportunity to appraise the family environment because parental cooperation is essential for proper postoperative care.

Most surgeons repair a cleft lip when the baby is 6 to 10 weeks old and repair a cleft palate at 6 to 12 months of age. The exact age of repair will depend on the size and health of the child and the surgeon's preference.

Because periosteoplasty and lip adhesions are carried out as soon as the segments are in alignment and the surgery is less extensive, the rule of 10 can be used with moderate license:

- *Weight*—approximately 10 lb
- *Hemoglobin*—10 g per dL or more
- *White blood cell count*—less than 10,000 per μL
- *Age*—can be less than 10 weeks

With open cleft palate, however, it is common to have crusting and low-grade infection of the nasopharynx because of food and fluid regurgitation through the cleft. It is nearly impossible to eliminate this completely. Unless an acute inflammation process is present, this does not lead to complications.

Barrett BM Jr, ed. *Patient Care in Plastic Surgery*. 2nd ed. St. Louis, MO: Mosby; 1996:343-344.

B.2. What preoperative orders are needed?

Preoperative fasting has been a prerequisite for elective surgery. An issue of particular importance to the pediatric patient is the wonderful changes that have taken place regarding preoperative fasting. Recent work has shown that prolonged fasting does not reduce the risk of aspiration pneumonitis during anesthesia. This has led to reduction in the fasting times. Reduced fasting increases patient comfort and may decrease the potential for intraoperative hypoglycemia. Fasting guidelines for infants and children are shown in Table 42.1.

Because multiple operations may be required, the emotional trauma of each hospital experience must be minimized. The most common premedication used at Weill Cornell Medical Center in pediatric patients is oral midazolam. Dose can range from 0.25 to 0.5 mg per kg orally. Children younger than 8 months rarely require premedication. Children with anticipated difficulty in airway management and those with a propensity toward airway obstruction are better off without premedication.

TABLE 42.1 Minimum Fasting Period (Hours) for Pediatric Patients

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	CLEAR FLUIDS	BREAST MILK	FORMULA OR COW'S MILK	SOLIDS
Children	2	—	6	6
3-12 mo	2	4	6	6
<3 mo	2	4	4	6

Special orders include antibiotics if the infant or child has associated congenital heart disease and the typing and crossmatching of a unit of blood for palatal surgery.

Coté CJ. Preparation, premedication and induction of anesthesia in children. In: *ASA Annual Meeting Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2001:243.

C. Intraoperative Management

C.1. What monitors will you need for cheiloplasty and palatoplasty?

Heart rate, respiration, blood pressure, temperature, and oxygen saturation are monitored at all times. An electrocardiogram provides visual and audible evidence of the electrical activity of the heart. A precordial stethoscope monitors both heart and respiratory sounds. It is particularly important in this patient because once the surgery has begun, the anesthesiologist no longer has easy direct access to the airway. The use of pulse oximetry and an end-tidal CO_2 monitor is indispensable. Temperature should be monitored per rectum or axilla. A warming blanket should be used in these patients to avoid hypothermia. Blood loss determination should be made by a calibrated catchment trap in the suction line and by weighing sponges. Blood loss rarely exceeds 10% of circulating blood volume; however, properly crossmatched and screened blood should be available but used only if absolutely necessary.

C.2. Discuss the induction and the anesthetic management for cleft lip and palate.

After suitable monitors are attached, the infant is induced with oxygen, nitrous oxide, and either sevoflurane or halothane. Because cardiac depressant effects of sevoflurane are less pronounced than that of halothane, we prefer to use sevoflurane for induction. In addition, the myocardium is more sensitive to exogenous epinephrine when halothane is used. Recommended maximal dose of lidocaine for palate or lip surgery is 5 mg per kg and of epinephrine 10 μg per kg. This epinephrine dose is for hypocarbic or normocarbic patients.

Once the patient is asleep, an intravenous line is established and appropriate intravenous fluids are started. Intubation can be facilitated with nondepolarizing muscle relaxant. Muscle relaxants should be withheld if any possibility of difficulty in intubation exists.

Laryngoscopy in patient with a cleft lip is generally straightforward, but the cleft palate has the capability to trap and immobilize a straight blade. Should this occur, the anesthesiologist must first recognize the problem and then consider inserting a gauze pack or a dental roll in the cleft before laryngoscopy.

To achieve a cosmetic repair, symmetry is essential, so the tube should exit the mouth in the midline without facial distortion from either the tube or the securing tape. Some surgeons prefer to suture the tube to the lower gum.

An orogastric tube should be passed to empty the stomach of gas and secretions, and it should be removed before preparation of the surgical field.

A pharyngeal pack of moistened ribbon gauze is inserted for a cleft lip repairs; as for a cleft palate repair, the surgeon inserts the gag before insertion of the pharyngeal pack. Following the gag and pack insertion, ventilation should be reassessed because tube compression may have occurred. To avert eye injury, an ocular lubricant is placed in the eyes, and the upper eyelids are splinted shut with tape.

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During the surgery, it is necessary to have good communication and cooperation between the surgeon and the anesthesiologist because the surgeon's tools and hands and the anesthesiologist's endotracheal tube and apparatus all occupy the same very small space.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. Chichester, United Kingdom: Wiley-Blackwell; 2012:832-834.

C.3. What positioning is recommended for cleft palate repair surgery?

Correct positioning of the child is important for the plastic surgeon, who sits at the head of the operating table. Head extension must be maximal for cleft palate surgery. The entire body is raised with a thick foam mat or folded blanket, allowing the head to drop back hyperextended into a stockinette head support. Not only does this position provide good exposure, but it also allows blood to flow away from larynx and toward the nasopharynx allowing it to be removed by suction.

C.4. What are the reported complications of this type of surgery and anesthesia?

Anesthetic complications include obstruction of the endotracheal tube, inadvertent extubation during the procedure, and cardiac arrest. Postanesthetic complications include airway obstruction, bleeding with or without aspiration, and pneumonia. Complications not related to anesthetic management are wound healing, diarrhea, and otitis media. The mortality rate has been reported to be less than 0.5%.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. Chichester, United Kingdom: Wiley-Blackwell; 2012:832-834.

C.5. Briefly describe the surgical techniques used to repair cleft defects.

The Furlow procedure is the most common technique for cleft palate closure. It involves opposing Z-plasties of the mucosa and the musculature of the soft palate. The goal is to separate the nonfunctioning attachments from the posterior border of the hard palate and to displace the mucosa and the musculature posteriorly.

Other basic surgical techniques include von Langenbeck technique, Schweckendiek technique, two-flap technique, and three-flap/V-Y technique.

Although most of the repairs do not involve repairing the muscular sling, doing so allows better palatal and eustachian tube function.

Sadove AM, van Aalst JA, Culp JA. Cleft palate repair: art and issues. *Clin Plast Surg*. 2004;31(2):231-241.

C.6. How does a pharyngeal flap affect anesthetic management or any subsequent anesthetic administered to this patient?

The presence of this flap prohibits nasoendotracheal intubation and makes many nasal techniques difficult (e.g., insertion of nasogastric tube). The degree of obstruction is related to the width of the flap. Traumatic rupture of this flap secondary to attempted nasotracheal intubation could produce bleeding, aspiration, and laryngospasm.

Traumatic rupture of soft palate can occur from placement of laryngeal mask airway.

Knowledge of prior surgery is essential to good anesthetic management. Following the pushback and pharyngeal flap operation (pharyngoplasty), significant airway obstruction has been noted in the early postoperative period. Sleeping pulse oximetry has demonstrated obstruction and desaturation in the first 48 to 72 hours.

Dearlove O, Perkins RJ, Briggs G. Anaesthesia after cleft palate repair. *Anaesthesia*. 2004;59(10):1032. Somerville NS, Fenlon S, Boorman J, et al. Disruption of cleft palate repair following the use of the laryngeal mask airway. *Anaesthesia*. 2004;59(4):401-403.

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C.7. What is an Abbe flap? What are its anesthetic implications?

An Abbe flap is a full-thickness pedicle flap taken from the lower lip and swung on its own artery to a position in the upper lip to replace a tissue deficit resulting from any cause, such as surgical excision of malignancy or loss of tissue in a bilateral cleft lip. The lips must remain closed until the flap "takes," and then, it can be detached from its blood supply. Usually this operation is performed in children of an older age under local anesthesia, but it occasionally requires general anesthesia if the patient is young. All the problems of a closed mouth, such as the possibility of vomiting and aspiration, are encountered in addition to those associated with preservation of the flap.

Koshy JC, Ellsworth WA, Sharabi SE, et al. Bilateral cleft lip revisions: the Abbe flap. *Plast Reconstr Surg*. 2010;126(1):221-227.

C.8. What is the crucial problem of anesthesia for cleft palate? What are the unique considerations of this surgical repair?

The establishment, maintenance, and protection of the airway are the crucial problems of anesthesia for palate surgery. Failure to establish, maintain, and protect the airway results in tachypnea, CO_2 retention, hypoxemia, increased bleeding, hypovolemia, arrhythmia, cardiac arrest, and death. The major cause of cardiac arrest in infants and children is hypoxia.

Positioning of the patient is usually supine with table rotated 90 to 180 degrees with a preformed oral RAE (Ring-Adair-Elwyn) or reinforced endotracheal tube extending down

the midline of the jaw taped to the chin. The mouth gag that is used for surgical exposure may be released intermittently to allow reperfusion of tongue. However, each manipulation may affect the endotracheal tube. Blood that collects in the oropharynx should be carefully suctioned at the end of the procedure without disrupting the suture line. Residual blood and secretions in the oropharyngeal cavity may irritate the larynx and cause laryngospasm.

Jaffe RA, Schmiesing CA, Golianu B, eds. *Anesthesiologist's Manual of Surgical Procedures*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2014:1460-1462.

C.9. What is laryngospasm? How would you make a diagnosis of laryngospasm?

This is defined as glottic closure resulting from a reflex constriction of the laryngeal muscles. It is much more common in pediatric than adult anesthesia. The incidence is twice that of adults in older children and three times that of adults in younger children. Airway complications are further increased in children with upper respiratory tract infections. In the pediatric patient, the oxygen consumption is greater, so the consequences of laryngospasm in children are more serious. The oxygen consumption is highest in the youngest patients.

Laryngospasm seems to occur during anesthesia for two reasons: first, a lack of inhibition of glottic reflexes because of central nervous system depression; and second, an increased number of stimuli—such as manipulation of the airway, secretions or blood irritating the cords, and stimulation of visceral nerve endings at an inadequate depth of anesthesia.

Bingham R, Lloyd-Thomas A, Sury M, eds. *Hatch & Sumner's Textbook of Paediatric Anesthesia* . 3rd ed. London: Hodder Arnold; 2008:288-289.

C.10. How would you manage the patient with laryngospasm?

Laryngospasm may be partial or complete. Partial spasm will be diagnosed by a characteristic stridulous noise and a mismatch between the patient's respiratory effort and the disappointingly small movements of the reservoir bag. Methods of overcoming laryngospasm include applying positive pressure to the airway, deepening anesthesia, and administering muscle relaxants or a bolus of propofol. Recently, it was found that a bolus of propofol works extremely quickly, without the side effects of succinylcholine. The exact mechanism of action of propofol is not clear, but it could be due to increasing the depth of anesthesia or direct effect on the glottis. When there is complete laryngospasm, there will be silence with regard to air movement. The application of positive pressure may not be helpful in these circumstances and indeed may make the situation worse by forcing the false cords against the tightly closed true cords. It is much better to relax the cords before the

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hypoxia is severe. Succinylcholine can be given intramuscular or intravenous.

Bingham R, Lloyd-Thomas A, Sury M, eds. *Hatch & Sumner's Textbook of Paediatric Anesthesia* . 3rd ed. London: Hodder Arnold; 2008:288-289.

D. Postoperative Management

D.1. What complications of cleft lip and cleft palate surgery may be seen in the recovery room?

Complications include airway obstruction, bleeding, and hypothermia. Airway obstruction is the result of closure of the cleft structures plus some edema secondary to trauma. In the case of a pushback procedure with or without a pharyngeal flap, the obstruction is due to the new posterior position of the palate and the pharyngeal flap.

Combination of a closed palate, a small mandible pushing the tongue into a small pharynx, edema, blood, and the residual effects of anesthesia make postextubation airway obstruction more likely. There could also be swelling of the tongue due to mouth gag placement during surgery.

The anesthesiologist must be aware of the potential problems such as subglottic edema, flap edema, increased oral secretions, posterior displacement of tongue, mucosal swelling of hypopharynx, and an overlooked throat pack.

Blood loss is not an anesthetic complication, but its replacement is an anesthesiologist's responsibility, as is prevention of aspiration.

Hypothermia delays emergence and produces metabolic acidosis and respiratory and myocardial depression. The most important problem for the anesthesiologist is maintenance of airway.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:832-835.

D.2. How do you protect the airway postoperatively?

Following palatoplasty, the pharynx and nasopharynx are suctioned before extubation. Some anesthesiologists advocate that this be done with the aid of the laryngoscope to ensure removal of any mucus, blood, or clots. If suctioning is done before removing the Dingman gag, the laryngoscope may not be necessary. The infant should be as awake as possible. A long traction suture is placed through the tongue and tied loosely. Traction on the suture stimulates respiration and clears the airway. Neither an oral nor a nasal airway should be inserted unless absolutely necessary; either one could disrupt the sutures and undo all the surgical work. The traction suture is removed when the infant leaves the recovery room.

Following palate surgery, the infant is placed in prone or lateral position with the head dependent, turned to the side, and hyperextended. This position can be achieved with a jack placed under the foot of the crib or by placing a bulky bath blanket under the hips of the infant. Any blood or mucus will accumulate in the dependent cheek or roll out of the mouth.

Following cleft lip surgery, a Logan bow is frequently used to take the tension off the newly sutured lip. The infant can still be placed in the lateral position. Elbow restraints are essential, and they are placed on the infant or the child before leaving the operating room. A high-humidity atmosphere is recommended postoperatively to reduce the incidence of tracheitis, but others have failed to show any correlation between the use of humidity and the incidence of tracheitis.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia, PA: Mosby Elsevier; 2011:832-835.

D.3. How would you control postoperative pain in patients following a cleft lip and cleft palate repair?

In patients with cleft lip or cleft palate repair, the continuum of pain management continues through to the recovery room, the pediatric intensive care unit, or to an inpatient bed. No child should be discharged from recovery room with uncontrolled pain. Cleft palate repair is associated with the risk of postoperative airway obstruction, which may be increased with administration of opioids. Nerve blocks may be used to improve pain relief, to decrease perioperative

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consumption of opioids, and to favor early feeding resumption after repair.

Infraorbital nerve block can be used for pain control after cleft lip repair. Nasopalatine and palatine nerve block will provide palatal hard and soft tissue anesthesia. Recently, bilateral maxillary nerve blocks using a suprazygomatic approach has been used for effective pain relief.

Opioid analgesics that can be used postoperatively are shown in Table 42.2

Nonopioid analgesics that can be used postoperatively are shown in Table 42.3.

Lonnqvist PA, Morton NS. Paediatric day-case anaesthesia and pain control. *Curr Opin Anaesthesiol*. 2006;19:617-621.

Mesnil M, Dadure C, Captier G, et al. A new approach for peri-operative analgesia of cleft palate repair in infants: the bilateral suprazygomatic maxillary nerve block. *Paediatr Anaesth*. 2010;20(4):343-349.

TABLE 42.2 Opioid Analgesics for Pediatric Patients

DRUGS	DOSAGE	FORM
Fentanyl	1 μg/kg	IV
Morphine	0.05-0.1 mg/kg	IV
Meperidine	1 mg/kg	IV
Codeine	1.5 mg/kg q4h	PO: 15-mg, 30-mg, 60-mg tablets; syrup 15 mg/mL
Oxycodone	0.15 mg/kg	PO: 5-mg tablets; syrup 5 mg/mL

IV, intravenous; PO, by mouth.

TABLE 42.3 Nonopioid Analgesics for Pediatric Patients

DRUG	DOSAGE	FORMS AVAILABLE
Acetaminophen (Tylenol)	10-15 mg/kg PO maximum 2,600 mg/day	Tablets: 80 mg Syrup: 325 mg/5 mL Suppositories: 120 mg, 325 mg, 650 mg
Ibuprofen (Motrin)	10-20 mg/kg PO q6h	Tablets: 300 mg, 400 mg Syrup: 100 mg/5 mL

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Ketorolac (Toradol)	0.5 mg/kg IV to load (maximum dose 30 mg)	Parenteral form used intramuscularly/intravenously
	0.5 mg/kg q8h intramuscularly or intravenously (limit use to 48 hr)	

IV, intravenous; PO, by mouth.

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Chapter 43
Congenital Heart Disease with a Cervical Mass in Infancy

Miles Dinner

Elizabeth M. Cudilo

A 1-week-old male infant was diagnosed shortly after birth with an interrupted aortic arch (IAA). The workup revealed the child to have a 22q11 deletion syndrome (formerly known as *DiGeorge syndrome*). An enlarging cervical mass was noted, and the child was brought to the operating room for exploration.

A. Medical Disease and Differential Diagnosis

1. What is 22q11 deletion syndrome?
2. What are the associated cardiovascular defects in 22q11 deletion syndrome?
3. What are the metabolic and endocrine abnormalities in patients with 22q11 deletion syndrome and the attendant manifestations?
4. What are the immunologic findings in 22q11 deletion syndrome?
5. What is the differential diagnosis of cervical masses in infancy?
6. What is a cystic hygroma? What are the complications? What is the treatment?
7. What is the IAA anomaly?
8. What is the pathophysiology of the IAA syndrome?
9. How is ductal patency maintained?
10. What are the side effects of prostaglandin infusion?
11. What is the hyperoxia test?

B. Preoperative Evaluation and Preparation

1. What preoperative studies should be obtained to evaluate the neck mass?
2. How would you categorize the difficult airway in children?
3. What features of the difficult airway can be noted on physical examination?
4. How would you preoperatively optimize the ability to secure the airway in the operating room?
5. What laboratory studies are necessary before surgery?
6. What are the causes of congestive heart failure (CHF) in the infant? How would you assess this infant in your preoperative evaluation for signs of CHF?
7. How would you optimize the preoperative treatment of CHF?
8. How would you premedicate this infant?
9. When is premedication useful in infants and children?
10. Before the planned surgery, the infant is scheduled for a magnetic resonance imaging (MRI) scan. You are asked to ensure that the baby remains immobile for 20 minutes to perform the scan adequately. How would you accomplish this?

C. Intraoperative Management

1. What anesthesia equipment, circuit, and monitors would you use?
2. Describe techniques other than direct laryngoscopy that would be useful for securing the airway in this baby.

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3. How would you monitor blood loss in this patient?
4. What anesthetic technique should be used in a patient who may experience severe loss of blood intraoperatively?
5. How would you induce and maintain anesthesia in this neonate?
6. Intraoperatively, the surgeon must dissect the tumor in the anterior mediastinum and needs to have a quiet surgical field. How would you accomplish this in the infant?

D. Postoperative Management

1. How would you manage this patient postoperatively?

A. Medical Disease and Differential Diagnosis

A.1. What is 22q11 deletion syndrome?

The 22q11 deletion syndrome is one of the most common multiple anomaly syndromes in humans and has historically been referred to as Velocardiofacial syndrome, DiGeorge sequence, conotruncal anomalies face syndrome, CATCH 22, and Sedlackova syndrome—different names describing the same disorder. This syndrome has an expansive phenotype with more than 180 clinical features that can involve every organ and system. The syndrome is caused by a microdeletion of chromosome 22 at the q11.2 band. The syndrome has a prevalence of approximately 1 in 2,000 in the United States, although incidence is higher. The majority of patients have a constellation of abnormalities resulting from an embryogenic disruption in the formation of the third and fourth aortic arches. The common clinical features are hypocalcemia, immunodeficiency, dysmorphic facial features, palatal and velopharyngeal dysfunction, renal anomalies, and congenital heart disease (CHD). The DiGeorge variant is characterized by thymic and parathyroid aplasia and/or hypoplasia, cardiovascular defects, and dysmorphic facies. Depending on the extent of the thymic hypoplasia, clinical manifestations can range from frequent upper respiratory tract infections to severe immunodeficiency that can only be corrected with cultured thymic tissue transplant, bone marrow transplant, or peripheral blood transplant.

Goldmuntz E. DiGeorge syndrome: new insights. *Clin Perinatol*. 2005;32:963-978.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics* . 20th ed. Philadelphia, PA: Elsevier Saunders; 2015:1019-1022.

Shprintzen RJ. Velo-cardio-facial syndrome: 30 years of study. *Dev Disabil Res Rev*. 2008;14(1):3-10.

A.2. What are the associated cardiovascular defects in 22q11 deletion syndrome?

Congenital heart defects are found in 80% of patients with this syndrome. Most of these patients have conotruncal defects with additional anomalies of the aortic arch, pulmonary arteries, infundibular septum, and semilunar valves. The most common abnormalities include tetralogy of Fallot, pulmonary atresia with ventricular septal defect (VSD), truncus arteriosus, IAA, isolated anomalies of the aortic arch, and VSD. These defects arise during the crucial developmental stages of the truncoconal parts of the heart from the pharyngeal pouch derivatives. Cardiac MRIs are invaluable in defining the cardiac and associated anatomy in detail.

Carotti A, Digilio MC, Piacentini G, et al. Cardiac defects and results of cardiac surgery in 22q11.2 deletion syndrome. *Dev Disabil Res Rev*. 2008;14(1):35-42.

Momma K. Cardiovascular anomalies associated with chromosome 22q11.2 deletion syndrome. *Am J Cardiol*. 2010;105:1617-1624.

A.3. What are the metabolic and endocrine abnormalities in patients with 22q11 deletion syndrome and the attendant manifestations?

Because of errors of embryogenesis of the third and fourth pharyngeal arches, parathyroid hypoplasia and/or aplasia is common and results in hypocalcemia. This can be transient in neonates or may be permanent requiring calcium and

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vitamin D supplementation. Because hypocalcemia can be difficult to detect in the neonate, a high index of suspicion is necessary if a neonate exhibits irritability, jitteriness, twitching, seizure activity, failure to thrive,

tachycardia, and hypotension. Stridor (which needs to be differentiated from laryngeal web which is also prevalent in 22q11 deletion syndrome) and carpopedal spasm may also occur. It is important to remember that in patients with this syndrome, hypocalcemia may be precipitated by the stress of surgery and by increased needs during puberty or pregnancy. Chronic hypocalcemia may result in poor dentition that is prone to caries.

The prevalence of thyroid disease is significantly higher in the pediatric population with 22q11 deletion syndrome than in the general pediatric population. Shugar et al. suggest that screening for thyroid disease should be added into the routine medical management of these children.

Bassett AS, Chow EW, Husted J, et al. Premature death in adults with 22q11.2 deletion syndrome. *J Med Genet*. 2009;46:324-330.

Brauner R, Le Harivel De Gonneville A, Kindermans C, et al. Parathyroid function and growth in 22q11.2 deletion syndrome. *J Pediatr*. 2003;142:504-508.

Chinnadurai S, Goudy S. Understanding velocardiofacial syndrome: how recent discoveries can help you improve your patient outcomes. *Curr Opin Otolaryngol Head Neck Surg*. 2012;20(6):502-506.

Habel A, Herriot R, Kumararatne D, et al. Towards a safety net for management of 22q11.2 deletion syndrome: guidelines for our times. *Eur J Pediatr*. 2014;173:757-765.

Shugar AL, Shapiro JM, Cytrynbaum C, et al. An increased prevalence of thyroid disease in children with 22q11.2 deletion syndrome. *Am J Med Genet A*. 2015;167:1560-1564.

Sperling MA, ed. *Pediatric Endocrinology*. 3rd ed. Philadelphia, PA: Saunders; 2008:690-696.

A.4. What are the immunologic findings in 22q11 deletion syndrome?

Patients with this syndrome demonstrate marked variability in their immune system ranging from complete thymic aplasia to reduced T-cell counts and function. The majority of patients (˜75% to 80%) have a decrease in the total number of T cells, whereas 20% have no laboratory evidence of reduced T-cells numbers, and ˜1% of patients have thymic aplasia requiring transplant. Reduced levels of immunoglobulin A (IgA) and immunoglobulin M (IgM) also occur more frequently compared to the general population. In most individuals, the T-cell deficiency undergoes spontaneous improvement, usually by 2 years of age. Nonetheless, almost all patients have a tendency toward infection, particularly of the respiratory tract. As long as there is a working thymus, patients with 22q11 deletion syndrome can be immunized and generate a good antibody response because humoral immunity is usually intact. Autoimmune conditions are found in up to a third of patients, the most common being juvenile chronic arthritis, autoimmune thrombocytopenia, hemolytic anemia, Raynaud phenomena, and autoimmune thyroid disease.

Gennery AR, Barge D, O'Sullivan JJ, et al. Autoantibody deficiency and autoimmunity in 22q11.2 deletion syndrome. *Arch Dis Child*. 2002;86:422-425.

Habel A, Herriot R, Kumararatne D, et al. Towards a safety net for management of 22q11.2 deletion syndrome: guidelines for our times. *Eur J Pediatr*. 2014;173:757-765.

Markert ML, Alexieff MJ, Li J, et al. Complete DiGeorge syndrome: development of rash, lymphadenopathy, and oligoclonal T cells in 5 cases. *J Allergy Clin Immunol*. 2004;113:734-741.

Sullivan KE. Chromosome 22q11.2 deletion syndrome: DiGeorge syndrome/velocardiofacial syndrome. *Immunol Allergy Clin North Am*. 2008:28:353-366.

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A.5. What is the differential diagnosis of cervical masses in infancy?

Neck masses can originate from a congenital anatomic anomaly, neoplasm, or infection. In the first category are branchial and thyroglossal duct cysts and failed thymic descents. In the embryo, branchial cysts arise from the thymic stalk or the pharyngeal pouch and may be present at birth or develop later. They lie beneath the sternocleidomastoid muscle and may bulge out from its anterior border. The branchial cysts can become infected and enlarge to the extent that they compress the airway or upper esophagus. Thyroglossal duct cysts are spherical, midline masses that may extend back to the base of the tongue and may represent all of the thyroid tissue that the neonate has. In the embryo, the thymus gland arises high in the neck and descends into the anterior mediastinum. If there is any interruption of this caudad movement, the thymus can appear as a soft, compressible mass anywhere along the anterior border of the sternocleidomastoid muscle.

Infectious masses can be due to tuberculosis, Kawasaki disease, Epstein-Barr viral infection, cellulitic facial infections (Ludwig angina), and subacute regional lymphadenitis (catscratch disease).

Neoplastic masses in the cervical region can be teratomas, hemangiomas, neurofibromas, lymphomas, goiters, or cystic hygromas. Teratomas are firm, midline masses arising adjacent to the thyroid isthmus. Hemangiomas may be extensive, consequently compressing vital structures. Neurofibromas may arise individually or as a consequence of neurofibromatosis (von Recklinghausen disease) and can be very large. Goiters are enlarged thyroid glands that may present a hypothyroid, hyperthyroid, or euthyroid state.

Long SS, Pickering LK, Prober CG, eds. *Principles and Practice of Pediatric Infectious Diseases*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:135-142.

Ungkanont K, Yellon RF, Weissman JL, et al. Head and neck space infections in infants and children. *Otolaryngol Head Neck Surg*. 1995;112:375-382.

A.6. What is a cystic hygroma? What are the complications? What is the treatment?

Cystic hygroma is a developmental malformation of the lymphatic system found most often in the posterior triangle of the neck and axilla of children. They are divided into suprahyoid and subhyoid masses. They are compressible masses that are most often found in infants younger than 1 year and can intermittently enlarge. Suprahyoid masses can be extremely difficult to manage because of the associated obstructive symptoms, feeding difficulties, and potential for infection, which further can compromise airway patency. Complete surgical removal of these masses is often impossible. Repeat debulking is sometimes the only treatment. Facial paresis is always a potential risk of the resection. The mortality of a prenatally diagnosed cystic hygroma with obstructing features exceeds 20% following delivery. Therefore, intubation of the neonate during delivery while maintaining uninterrupted maternal-fetal circulation until the airway is secured (ex utero intrapartum treatment [EXIT] procedure) has been performed to prevent the fatal consequences of immediate postnatal airway obstruction. Bleomycin or derivatives of *Streptococcus pyogenes* have been used as sclerosing agents with favorable results.

Burezq H, Williams B, Chitte SA. Management of cystic hygromas: 30 year experience. *J Craniofac Surg*. 2006;17:815-818.

Descamps P, Jourdain O, Paillet C, et al. Etiology, prognosis and management of nuchal cystic hygroma: 25 new cases and literature review. *Eur J Obstet Gynecol Reprod Biol*. 1997;71:3-10.

Townsend CM, Beauchamp D, Evers MB, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:1819, 1832.

A.7. What is the IAA anomaly?

An IAA anomaly is extremely rare and represents approximately 1% of CHD. In IAA, there is complete aorta atresia somewhere along its arch, which is usually associated with a VSD and other complex cardiovascular anomalies. This

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defect is categorized into three types depending on where the atresia occurs. Left untreated, it is uniformly lethal within 1 week of life as a result of closure of the ductus arteriosus. In type A (43%), the aorta is interrupted between the left subclavian artery and the aortic isthmus. In type B (the most common, 57%), the interruption lies between the left common carotid and the left subclavian arteries. With type C (least common type, <1%), the arch is interrupted between the innominate and the left common carotid arteries. Forty percent to 50% of patients with IAA have the 22q11.2 deletion, which is usually associated with a more proximal location of the arch interruption (type C or type B).

Brown JW, Ruzmetov M, Okada Y, et al. Outcomes in patients with interrupted aortic arch and associated anomalies: a 20-year experience. *Eur J Cardiothorac Surg*. 2006;29:666-673.

Carotti A, Digilio MC, Piacentini G, et al. Cardiac defects and results of cardiac surgery in 22q11.2 deletion syndrome. *Dev Disabil Res Rev*. 2008;14(1):35-42.

Goldmuntz E, Clark BJ, Mitchell LE, et al. Frequency of 22q11 deletions in patients with conotruncal defects. *J Am Coll Cardiol*. 1998;32:492-498.

Matsuoka R, Kimura M, Scambler PJ, et al. Molecular and clinical study of 183 patients with conotruncal anomaly face syndrome. *Hum Genet*. 1998;103:70-80.

Momma K. Cardiovascular anomalies associated with chromosome 22q11.2 deletion syndrome. *Am J Cardiol*. 2010;105:1617-1624.

Reardon MJ, Hallman GL, Cooley DA. Interrupted aortic arch: brief review and summary of an eighteen-year experience. *Tex Heart Inst J*. 1984;11(3):250-259.

A.8. What is the pathophysiology of the IAA syndrome?

IAA is a neonatal medical emergency. It warrants immediate infusion of prostaglandin E_1 (PGE_1) to maintain ductal patency as well as stabilizing coexisting CHF. Due to the discontinuity between the descending aorta and the arch, blood flow to the descending aorta and its tributaries cannot occur unless the ductus arteriosus stays open. After medical stabilization, surgical correction should occur as soon as possible because the median age of death in untreated IAA with associated cardiac anomalies is 10 days. The cause of death is usually a combination of greatly increased left-to-right shunt with increased pulmonary blood flow, which results in biventricular failure, pulmonary edema, ductal stenosis, the sequelae of renal failure, and metabolic acidosis. Pulse oximetry will reveal normal saturation in the right arm, with a decreased saturation in the lower extremities. If there is inadequate perfusion to the lower body because of ductal closure, death quickly ensues from the combination of increased left-to-right shunt with increased pulmonary blood flow via the VSD, biventricular CHF, pulmonary edema, renal insufficiency, severe metabolic acidosis, and shock. Symptoms of ductal closure include tachypnea, lethargy, and poor feeding. A transthoracic echocardiography is diagnostic.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2015:2235-2239.

Luciani GB, Ackerman RJ, Chang AC, et al. One-stage repair of interrupted aortic arch, ventricular septal defect, and subaortic obstruction in the neonate: a novel approach. *J Thorac Cardiovasc Surg*. 1996;111:348-358.

Reardon MJ, Hallman GL, Cooley DA. Interrupted aortic arch: brief review and summary of an eighteen-year experience. *Tex Heart Inst J*. 1984;11(3):250-259.

A.9. How is ductal patency maintained?

The ductus arteriosus is kept open by the infusion of PGE_1. Both PGE_1 and prostaglandin E_2 are produced endogenously in the ductus and are metabolized in the lungs. Among the endogenous prostaglandins, prostaglandin E_2 is

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the most important. Postnatally, the levels fall dramatically secondary to increased metabolism resulting from the increase in pulmonary blood flow. A prostaglandin infusion will delay the natural closure of the ductus and improve systemic arterial perfusion and oxygenation. Less acidosis will also be seen in arterial blood gases compared to those obtained prior to PGE_1 infusion administration. In the case of an IAA, circulation to the lower body is completely dependent on the patency of the ductus; therefore, PGE_1 infusion must be continuously infused to keep the infant alive. Of note, the PGE_1 infusion has a relatively long half-life, and its inadvertent discontinuation will not acutely cause ductal closure (but should be maintained until surgical repair is complete).

Freed MD, Heymann MA, Lewis AB, et al. Prostaglandin E_1 in infants with ductus arteriosus-dependent congenital heart disease. *Circulation*. 1981;64:889-905.

Hermes-DeSantis ER, Clyman RI. Patent ductus arteriosus: pathophysiology and management. *J Perinatol*. 2006;26(suppl 1):S14-S18.

Kliegman RM, Behrman RE, Jenson HB, et al, eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia, PA: Saunders; 2007:2956.

A.10. What are the side effects of prostaglandin infusion?

Prostaglandin has a wide array of side effects ranging from fever, seizure-like activity, and hypotension, to flushing and edema. Platelet aggregation may also be reduced, and apnea with associated bradycardia can occur. This is most often seen in neonates weighing less than 2 kg at birth and usually appears during the first hour of initiating the drug infusion. Therefore, respiratory status should be monitored throughout treatment with mechanical ventilation as a consideration. It is recommended that a prostaglandin infusion be continuously administrated via a separate intravenous line that can be monitored for any disruptions in flow.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2015:2211-2222.

A.11. What is the hyperoxia test?

This test is performed to distinguish pulmonary causes from cardiac causes of cyanosis. To perform the test, the patient is first placed on 100% oxygen for 10 minutes. A preductal arterial blood gas is then taken from the patient's right arm. In patients with pulmonary disease, this supplemental oxygen significantly augments systemic oxygenation, which is not the case in cyanotic congenital heart defects. However, in some pulmonary conditions, the oxygen tension may not rise significantly. In these patients, a chest radiograph is invaluable for affirming pulmonary pathology. In some congenital heart lesions with mixing (i.e., truncus arteriosus), the supplemental oxygen decreases the pulmonary vascular resistance, which results in an increase in oxygen tension but is rarely greater than 150 mm Hg.

Keane JF, Lock JE, Fyler DC, eds. *Nadas' Pediatric Cardiology*. 2nd ed. Philadelphia, PA: Saunders Elsevier; 2006:141-142.

B. Preoperative Evaluation and Preparation

B.1. What preoperative studies should be obtained to evaluate the neck mass?

Because cervical masses have a variable nature and the potential for airway compression, studies need to be done preoperatively. A flexible neonatal bronchoscopy can define any extrinsic compressive deformations of the airway. Sonography and MRI of the head and neck can define the nature of the cystic hygroma and elucidate the degree of airway compression. These cysts are known to invade the anterior mediastinum and can cause extrinsic distortion of the lower airway anywhere from the cricoid ring to the carina. Under sonographic guidance, cystic fluid can be aspirated to reduce the size of the mass and potentially relieve compressive symptoms. Rarely, there may be invasion into the pericardium

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and displacement of the lung. If the mass is suprahyoid, radiologic studies will reveal the degree of laryngeal compression and retropharyngeal involvement, which are vital to know prior to intubation.

B.2. How would you categorize the difficult airway in children?

Children with difficult airways can be grouped into four main groups. The first group includes children who have congenital anomalies affecting the airway such as vascular rings, laryngomalacia, micrognathia, or neurofibromatosis. The second group includes patients with an acutely acquired obstruction of the airway such as trauma or foreign body. The third group includes infectious etiologies such as retropharyngeal abscess, laryngotracheobronchitis, or peritonsillar abscess. The last group is composed of children without known congenital or anatomic abnormalities that have unanticipated difficulty with intubation secondary to glottic visualization problems on direct laryngoscopy.

Hall SC. The child with a difficult airway: recognition and management. In: *ASA Annual Meeting Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2006:412.

B.3. What features of the difficult airway can be noted on physical examination?

Many anatomic abnormalities can be noted simply by performing a thorough airway exam. Visual inspection of the size of the patient's mouth can alert the anesthesiologist to a constricted oral opening that may be seen in conditions, such as scleroderma, epidermolysis bullosa, burn cicatrization, or congenital microstomia, which could prevent insertion of the laryngoscope. Micrognathia or maxillary protrusion often accompany an anterior larynx, making glottic visualization during direct laryngoscopy impossible. This is seen in children with craniofacial syndromes, such as Pierre Robin sequence, Treacher Collins syndrome, Apert syndrome, or Crouzon syndrome. Macroglossia as a consequence of certain metabolic storage diseases (i.e., Hurler syndrome, Hunter syndrome), cystic abnormalities, and/or hamartomatous tumors of the tongue (Goltz syndrome) can also make effective laryngoscopy impossible. Assessing the temporomandibular joint can reveal signs of ankylosis, which can occur in patients with juvenile rheumatoid arthritis and other autoimmune processes that may prevent adequate mouth opening. A narrow, high-arched palate may also suggest a difficult intubation. One should evaluate range of motion of the neck to reveal any decreased

neck extension, which may accompany some neuromuscular disorders, arthritic conditions, trauma, Klippel-Feil syndrome, or Goldenhar syndrome. Lastly, one should attempt to palpate the patient's neck to access for tracheal deviation. A preoperative chest radiograph may better serve to note tracheal deviation as well as provide a baseline for the state of the lungs.

Berry FA, ed. *Anesthetic Management of Difficult and Routine Pediatric Patients*. New York: Churchill Livingstone; 1986:167.

Wetmore RF, Muntz HR, McGill TJ. *Pediatric Otolaryngology: Principles and Practical Pathways*. 2nd ed. New York: Thieme Medical; 2012.

B.4. How would you preoperatively optimize the ability to secure the airway in the operating room?

Because there are inherent risks in inducing anesthesia and securing the airway in this neonate, one would prepare for a fiberoptic-guided intubation. The infant bronchoscope is so small in diameter that it does not allow the presence of a suction port, which can impair visualization if there are excessive secretions. An antisialagogue should be given at least 15 to 20 minutes before beginning the fiberoptic intubation to facilitate recognition of the anatomy. Glycopyrrolate (0.01 mg per kg) will limit secretions without causing the excessive tachycardia that may occur with atropine. In this neonate with cardiac compromise, any unnecessary stress on the heart should be avoided. In addition to the fiberoptic bronchoscope being available, an appropriate laryngeal mask airway (LMA) and equipment trays for an emergency cricothyrotomy should also be ready. Having a pediatric otolaryngologist present for the induction of anesthesia as well as a rigid infant bronchoscope with video imaging capability should also be strongly considered. The rigid bronchoscope cannot only facilitate visualization of the laryngeal inlet, but it can also provide a route to temporarily ventilate the patient and hold the endotracheal tube as an introducing stylet to facilitate intubation.

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American Society of Anesthesiologists Task Force on Management of Difficult Airway. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of Difficult Airway. *Anesthesiology*. 2003;98:1269-1277.

Apfelbaum JL, Hagberg CA, Caplan RA, et al. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of Difficult Airway. *Anesthesiology*. 2013;118(2):251-270.

DeLeo A, Dimmitt P. Pediatric upper airway endoscopy. *ORL Head Neck Nurs*. 2005;23:29-30.

Enterlein G, Byhahn C. Practice guidelines for management of difficult airway: update by the American Society of Anesthesiologists task force [in German]. *Anaesthetist*. 2013;62(10):832-835.

B.5. What laboratory studies are necessary before surgery?

Serum calcium should be measured because of the strong association of 22q11 deletion syndrome with hypocalcemia. Also, the inherent dysphagia caused by the cystic hygroma will have resulted in the infant having been on total parenteral nutrition due to the inability of oral feeding. To ensure that adequate parenteral nutrition and hydration have been provided, serum glucose and sodium levels should be reviewed. Because there is also the potential for severe metabolic acidosis secondary to underperfusion of the lower body as a result of the IAA, serum pH and bicarbonate concentrations must be obtained. The $PaCO_2$ level will indicate the baseline adequacy of ventilation in the face of a potentially obstructing mass, and the PaO_2 level will serve as a guide in assessing the neonate's degree of CHF, pulmonary insufficiency, and central shunting. Because the surgery can be extensive, with a significant loss of blood, a baseline complete blood count with hematocrit should be obtained. In addition, the prothrombin time and partial thromboplastin time should be obtained before surgery because of the possibility of baseline immaturity in coagulation factor production and the inherent bleeding potential from the large dissection that will be done.

B.6. What are the causes of congestive heart failure (CHF) in the infant? How would you assess this infant in your preoperative evaluation for signs of CHF?

The causes of CHF can be divided into five major areas:

- Cardiac rhythm disturbances (heart block and supraventricular tachycardia)
- Volume overload (anemia, sepsis, and VSD)

- Systolic ventricular dysfunction (myocarditis, malnutrition, and dilated cardiomyopathy)
- Pressure overload (aortic stenosis and coarctation)
- Diastolic ventricular dysfunction (pericardial tamponade and restrictive cardiomyopathy)

CHF occurs either in response to an excessive volume or pressure load or as a consequence of myocardial muscle impairment. Volume overload is due to factors causing a large increase in cardiac output (e.g., large VSD or ductus arteriosus). In these circumstances, there must be a sufficiently large left-to-right shunt to cause a severe strain on the heart. In the normal newborn, these lesions do not usually produce heart failure until 1 to 2 months of age because it takes longer than usual for the pulmonary vascular resistance to fall. The elevated pulmonary vascular resistance protects the left ventricle from the stress of overcirculation. This is not true in premature neonates who do not manifest the same degree of pulmonary arteriolar constriction; therefore, they are susceptible to large left-to-right shunts early and show CHF more readily.

Regurgitant valvular lesions can also lead to CHF. In complex CHD (i.e., truncus arteriosus or tricuspid atresia with transposition), the additional stress of hypoxemia or univentricular overload may herald the early onset of CHF. Large arteriovenous malformations may also occur intracranially and cause CHF. Excessive pressure loads are seen in obstruction to cardiac output from aortic stenosis, aortic coarctation, and aortic interruption.

In the immediate newborn period, right-sided CHF is seen with greater frequency because of severe pulmonary hypertension. Pulmonary hypertension has many causes including intrinsic lung parenchymal insufficiency or pathology

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(i.e., diaphragmatic hernia, meconium aspiration, or hyaline membrane disease), chronic hypoxemia, hypervolemia, and polycythemia.

Primary myocardial failure is unusual and rare in the newborn. If it occurs, it is likely due to endocardial fibroelastosis and anomalous coronary circulation. Nonetheless, the myocardium in the infant is susceptible to depression from metabolic derangements such as hypoglycemia, hypocalcemia, hypoxemia, and hypercarbia. Also, severe anemia with the associated decreases in systemic and myocardial oxygen supply forces an increase in myocardial work that can lead to CHF.

Infants are different from adults in their manifestations of CHF. Signs of cardiac dilation may be absent because of decreased systemic venous return from the elevated intrathoracic pressure as a consequence of coexisting lung disease in premature infants. Although immature, the carotid baroreceptors still initiate an increase in sympathetic outflow in response to reduced perfusion. The increased α-adrenergic stimulation impairs blood flow to the systemic arteriolar beds, resulting in cold, underperfused extremities, and diminished splanchnic perfusion. Fatigue, loss of appetite, and failure to thrive quickly follow. Tachycardia from β-adrenergic receptor stimulation occurs. Generalized sweating results from sympathetic cholinergic fiber stimulation. Extracellular water increases because of decreased renal excretion of sodium due to a decreased glomerular filtration rate; however, peripheral pitting edema is much less common in infants compared to older children and adults. The venous system in infants is extremely distensible, so much so that elevated right atrial pressures may not show jugular venous engorgement. The most prominent manifestation of CHF in the infant is tachypnea. Because pulmonary venous pressure is elevated from left ventricular failure, the lung compliance decreases because of the augmented interstitial fluid. Breathing becomes rapid and shallow further increasing the body's oxygen requirement, which leads to a cyclic dependency to maintain both tachycardia and tachypnea. It is common to see subcostal retractions due to the increase in respiratory effort in infants with CHF.

Infants have a greater lymphatic drainage capacity compared to adults and can clear interstitial accumulations more readily. Therefore, rales are less often appreciated in infants with CHF as opposed to adults with CHF. The bronchial mucosa may become swollen because of engorgement of the bronchial venous system resulting in narrowing of the airway lumen. This can produce an audible wheeze that is often seen in infantile CHF. Lastly, hepatomegaly is a cardinal sign of right ventricular failure in infants.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2015:2282-2288.

B.7. How would you optimize the preoperative treatment of CHF?

The typical manifestations of CHF in infants (i.e., tachycardia, tachypnea, subcostal retractions, and rhonchi) are also cardinal signs of pulmonary infection in this age group. They can be difficult to distinguish. Often, they coexist and treatment must address both conditions. In this patient, the structural abnormality of the IAA, needs surgical correction; however, correction must be deferred until the neck mass is resected. In this infant, the CHF is caused by pressure overload from the IAA, and the hypocalcemia is due to parathyroid hormone insufficiency. Calcium must be normalized by intravenous infusion. If glucose is low, as would be expected in an infant who is unable to feed by mouth, has glycogen depletion from the stress of illness, has an immature liver that is unable to generate sufficient gluconeogenesis, and has an increased utilization from a baseline higher metabolic rate (compared to adults), a glucose source should be continuously supplemented by slow intravenous administration. Myocardial work is compromised by the presence of metabolic acidosis, which occurs as a consequence of the increased lactic acid production during anaerobic metabolism resulting from lower body hypoperfusion. The pH should be normalized with sodium bicarbonate. Because of the attendant sodium load, tromethamine may be an alternative.

With the guidance of a pediatric cardiologist, myocardial function should be optimized with digitalis in most infants with CHF; although in the IAA syndrome, there may be decreased renal perfusion. As a consequence, the digoxin levels may rise and toxicity is more likely to occur. A catecholamine (e.g., dopamine or dobutamine) can be infused to boost contractility. Pulmonary symptoms should be treated with antibiotics and positive pressure ventilation (i.e., high-flow nasal cannula, nasal continuous positive airway pressure [CPAP]) with oxygen titrated to arterial blood gas measurements. Intubation and mechanical ventilation may be necessary in many infants with CHF. Diuresis, with furosemide in conjunction with fluid restriction, will promote restoration of pulmonary compliance by decreasing lung water.

Balaguru D, Artman M, Auslender M. Management of heart failure in children. *Curr Probl Pediatr*. 2000;30:1-35.

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McMillan JA, Feigin RD, DeAngelis C, et al, eds. *Oski's Pediatrics: Principles and Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:357.

B.8. How would you premedicate this infant?

Infants younger than 2 years do not routinely require preoperative anxiolytics or narcotics. An infant with a compromised airway and abnormal circulation cannot tolerate any degree of respiratory depression; therefore, no sedative premedication should be given at all. Because a fiberoptic intubation is planned, glycopyrrolate should be given preoperatively for its antisialagogue activity.

B.9. When is premedication useful in infants and children?

Patients with dynamically responsive cyanotic CHD (i.e., tetralogy of Fallot) benefit from premedication before coming to the operating room. In these children, the inherent anxiety of transfer to unfamiliar surroundings, change in temperature, and parental separation may trigger infundibular spasm and reduce pulmonary blood flow, thereby leading to a “tet spell.” This transient increase in pulmonary vascular resistance dramatically decreases pulmonary blood flow and increases the flow of desaturated blood to the body via VSD. Acute hypoxemia is not an optimal state in which to initiate an anesthetic induction. Therefore, sedation with oral midazolam or nasal dexmedetomidine is useful to allay preoperative anxiety and reduce the risk of provoking a hypoxemic spell. Premedication can make the perioperative experience for a child less frightening, produce variable degrees of amnesia, and decrease the risk of emergence delirium. However, it is one of many tools a pediatric anesthesiologist has at his or her disposal to ensure a positive perioperative experience for the patients and their family.

Fortier MA, Blount RL, Wang SM, et al. Analysing a family-centred preoperative intervention programme: a dismantling approach. *Br J Anaesth*. 2011;106(5):713-718.

Kain ZN, Caldwell-Andrews AA, Mayes LC, et al. Family-centered preparation for surgery improves perioperative outcomes in children: a randomized controlled trial. *Anesthesiology*. 2007;106(1):65-74.

Sun Y, Lu Y, Huang Y, et al. Is dexmedetomidine superior to midazolam as a premedication in children? A meta-analysis of randomized controlled trials. *Paediatr Anaesth*. 2014;24(8):863-874.

B.10. Before the planned surgery, the infant is scheduled for a magnetic resonance imaging (MRI) scan. You are asked to ensure that the baby remains immobile for 20 minutes to perform the scan adequately. How would you accomplish this?

Because this neonate has an already severely compromised airway while awake, the safest anesthetic plan to assure immobility and adequate ventilation is to perform a general anesthetic via an endotracheal tube. Any form of sedation without an endotracheal tube already in place puts this patient at risk for complete airway obstruction and should not be used here. Section C.2 details the fiberoptic intubation for an infant. If the neonate has demonstrated a postprandial sleep cycle and can take oral fluids, it may be well worth an attempt to perform the MRI scan while the neonate is swaddled in a warm baby blanket sucking on a pacifier filled with dextrose solution (“Sweetie pacifier”). In this manner, the patient remains “motionless” from the inherent feeling of wellness of being able to feed and being bundled in a warm blanket.

Arthurs OJ, Edwards A, Austin T, et al. The challenges of neonatal magnetic resonance imaging. *Pediatr Radiol*. 2012;42(10):1183-1194.

C. Intraoperative Management

C.1. What anesthesia equipment, circuit, and monitors would you use?

This patient is especially susceptible to infection because of the baseline depressed cellular immunity. As with every patient, strict attention must be paid to maintaining a sterile technique during the central line placement and instrumentation of the patient. The anesthesiologist must wear a sterile gown and gloves to protect the neonate. Sterility of

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the disposable circle system, mask, endotracheal tube, fiberoptic bronchoscope, and laryngoscope should be ensured. Routine monitors for all surgery on infants include pulse oximetry, electrocardiogram, blood pressure, capnograph, spirometer, precordial stethoscope, and rectal temperature probe. Multiple pulse oximeters should be available to offer flexibility in the event of monitor dysfunction. In this neonate, the IAA prevents the ability to obtain saturation data from the lower body and left arm. End-tidal expired gas concentrations should be recorded for anesthetic gases, nitrogen, and oxygen. Accurate capnography in small infants may be hampered by side-arm gas sampling resulting from the relatively high gas flows relative to the expired gas flow from the infant.

In this procedure, an arterial line should be inserted in the right upper extremity because the IAA will not allow for blood pressure determination on the left side. Because there is potential for significant blood loss, a central line should be placed under ultrasound guidance at the best available site (i.e., internal jugular, subclavian, or femoral). With such a small patient with distorted anatomy, obtaining central access maybe very difficult. If an internal jugular or subclavian central line is placed, a postline placement chest radiography should be obtained and reviewed (to rule out pneumothorax and correct position) before proceeding with this complicated case. Catheter length must be taken into consideration because it is very easy in an infant to inadvertently place the central line inside the right atrium or across the tricuspid valve leading to arrhythmias and misleading right ventricular pressures. The arterial line and central venous pressure transducers should be placed at the approximate level of the right atrium and adjusted accordingly as the table height is changed. Cerebral and somatic oximetry are useful in providing early recognition of intraoperative hypoperfusion to the brain and body.

Schreiber C, Eicken A, Vogt M, et al. Repair of interrupted aortic arch: results after more than 20 years. *Ann Thorac Surg*. 2000;70:1896-1899.

Tobias JD. Cerebral oximetry using near-infrared spectroscopy aids in the diagnosis of interrupted aortic arch. *J Intensive Care Med*. 2008;23:335-337.

C.2. Describe techniques other than direct laryngoscopy that would be useful for securing the airway in this baby.

It is highly unlikely that glottic visualization could be accomplished in this neonate with direct laryngoscopy alone. On the computed tomography scan, the mass is seen to elevate the tongue

and deviate the larynx to the side. The following alternative forms of securing the airway can be used when direct laryngoscopy is not expected to provide easy visualization of the glottis.

Infant Video Laryngoscope

The various forms of this device on the market allow for excellent glottic visualization and facilitation of intubation if the patient's mouth opening is large enough to accommodate the blade and may provide a superior visualization compared to conventional direct laryngoscopy in some patients.

Intubation through a Laryngeal Mask Airway

First, securing the airway with an LMA and demonstrating that one can ventilate through it can add an extra margin of safety when performing an anticipated difficult pediatric intubation. The LMA is then used as a conduit for insertion of the fiberoptic-guided endotracheal tube into the glottis.

Retrograde Cricothyroid Wire

This technique is not ideal for this patient for many reasons. First, the size of the patient would make it technically difficult. Second, the large cystic hygroma is distorting the external anatomy landmarks that facilitate this type of intubation; nonetheless, for completeness, this method will be described. The retrograde cricothyroid wire technique is best for oral intubations. A guidewire is inserted through a large-gauge needle that is used to puncture the cricothyroid membrane. The guidewire is threaded cephalad until it visualized and retrieved through the mouth. Then, the guidewire is tied to “Murphy eye” of the endotracheal tube. Then, the other end of the guidewire (that is sticking out through the cricothyroid membrane) is slowly pulled caudally to guide the endotracheal through the vocal cords. Even after the endotracheal tube is in correct position, the guidewire remains attached externally to the neck in case of unplanned extubation (to facilitate reintubation).

Blind Nasal Intubation

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Although very successful in adult patients, the blind nasal intubation technique can be very challenging in infants or small children. Certainly, performing an awake, sedated intubation in this manner mandates giving adequate topical anesthesia to a less than cooperative infant. In addition, the smaller endotracheal tubes used in pediatrics are far more compliant than adult-sized tubes, especially when warmed with nasopharyngeal respiratory gases, which makes it difficult to maintain the anterior curve on the tube to enter the larynx.

Nasal Intubation with Laryngoscope and Magill Forceps

If the larynx cannot be visualized by direct laryngoscopy, an anesthetized, spontaneously breathing nasal intubation with laryngoscopic assistance can be carried out in some patients. In this case, great care is taken to ensure that the patient continues to maintain spontaneous and adequate ventilatory exchange during the inhalational induction. Sevoflurane is used for pediatric inhalational inductions because it is less pungent and more easily tolerated than other agents. The pediatric anesthesiologist should be mindful that total airway obstruction can happen at any point during the inhalation induction due to relaxation of pharyngeal tone and other airway abnormalities. If spontaneous breathing can be maintained, the intubation should be attempted after a surgical plane of anesthesia is achieved. The laryngoscope is then used to visualize the epiglottis. Using Magill forceps, the tip of the endotracheal tube is aligned with the subepiglottic region and slowly advanced. Capnographic monitoring during this maneuver can help verify the direction of the endotracheal tube tip.

Fiberoptic Intubation

Fiberoptic intubation is most successful when it is carried out as the initial maneuver (before the airway is traumatized from previous attempts at intubation). It may be nearly impossible to use after several unsuccessful attempts because the upper airway becomes hypersecretory and may ooze blood. The appropriate fiberoptic technology may not be widely available unless one is practicing at a tertiary pediatric hospital with a wide range of bronchoscopes on hand (including the smallest, “ultrathin” 2.2 mm in diameter scope necessary for this neonate). Due to their small size, pediatric bronchoscopes lack a suction port and need to be lubricated to facilitate the sliding of the endotracheal tube off the scope once it is through the glottis.

In older patients, three specialized fiberoptic methods can be useful in intubating pediatric patients with difficult airways. First, the clinician can pass a guidewire through the suction port of the larger instrument to serve as a stylet for the endotracheal tube. Second, the scope can be used to visualize and guide a nasal endotracheal tube inserted into the opposite nostril. Finally, a 4.5-mm tube can be placed at the laryngeal orifice to be used as a stent for inserting a small guidewire, which can in turn be used to place a smaller endotracheal tube.

Transtracheal jet ventilation can be used when applicable. In this technique, a 16-gauge intravenous catheter is placed through the cricothyroid membrane and jet ventilation with 100% oxygen is provided. A second intravenous catheter is placed through the cricothyroid membrane and a guidewire (0.021 in. diameter J-tip) is introduced with cephalad angulation. Jet ventilation continues as the guidewire is threaded through the nose and connected to the working part of a fiberoptic scope. The scope is then advanced through the laryngeal inlet, and a tube is threaded over the scope; then, the guidewire is removed. Sedation can be provided with a remifentanil drip (0.1 to 0.2 μg/kg/min). Because patient safety is the foremost consideration in any technique for inserting an artificial airway, the anesthesiologist and/or otolaryngologist should be immediately available to perform an emergent cricothyrotomy in case of a life-threatening loss of airway.

Of note, in the pediatric patient with a known difficult airway, a preemptive collaborative approach of securing the airway with a pediatric otolaryngologist can greatly increase the degree of safety and minimize harm done to the patient. When performing an emergency cricothyrotomy, a longitudinal incision is made in the skin and fascia above the cricothyroid membrane, after which the cricothyroid membrane is punctured and entered with a small endotracheal tube. Another technique utilizes a 14-gauge angiocatheter, which is inserted into the cricothyroid membrane. Intratracheal location is verified by the loss of resistance with an attached syringe and the aspiration of air. The catheter is attached to a 3-mL syringe (without plunger), which is then connected to the Y-piece of the anesthesia circuit by an adapter from a 7.0-mm internal diameter endotracheal tube.

Auden SM. Additional techniques for managing the difficult pediatric airway. *Anesth Analg*. 2000;90:878-880.

Hall SC. The child with a difficult airway, recognition and management. In: *ASA Annual Meeting Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2006:412.

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Jagannathan N, Wong DT. Successful tracheal intubation through an intubating laryngeal airway in pediatric patients with airway hemorrhage. *J Emerg Med*. 2011;41(4):369-373.

C.3. How would you monitor blood loss in this patient?

In many of these procedures, the blood loss can be significant and easily exceed the patient's calculated blood volume. It is difficult to accurately measure blood loss when it is lost under the drapes or irrigated away. Meticulous weighing of the sponges and observation of suction canisters are important, but blood loss can be continuous from the time of skin incision and may be seemingly relentless for an inexperienced clinician. Absolute changes in the CVP are a relative guide to the volume in the central compartment, but no one isolated value correlates with a known blood volume. A steady decrease CVP in association with a downward trend in mean arterial blood pressures during periods of surgical intervention known to produce significant bleeding should be treated aggressively with crystalloid (20 mL per kg) or colloid (i.e., 5% albumin) replacement first, followed by a vasopressor supplementation as necessary. Ideally, with an arterial line in place and point of care testing, one can trend the hemoglobin and/or hematocrit prior to the initiation of a blood transfusion. Persistent hypotension with a normal hematocrit could be due to hypocalcemia either from parathyroid hormone insufficiency and/or from the citrate (used as an anticoagulant in the blood products) which binds ionized calcium if the patient was recently transfused.

C.4. What anesthetic technique should be used in a patient who may experience severe loss of blood intraoperatively?

Blood loss should be replaced milliliter for milliliter to prevent falling behind in volume. It is wise to choose an anesthetic technique that produces a relatively stable blood pressure throughout the surgery, so that any new downward trend in blood pressure can be easily

attributable to blood loss and not to pharmacologic action. For instance, if a steady level of desflurane or sevoflurane is given at 1.25 minimal alveolar concentration (MAC) with a resultant mean arterial pressure (MAP) 15% lower than awake, further dips in MAP during surgical intervention can be taken as intravascular volume depletion secondary to bleeding and replaced accordingly. This interpretation would be obscured if there were frequent anesthetic interventions associated with MAP changes, such as intermittent narcotization, relaxant titration, or up and down titration of hypotension-inducing agents. An important clue to the blood volume loss of the patient is the blood pressure at a MAC of anesthesia. If a stable pressure is established at a given MAC of inhalational agent, a lower than expected blood pressure at this MAC is almost always indicative of hypovolemia and therefore calls for fluid or blood replacement. Another anesthetic technique for this procedure on a neonate is to use a high-dose narcotic technique with paralysis, which will lessen the impact of inhalational agents on the MAP. Serial hematocrit determinations drawn throughout the case should guide management. Remember, it is most unusual in an otherwise healthy infant to produce hypotension with intravascular overload unless there are other attendant problems.

C.5. How would you induce and maintain anesthesia in this neonate?

After securing the airway and verifying bilateral breath sounds, narcotic titration with fentanyl should be given in repeated doses. Remember, this neonate may be sensitive to any anesthetic agent because of his cardiovascular anomalies; therefore, titrating fentanyl to the patient's arterial blood pressure via the arterial line decreases the chance of inadvertent drops in perfusion. Because the neonate is not going to be extubated, fentanyl can be safely given 50 μg per kg or higher to allow for dense analgesia. Along those lines, vecuronium and cisatracurium can be given and re-dosed at regular intervals to facilitate the surgical dissection. If tolerated, small concentrations of approximately 0.5% to 4% desflurane or sevoflurane 0.25% to 1.5% can be administered to synergize with the narcotic. The prostaglandin infusion should be maintained throughout the entire surgery.

C.6. Intraoperatively, the surgeon must dissect the tumor in the anterior mediastinum and needs to have a quiet surgical field. How would you accomplish this in the infant?

Double-lumen tubes are not used in the neonatal age group because of the exceedingly small lumen and the technical difficulties of securing both lungs. Instead, a single-lumen endotracheal tube can be advanced to the right or left mainstem bronchus to allow for one-lung ventilation. This may be fraught with consequences in this infant with IAA, but it can still be attempted. Keep in mind that hypoxic pulmonary vasoconstriction may not occur readily in the neonate and excessive shunting may happen. In addition, having an infant on one-lung ventilation may lead to an elevated $PaCO_2$ from the

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pulmonary insufficiency. During thoracotomies in infants for pulmonary banding or Blalock-Taussig shunts, it is not uncommon to see extremely elevated $PaCO_2$ values from lung retraction, especially the right side, which has almost 60% of the total lung surface area.

Engum SA. Minimal access thoracic surgery in the pediatric population. *Semin Pediatr Surg*. 2007;16:14-26.

Lew YS. Paediatric one lung anesthesia by selective bronchial intubation. *Singapore Med J*. 2000;41:398-400.

McGahren ED, Kern JA, Rodgers BM. Anesthetic technique for pediatric thoracoscopy. *Ann Thorac Surg*. 1995;60:927-930.

D. Postoperative Management

D.1. How would you manage this patient postoperatively?

Multiple factors about this case mandate that the neonate remain intubated or have a tracheostomy placed at the end of the case. This surgery involves an extensive dissection of the patient's neck and upper thorax that will result in a tremendous amount of upper airway and neck edema. Consequently, this would make extubation life-threatening. As described in sections C.5 and C.6, high-dose narcotics and paralytics have been used which also hamper

safe extubation. The neonate should continue to remain well-narcotized and paralyzed to coordinate effective mechanical ventilation. Artificial ventilation and oxygen supplementation should be titrated to serial arterial blood gases. In addition, the prostaglandin drip must be continued to ensure ductal patency. The generous narcotic supplementation will ensure that the pulmonary vascular resistance stays in a state of relative quiescence. Approximately 24 hours postoperatively, a leak test can be performed to assess residual vocal cord edema. Fiberoptic visualization of the laryngeal inlet can provide useful information about the state of the laryngeal inlet for extubation.

Anatomic airway factors aside, the IAA and associated CHF will make extubation of this baby more challenging. Assuming all other factors are under control, the following ventilatory parameters should be met before extubation: normal arterial blood gases with satisfactory oxygenation on 28% oxygen, spontaneous tidal volume greater than 5 mL per kg, and inspiratory force greater than 12 cm H_2O. One needs to be vigilant for early signs of airway obstruction and be ready to reintubate or perform emergent tracheostomy if prompt desaturation occurs.

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Chapter 44
Patent Ductus Arteriosus and Prematurity

David Stein

Fun-Sun F. Yao

A 2-week-old male infant weighing 900 g was scheduled for ligation of patent ductus arteriosus (PDA). He was born at 27 weeks' gestation as part of a triplet pregnancy complicated by preterm labor. Immediately after delivery, he was intubated because of respiratory distress. He was given indomethacin prophylactically because of his prematurity and presumed PDA. A transthoracic echocardiogram (TTE) confirmed the patency of the ductus arteriosus and demonstrated its closure after one course of indomethacin. His respiratory function was gradually improving with ventilatory support until 2 weeks later when his oxygenation and ventilation suddenly worsened. A murmur was heard over his chest. A repeat TTE demonstrated left-to-right shunting through the ductus arteriosus. Another course of indomethacin was administered, but the ductus remained patent. His blood pressure was 50/20 mm Hg; heart rate, 165 beats per minute. The laboratory data were as follows: white blood cell (WBC) count, 17,000 per μL; hemoglobin, 11 g per dL; hematocrit, 34%; urine specific gravity, 1.005; protein, 1+; sugar, 1+; serum calcium, 6.0 mg per dL; blood glucose, 60 mg per dL; arterial blood gases: pH, 7.30; $PaCO_2$, 60 mm Hg; PaO_2, 49 mm Hg on FIO_2 50%, inspiratory pressure, 19/6 cm H_2O; and ventilation rate, 40 breaths per minute.

A. Medical Disease and Differential Diagnosis

1. How would you classify prematurity? What are the common problems associated with prematurity?
2. What are the survival rates of preterm infants?
3. What are the incidence and survival rates of respiratory distress syndrome (RDS)? Discuss its pathophysiology.
4. What is bronchopulmonary dysplasia (BPD)? How would you treat it?
5. What are apnea spells? What are the possible causes of apneic spells?
6. Discuss the incidence and pathophysiology of PDA in preterm infants.
7. How would you make a diagnosis of PDA? Describe its treatment.
8. Would you give digitalis to treat congestive heart failure in preterm infants? Why?
9. How does indomethacin close the ductus? What are the adverse effects of indomethacin?
10. What is retinopathy of prematurity (ROP) (retrolental fibroplasia [RLF])? Discuss its etiology, pathophysiology, prognosis, and prevention.
11. Define neutral and critical temperatures. What are these values in the preterm neonate, in the term neonate, and in the adult? Discuss temperature regulation in the neonate.

B. Preoperative Evaluation and Preparation

1. How would you evaluate this patient preoperatively?
2. What are the normal values of arterial blood gases and pH in preterm and term pediatric patients?

3. Interpret the arterial blood gases: pH, 7.30; $PaCO_2$, 60 mm Hg; PaO_2, 49 mm Hg; HCO_3^-, 20 mEq per L on 50% oxygen; and 6 cm H_2O of positive end-expiratory pressure (PEEP). How would you improve them?
4. What are the normal values of arterial blood pressure, heart rate, and respiratory rate for preterm infants?
5. What are the normal values of WBC, red blood cells (RBCs), hemoglobin, glucose, electrolytes, calcium, blood urea nitrogen, and creatinine for preterm infants?
6. Would you transfuse blood to this patient preoperatively?

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7. How would you interpret the urinalysis: specific gravity, 1.005; sugar, 1+; and protein, 1+?
8. Would you correct a serum calcium level of 6.0 mg per dL? What other information would you like to have? Which contains more calcium, 10 mL of 10% calcium chloride or 10 mL of 10% calcium gluconate? Could you hyperventilate this child safely?
9. How would you premedicate this patient?

C. Intraoperative Management

1. What monitors would you use for this child during surgery?
2. How does the oxygen analyzer work?
3. What is the Doppler effect? How does the Doppler transducer measure blood pressure?
4. What is the mechanism of pulse oximetry? Why is it important to monitor arterial oxygen saturation? What levels of arterial oxygen saturation would you like to keep during surgery?
5. How would you maintain the patient's body temperature?
6. How do the anesthetic requirements of the preterm infant differ from those of the adult?
7. What size endotracheal tube would you have used if the patient had not been intubated?
8. How would you have induced anesthesia if the patient had not been intubated?
9. How would you maintain anesthesia?
10. How would you ventilate the patient? What tidal volume, respiratory rates, and FIO_2 would you set for the infant?
11. Discuss blood and fluid therapy in this preterm infant.
12. During dissection of the ductus arteriosus, the arterial oxygen saturation dropped from 92% to 80% and the heart rate decreased from 140 beats per minute to 80 beats per minute. What were the causes? How would you correct this situation?

D. Postoperative Management

1. Would you reverse the muscle relaxants and extubate the patient at the end of surgery?
2. How can one minimize the risk of transporting the patient to the neonatal intensive care unit (ICU) after surgery?
3. The patient's condition deteriorated postoperatively in the ICU. Physical examination revealed persistent cardiac murmur. What was the possible diagnosis?

A. Medical Disease and Differential Diagnosis

A.1. How would you classify prematurity? What are the common problems associated with prematurity?

Live born infants delivered before 37 weeks from the first day of the last menstrual period are termed premature by the World Health Organization. Preterm infants can be classified into three groups, as shown in Table 44.1. Infants of borderline prematurity usually require no special care, but, because of their susceptibility to RDS, they should be observed closely

for 24 to 48 hours in the newborn nursery. Further, those with a poor suck reflex may require gavage feedings. Infants classified as moderately premature require intense neonatal care, and neonatal mortality correlates inversely with gestational age. Neonates of extreme prematurity constitute only 1% of all preterm infants; however, mortality in this group is extremely high, accounting for greater than 70% of all neonatal deaths. Furthermore, morbidity in surviving infants is substantial, often secondary to irreversible neurologic or respiratory insult.

TABLE 44.1 Classification of Prematurity

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	BORDERLINE PREMATURITY	MODERATE PREMATURITY	EXTREME PREMATURITY
Gestational age (wk)	36-37	31-35	24-30
Percentage live births	16%	6%-7%	<1%
Weight (g)	2,500-3,200	1,500-2,500	500-1,500
Associated problems	Poor suck	Poor suck	Poor suck
	RDS	RDS	RDS
	Temperature regulation	Temperature regulation	Temperature regulation
		Sepsis	Sepsis
		Intracranial hemorrhage	Intracranial hemorrhage
			Necrotizing enterocolitis
			Congestive heart failure
			Birth asphyxia
Level of care	Careful observation in newborn nursery	Neonatal ICU	Neonatal ICU

ICU, intensive care unit; RDS, respiratory distress syndrome.

Coté C, Lerman J, Anderson B. *Coté and Lerman's A Practice of Anesthesia in Infants and Children* . 5th ed. Philadelphia, PA: Saunders/Elsevier; 2013:733.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:475-476.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics* . 20th ed. Philadelphia, PA: WB Saunders; 2015:818.e1-831.e1.

A.2. What are the survival rates of preterm infants?

The survival rates of preterm infants depend mainly on their maturity or birth weights. Because of the advancement in neonatal care, survival rates have increased twofold in the last two decades. Recently, the survival rates for infants with birth weights 500 to 750 g, 750 to 1,000 g, 1,000 to 1,250 g, 1,250 to 1,500 g, and 1,500 to 2,000 g have been approximately 53.9%, 86.3%, 94%, 96.8%, and 97%, respectively. Recent reports showed the survival rates for premature infants born at 24, 25, and 26 weeks' gestation to be 43%, 74%, and 83%, respectively.

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Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: WB Saunders; 2015:819.

Lemons JA, Bauer CR, Oh W, et al; for the NICHD Neonatal Research Network. Very low birth weight outcomes of the National Institute of Child Health and Human Development Neonatal Research Network, January 1995 through December 1996. *Pediatrics*. 2001;107:E1.

A.3. What are the incidence and survival rates of respiratory distress syndrome (RDS)? Discuss its pathophysiology.

RDS, formerly called hyaline membrane disease, is common in preterm infants. RDS is a life-threatening condition associated with 50% to 75% of all deaths of premature infants. It occurs three times more often in those born by cesarean section than in those born vaginally. The incidence of RDS depends on the birth weight. It happens in 86% of preterm infants

weighing 501 to 750 g; 79% of preterm infants weighing 751 to 1,000 g; 48% of preterm infants weighing 1,001 to 1,250 g; and 27% of preterm infants weighing 1,251 to 1,500 g.

The survival rate has increased dramatically over the last 50 years. Survival depends on the infant's size. Ninety percent of those weighing 900 to 1,000 g survive, whereas approximately 70% of those weighing 500 to 700 g survive. Recently, an increase in survival and a decrease in severity of RDS have been associated with maternal steroid administration and routine administration of exogenous surfactant into the lungs of neonates of less than 28 weeks' gestation at birth. This may pose a problem for the anesthesiologist if these patients require surgery. Ventilation with high positive pressures and large volumes increases the likelihood of pulmonary gas leaks, pneumothorax, and lung injury.

Physical examination of the infant with RDS will likely reveal cyanosis, tachypnea, intercostal retractions, and bilateral rales that fail to clear with suctioning. An arterial blood gas sample will demonstrate hypoxemia, metabolic acidosis, and respiratory alkalosis; a chest radiograph will show diffuse, hazy (“ground glass”) infiltrates.

Deficiency of the alveolar phospholipid surfactant is thought to be the cause of RDS. The surfactant is produced by the type II alveolar cells and is necessary for the maintenance of alveolar stability. Surfactant production is usually inadequate before 35 weeks of gestational age. In its absence, alveolar collapse and a decrease in functional residual capacity (FRC) occur, with consequent right-to-left shunting, arterial hypoxemia, and metabolic acidosis. Administration of betamethasone to women 48 hours before the delivery of fetuses less than 34-week gestation significantly reduces the incidence, mortality, and morbidity of RDS.

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Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:477-478.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:589-590.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: WB Saunders; 2015:848.e2-867.e2.

A.4. What is bronchopulmonary dysplasia (BPD)? How would you treat it?

BPD is defined as oxygen dependence at 36 weeks' postconceptual age with oxygen requirements to maintain PaO_2 >50 mm Hg beyond 28 days of life in infants with birth weight less than 1,500 g. BPD is a chronic lung disease as a result of mechanical ventilation, oxygen toxicity, infection, or a combination of these factors. It includes interstitial fibrosis, lobar emphysema, and components of reactive airway disease, and may render the baby oxygen, steroid, or ventilator dependent. With progressive disease, it may lead to pulmonary hypertension and right heart failure. It usually progresses

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through four stages:

Stage I: At 2 to 3 days of age, the chest radiograph shows classic RDS. There are atelectasis, hyaline membrane, hyperemia, lymphatic dilation, metaplasia, and necrosis of bronchiolar mucosa.

Stage II: At 4 to 10 days of age, the chest radiograph shows obscure cardiac borders and nearly complete opacification of lung fields. The pathology reveals necrosis and repair of epithelium, persisting hyaline membrane, emphysematous coalescence of alveoli, and thickening of alveolar and capillary membranes.

Stage III: At 10 to 20 days of age, the chest radiograph shows small rounded areas of spongelike radiolucency. There are few hyaline membranes, regeneration of clear cells, bronchiolar metaplasia, mucus secretion, emphysematous alveoli, and focal thickening of basement membrane.

Stage IV: After 30 days of age, the radiolucent areas seen in stage III enlarge and alternate with thin strands of radiodensity. The pathology reveals emphysematous alveoli and marked hypertrophy of epithelium.

BPD causes maldistribution of ventilation and perfusion, resulting in hypoxemia and hypercarbia. The treatment is supportive. The goals of treatment are to minimize the FIO_2 and

mean airway pressure, reduce the amount of lung water with diuretics (furosemide 5 to 10 mg per kg every 6 hours), and support cardiac contractility with inotropes.

Andropoulos D, Stayer S, Russell I, et al, eds. *Anesthesia for Congenital Heart Disease*. 2nd ed. West Sussex, United Kingdom: Wiley-Blackwell; 2010:253.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:478.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:590-591.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: WB Saunders; 2015:848.e2-867.e2.

A.5. What are apnea spells? What are the possible causes of apneic spells?

Apnea spells are defined as cessation of breathing lasting more than 20 seconds or more than 10 seconds and produces oxygen desaturation and bradycardia. Apneic spells are common in preterm infants, especially after the first week of life and almost universal in infants who are less than 1,000 g at birth. The causes are multiple and include the following:

- Hypothermia or hyperthermia
- Hypoglycemia or hyperglycemia
- Hypocalcemia or hypercalcemia
- Hypovolemia or hypervolemia
- Anemia
- Decreased FRC
- PDA
- Constipation
- Hypothyroidism
- Immature brainstem function
- Lack of type I muscle fibers in diaphragm
- Excessive handling

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- Sepsis
- Gastroesophageal reflux disease

Repeated apnea increases the likelihood of central nervous system damage because of repeated episodes of hypoxemia. Infants who have apneic spells do not breathe during anesthesia; therefore, they should be ventilated throughout anesthesia, including the induction phase. Inhaled and intravenous anesthetics affect the control of breathing and contribute to upper airway obstruction, thereby increasing the likelihood of apnea during the postoperative period, especially in preterm infants less than 60 weeks postconception age.

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Finer NN, Higgins R, Kattwinkel, et al. Summary proceedings from the apnea-of-prematurity group. *Pediatrics*. 2006;117:47-51.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:478-479.

A.6. Discuss the incidence and pathophysiology of PDA in preterm infants.

Fifty percent of infants weighing less than 1,000 g and 20.2% of infants under 1,750 g have hemodynamically significant PDA. In term infants, the ductus arteriosus closes soon after birth in response to the increased arterial oxygen tension. However, in preterm infants, it has a thinner, poorly contractile muscular layer with diminished responsiveness to the increasing oxygen levels after birth. In addition, preterm infants often suffer from hypoxemia because of RDS, so that there are both a reduced stimulus to and a reduced response to physiologic closure. As many as 20% of neonates with RDS have a PDA. However, on the third to fifth day of life, some resolution of the RDS usually occurs, with a concurrent decrease in pulmonary

resistance. This allows blood shunting from the systemic to the pulmonary circulation by way of the PDA, resulting in pulmonary vascular overload and ultimately left heart failure. The pulmonary congestion worsens respiratory failure, resulting in further hypoxemia and CO_2 retention.

Andropoulos DN, Stayer SA, Russell IA, et al, eds. *Anesthesia for Congenital Heart Disease*. 2nd ed. West Sussex, United Kingdom: Wiley-Blackwell; 2010:253.

Coté C, Lerman J, Anderson B. *Coté and Lerman's A Practice of Anesthesia in Infants and Children* . 5th ed. Philadelphia, PA: Saunders/Elsevier; 2013:742-743.

A.7. How would you make a diagnosis of PDA? Describe its treatment.

The diagnosis of PDA in preterm infants may be suspected when there is sudden increase in respiratory failure, tachycardia, tachypnea, and a widened pulse pressure. The typical continuous or machinery murmur of PDA is usually not present in this population, but a systolic murmur, sometimes extending into diastole, and a hyperdynamic precordium are nearly always present. The diagnosis is confirmed by echocardiography that demonstrates left atrial enlargement. Two-dimensional echocardiography can identify the aortic end of the ductus. Continuous-wave Doppler can detect abnormal flow in the pulmonary artery. Color Doppler can visualize the jet of abnormal flow.

The initial treatment of PDA is medical. It includes fluid restriction and administration of diuretics and indomethacin. Indomethacin, 0.1 to 0.2 mg per kg, three doses for every 12 hours, usually closes the ductus within 24 hours. If the ductus fails to close with medical treatment, surgical ligation is indicated. There is now the option of percutaneous closure of PDA with an AMPLATZER Duct Occluder.

Andropoulos D, Stayer S, Russell I, et al, eds. *Anesthesia for Congenital Heart Disease*. 2nd ed. West Sussex, United Kingdom: Wiley-Blackwell; 2010:374.

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Pass RH, Hijazi Z, Hsu DT, et al. Multicenter USA Amplatzer patent ductus arteriosus occlusion device trial: initial and one-year results. *J Am Coll Cardiol*. 2004;44:513-519.

A.8. Would you give digitalis to treat congestive heart failure in preterm infants? Why?

Digitalis should not be given to small preterm infants because it does not effectively improve stroke volume or ventricular emptying. However, it does decrease the heart rate, resulting in detrimental decrease in cardiac output. Meanwhile, digitalis toxicity increases mortality in preterm infants.

Berman W Jr, Dubynsky O, Whitman V, et al. Digoxin therapy in low-birth-weight infants with patent ductus arteriosus. *J Pediatr*. 1978;93:652-655.

A.9. How does indomethacin close the ductus? What are the adverse effects of indomethacin?

The ductus arteriosus functionally closes shortly after birth in term infants when the vascular smooth muscle contracts. The muscular contraction of the ductus is initiated by the increased oxygen content and is influenced by other factors, such as release of vasoactive substances, the relative resistances in the aorta and pulmonary artery, and the differences in sensitivity of the vessel to oxygen. The ductus arteriosus produces several prostaglandins, including PGI_2 and PGE_2; both prostaglandins relax the smooth muscle of the ductus and keep the ductus patent. Meanwhile, the ductus of preterm infants is far more sensitive to the vasodilating effects of prostaglandins than is the ductus of term infants. Indomethacin is one of the most potent inhibitors of the prostaglandin-forming cyclooxygenase. Therefore, indomethacin decreases the synthesis of prostaglandins, resulting in closure of the ductus. Adverse effects of indomethacin include decreased mesenteric, renal, and cerebral blood

flow. Ibuprofen is another nonselective cyclooxygenase inhibitor that can be used effectively to treat PDA and has less side effects on organ blood than indomethacin, although there is no clinical data to support its use in place of indomethacin.

Clyman RI. Ontogeny of the ductus arteriosus response to prostaglandins and inhibitors of their synthesis. *Semin Perinatol*. 1980;4:115-124.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:53.

Wyllie J. Treatment of patent ductus arteriosus. *Semin Neonatol*. 2003;8:425-432.

A.10. What is retinopathy of prematurity (ROP) (retrolental fibroplasia [RLF])? Discuss its etiology, pathophysiology, prognosis, and prevention.

Some degree of ROP occurs in approximately 50% of infants weighing 1,000 to 1,500 g at birth, 78% of those weighing 750 to 999 g, and more than 90% of those weighing less than 750 g. At stage 3, ROP was not noted in infants with birth weight more than 1,500 g. No ROP was noted in infants born more than 32 weeks' gestational age. ROP begins with retinal vascular obliteration, which is followed by increased vascularity, hemorrhage, cicatrization, and finally retinal detachment. ROP refers to all stages of the disease and its sequelae. RLF, the term previously used for this disease,

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described only the cicatricial stages.

The factors that cause ROP and determine its outcome are not fully known, but prematurity, the degree of retinal immaturity at birth, and days on supplemental oxygen therapy are major factors. Other contributing factors include respiratory distress, apnea, bradycardia, heart disease, infection, hypoxia, hypercarbia, acidosis, anemia, and the need for transfusion. The presence of fetal hemoglobin may protect against ROP, and patients transfused with adult blood may be at great risk for developing ROP. Generally, the lower the birth weight and the sicker the infant, the greater the risk for ROP.

The retinal vasculature in the developing fetus spreads outward from the optic disc, reaching the nasal side of the retinal periphery by 36 weeks' gestational age and the temporal side at 40 weeks. Classically, it was postulated that hyperoxia constricts the retinal arterioles, resulting in swelling and degeneration of the endothelium. This causes paradoxical retinal ischemia in spite of systemic hyperoxia. When normoxic conditions are restored, vascularization resumes in an aberrant manner, leading to retinal detachment and blindness. ROP is divided into five stages:

Stage 1: A thin white line separates the posterior vascularized portion of the retina from the anterior avascular retina.

Stage 2: The demarcation line increases in volume and elevates. At this point, it is known as the “ridge.” The changes in stage 1 and 2 regress in 80% of patients. Between 5% and 10% of premature infants with stage 1 and 2 disease progress to stage 3.

Stage 3: Tissue proliferation develops from the ridge, usually posteriorly. Stage 3 can be mild, moderate, or severe, depending on the volume of the extraretinal tissue.

Stage 4: Partial retinal detachment occurs with the macula still attached (stage 4a). The macula is detached in stage 4b.

Stage 5: Total retinal detachment occurs.

Eighty-five percent of ROP cases undergo spontaneous recovery. Mild ROP regresses in 2 to 3 months, and moderate ROP in 6 months. The most severe ROP usually results in blindness or limited vision.

It is unclear what level of PaO_2 causes ROP, but a PaO_2 of 150 mm Hg for as short a time as 1 to 2 hours can do so. Furthermore, the retinal vessels of these neonates certainly constrict maximally with a PaO_2 of 100 mm Hg. In addition, it is also possible that ROP will develop at lower PaO_2 levels because infants of this age are normally exposed to a much lower PaO_2 (30 to 40 mm Hg) in utero than the levels found during the neonatal period. Therefore, in order to reduce the possibility of ROP, it is wise to maintain the PaO_2 levels between 50 and 70 mm Hg or the saturation of oxygen (SaO_2) between 87% and 92% for infants <44 to 50 weeks' gestation.

TABLE 44.2 Neutral and Critical Temperature

	NEUTRAL TEMPERATURE (°C)	CRITICAL TEMPERATURE (°C)
Preterm neonate	34	28
Term neonate	32	23
Adults	28	1

However, prevention of ROP ultimately depends on the prevention of premature birth and its attendant problems. Oxygen alone is neither sufficient nor necessary to produce ROP, and no safe level of oxygen has yet been determined. Each infant must be treated with whatsoever is necessary to sustain life and neurologic function. Some investigations have suggested the use of vitamin E for its antioxidant effects in infants at risk for ROP. However, its efficacy has not been proved.

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Betts EK, Downes JJ, Schaffer DB, et al. Retrolental fibroplasia and oxygen administration during general anesthesia. *Anesthesiology*. 1977;47:518-520.

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Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:482-483.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:591-592.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics* . 20th ed. Philadelphia, PA: WB Saunders; 2015:3049.e1-3057.e1.

A.11. Define neutral and critical temperatures. What are these values in the preterm neonate, in the term neonate, and in the adult? Discuss temperature regulation in the neonate.

Neutral temperature is the ambient temperature that results in minimal oxygen consumption. Critical temperature is the ambient temperature below which an unclothed, unanesthetized individual cannot maintain a normal core temperature (see Table 44.2).

Normally, body heat is lost by conduction, convection, radiation, and evaporation. The neonate is particularly susceptible to heat loss owing to a large surface: volume ratio, lack of insulating fat, and naturally flaccid and open posture. When stressed by a cold environment, vasoconstriction occurs, but the neonate is unable to shiver. Further cold stress stimulates norepinephrine release, promoting the exothermic metabolism of brown fat deposits in an attempt to maintain core temperature. Continued cold stress often results in episodes of bradycardia, apnea, hypoglycemia, and metabolic acidosis.

When the infant's rectal temperature reaches 36.6°C to 37.3°C (97.88°F to 99.14°F), dilation of peripheral vessels occurs. The term neonate will perspire at 37.2°C (98.96°F) in an attempt to maintain a normal core temperature, whereas those infants born before 37 weeks' gestation are unable to sweat.

Coté C, Lerman J, Anderson B. *Coté and Lerman's A Practice of Anesthesia in Infants and Children* . 5th ed. Philadelphia, PA: Saunders/Elsevier; 2013:737.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:477.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:584-585.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate this patient preoperatively?

The preoperative evaluation of preterm infants should be based on a clear understanding of the pathophysiology of prematurity. The preoperative evaluation of this patient should begin

with a careful review of the medical record, followed by a systematic physical examination and laboratory evaluation, specifically:

- *History*—birth trauma, asphyxia, maternal drug history, respiratory, cardiovascular, and fluid status
- *Physical examination*—evaluation of the airway, cardiopulmonary system, fluid status (skin texture, turgor, mucous

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membranes, and fontanelles), and abdominal examination

- *Laboratory data*—WBC count; hemoglobin and hematocrit; serum electrolytes; serum coagulation profile, including prothrombin time, partial thromboplastin time, and platelet count; serum calcium and serum protein; arterial blood gases; urinalysis and urine-specific gravity; and chest and abdominal radiographs

B.2. What are the normal values of arterial blood gases and pH in preterm and term pediatric patients?

The normal blood gas and pH values for pediatric patients are shown in Table 44.3. The normal pH and $PaCO_2$ values for pediatric patients are similar to those for adults, whereas the normal PaO_2 values are lower in pediatric patients than in adult patients.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:485,1302-1303.

B.3. Interpret the arterial blood gases: pH, 7.30; $PaCO_2$, 60 mm Hg; PaO_2, 49 mm Hg; HCO_3^-, 20 mEq per L on 50% oxygen; and 6 cm H_2O of positive end-expiratory pressure (PEEP). How would you improve them?

The blood gases show respiratory and metabolic acidosis. The PaO_2 of 49 mm Hg is low but acceptable for preterm infants with chronic lung disease. In order to prevent ROP, it is wise to keep PaO_2 between 50 and 70 mm Hg. $PaCO_2$ of 60 mm Hg indicates hypoventilation, which can be corrected by increasing respiratory rate or tidal volume. In order to avoid the pulmonary oxygen toxicity, FIO_2 should be lowered to less than 40% by increasing levels of PEEP. Mild metabolic acidosis may be corrected by hyperventilation and by improving fluid balance and circulation.

B.4. What are the normal values of arterial blood pressure, heart rate, and respiratory rate for preterm infants?

The blood pressure is related to the size of infants, as shown in Table 44.4. The heavier the birth weight, the higher the blood pressure is. The normal heart rate is 120 to 160 beats per minute. The respiratory rate is normally between 30 and 60 breaths per minute. However, it can increase to 100 to 150 breaths per minute depending on how severely the lung compliance is decreased.

Coté C, Lerman J, Anderson B. *Coté and Lerman's A Practice of Anesthesia in Infants and Children* . 5th ed. Philadelphia, PA: Saunders/Elsevier; 2013:14-15.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:210-211.

B.5. What are the normal values of WBC, red blood cells (RBCs), hemoglobin, glucose, electrolytes, calcium, blood urea nitrogen, and creatinine for preterm infants?

The WBC count usually ranges from 9,000 to 30,000 per μL at birth and decreases to 5,000 to 20,000 per μL during the fifth week of life.

TABLE 44.3 Normal Values of Arterial Blood Gases and pH in Pediatric Patients

AGE	PRETERM	TERM	1 MONTH	1 YEAR
pH	7.37 ± 0.03	7.40 ± 0.02	7.41 ± 0.04	7.39 ± 0.02

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PaO_2 (mm Hg)	60 ± 8	70 ± 11	95 ± 8	93 ± 10
$PaCO_2$ (mm Hg)	37 ± 6	39 ± 7	40 ± 6	41 ± 7

TABLE 44.4 Normal Blood Pressure of Infants Weighing between 1,000 and 4,000 g

	BIRTH WEIGHT (g)			
	1,000	**2,000**	**3,000**	**4,000**
Systolic BP (mm Hg)	50 ± 10	55 ± 10	60 ± 10	70 ± 10
Diastolic BP (mm Hg)	25 ± 10	30 ± 10	35 ± 10	40 ± 10
Mean BP (mm Hg)	35 ± 10	40 ± 10	45 ± 10	50 ± 10

BP, blood pressure.

The normal RBC and hemoglobin are 5.1 ± 1.0 × 10^6 per μL and 19.5 ± 5.0 g per dL, respectively, at birth and decrease to 4.5 ± 0.7 × 10^6 per μL and 12.2 ± 2.3 g per dL, respectively, at 3 months of age. At birth, most of the hemoglobin is fetal hemoglobin, which has a greater affinity for oxygen. Therefore, the oxygen saturation (and content) of blood for a given PaO_2 is higher. By 7 months of age, the circulating hemoglobin is of the adult type.

The normal blood glucose level is between 45 and 90 mg per dL. A glucose level below 40 mg per dL is common in preterm infants. It should be corrected with a bolus of 10% to 20% glucose (2 to 5 g per kg) given over 5 minutes, followed by a continuous infusion of glucose. Severe hypoglycemia (<10 mg per dL) may cause brain damage.

The serum calcium concentration of preterm infants is normally lower than that of term infants because preterm infants have decreased serum proteins. Normal calcium level is over 8.0 mg per dL.

The normal values of sodium, potassium, and chloride are 135 to 145, 3.0 to 5.0, and 105 to 115 mEq per L, respectively.

The creatinine levels of term infants at birth are 0.6 to 1.2 mg per dL but, within 1 month, fall to levels of 0.1 to 0.2 mg per dL. Preterm infants have relatively high serum creatinine levels compared with term infants. They are 0.8 to 1.8 mg per dL at birth and fall to 0.2 to 0.8 mg per dL in 1 month.

The normal blood urea nitrogen level is 10 to 20 mg per dL in term infants, whereas it is 16 to 28 mg per dL in preterm infants.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:1300-1314.

B.6. Would you transfuse blood to this patient preoperatively?

The patient had a hemoglobin of 11 g per dL; we would not transfuse blood to this patient. To ensure oxygen-carrying capacity, most clinicians agree that a hemoglobin of 10 g per dL is the lowest acceptable level if cardiorespiratory disease exists. If infants are well, a hemoglobin level of above 7.0 g per dL is usually tolerable.

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Coté C, Lerman J, Anderson B. *Coté and Lerman's A Practice of Anesthesia in Infants and Children* . 5th ed. Philadelphia, PA: Saunders/Elsevier; 2013:737.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:244.

B.7. How would you interpret the urinalysis: specific gravity, 1.005; sugar, 1+; and protein, 1+?

In infants weighing 1,000 to 3,300 g, the normal urine-specific gravity is 1.005 to 1.010. A urine specific gravity of greater than 1.020 suggests dehydration.

Glucosuria 1+ normally presents in 13% of preterm infants who are less than 34 weeks' gestational age because the preterm infant has a decreased renal tubular reabsorption for glucose. After 34 weeks of gestational age, glucosuria is usually associated with serum hyperglycemia.

Albumin is normally filtered by the glomerulus and is completely reabsorbed. However, because of tubular immaturity, 16% to 21% of preterm infants have proteinuria.

Coté C, Lerman J, Anderson B. *Coté and Lerman's A Practice of Anesthesia in Infants and Children* . 5th ed. Philadelphia, PA: Saunders/Elsevier; 2013:555-568, 737.

B.8. Would you correct a serum calcium level of 6.0 mg per dL? What other information would you like to have? Which contains more calcium, 10 mL of 10% calcium chloride or 10 mL of 10% calcium gluconate? Could you hyperventilate this child safely?

Normally, the serum calcium is maintained at 8.0 mg per dL; however, in the preterm infant, a level of 7.0 mg per dL is acceptable. This child's serum calcium is 6.0 mg per dL. Therefore, supplementation with 30 to 100 mg per kg of calcium gluconate or 10 to 20 mg per kg of calcium chloride is appropriate.

Hypocalcemia in neonate is defined as serum calcium less than 3.5 mEq per L or serum ionized calcium less than 1.5 mEq per L. When evaluating the serum calcium levels, it is important to know the serum protein concentration; neonatal hypocalcemia is usually due to hypoproteinemia. It is also important to determine the ionized calcium concentration (usually 45% of the total calcium concentration) because this is the calcium immediately available at the cellular level. The chloride molecule is approximately one-third the weight of the gluconate molecule. For this reason, approximately three times more calcium is given when an equivalent volume of calcium chloride is administered instead of 10% calcium gluconate. Respiratory alkalosis following hyperventilation will reduce serum ionized calcium levels and, for this reason, should be avoided in this infant.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:481.

B.9. How would you premedicate this patient?

Children under 1 year of age do not usually need sedation. However, atropine, 0.01 to 0.02 mg per kg, may be given to attenuate the vagal response to a host of different stimuli.

Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:412-416.

C. Intraoperative Management

C.1. What monitors would you use for this child during surgery?

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Proper monitoring of this child for safe administration of anesthesia includes the following:

- *Respiratory*—precordial or esophageal stethoscope, end-tidal CO_2, inspiratory oxygen monitor, pulse oximeter, arterial blood gases, inspiratory pressure gauge
- *Cardiovascular*—precordial or esophageal stethoscope, electrocardiogram, blood pressure cuff and Doppler transducer, and urinary bag
- *Thermoregulatory*—esophageal or axillary temperature probe with servoloop overhead heater, and thermal blanket

If the patient has an umbilical artery catheter in place, it is useful for the measurement of blood pressure and arterial blood gases. However, it is probably unnecessary to establish an arterial line for the surgery alone because invasive monitoring in this age group is not without risk.

C.2. How does the oxygen analyzer work?

Oxygen analysis can be done by either parametric or amperometric analysis. Parametric analysis is based on the fact that oxygen is a dipole molecule. When a gas containing oxygen is passed through a magnetic field, the gas is deflected in proportion to the concentration of oxygen. Sensors can detect this deflection and give a readout of oxygen concentration. Amperometric analysis can be done with one of the two devices: the galvanic cell analyzer and the polarographic cell analyzer. In the galvanic or fuel cell analyzer, oxygen diffuses through a membrane of the sensor into an electrolyte solution from which the oxygen absorbs electrons and forms hydroxide ions. The hydroxide ions then diffuse to a lead anode where oxidation to lead oxide and water occurs with the resultant liberation of free electrons. An electron flow (current) is thereby generated between the anode and the cathode, which

is proportional to the oxygen level at the sensor. This current is directly displayed by a meter that indicates oxygen percentage. These devices are relatively inexpensive to purchase but carry a high operating cost because the sensor is eventually exhausted and must be replaced.

The polarographic cell, or Clark electrode, uses a battery to induce a negative potential of 0.75 V between the anode and the cathode. As oxygen diffuses across a membrane and into the electrolyte solution separating the anode and cathode, the polarizing voltage at the cathode causes electrons to combine with oxygen molecules, reducing them to hydroxide ions. The hydroxide ions then move to the anode, causing electron flow (current) that is proportional to the initial oxygen concentration. This flow is read by a meter that translates to oxygen percentages. These monitors are initially more expensive than galvanic cell monitors, but they are less expensive to maintain, requiring only inexpensive electrolyte solution and battery replacement.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier; 2015:1315-1344. Saidman LJ, Smith NT, eds. *Monitoring in Anesthesia*. 3rd ed. Boston, MA: Butterworth-Heinemann; 1993:384.

C.3. What is the Doppler effect? How does the Doppler transducer measure blood pressure?

In 1841, Christian Doppler noted the change in observed frequency from a constant frequency sound generator when the source moved with respect to the observer. Ballot confirmed this “Doppler effect” in 1845 with the simple example of the frequency increase in a train's steam whistle as the train approached an observer. In the 1960s, a practical ultrasonic system for transducing arterial wall motion was described to obtain blood pressure. The ultrasonic system consists of an occlusive cuff and a dual crystal ultrasonic transducer placed over the artery distal to the occlusion. One crystal transmits the ultrasonic signal, whereas the other receives the signal reflected from the artery. Although the cuff occludes the artery, there is no arterial wall movement and the crystal receives a signal with an unchanged frequency. When the cuff pressure falls below systolic pressure, arterial wall motion occurs, causing a Doppler frequency shift, indicating systolic blood pressure. When the cuff pressure falls to diastolic pressure, the artery is open throughout the cycle: Rhythmic arterial opening and closing does not occur and there is a loss of Doppler frequency shift. Therefore, one can easily and accurately obtain systolic and diastolic blood pressure.

Miller RD, Cohen NH, Eriksson L, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier; 2015:1325. Saidman LJ, Smith NT, eds. *Monitoring in Anesthesia*. 3rd ed. Boston, MA: Butterworth-Heinemann; 1993:121.

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C.4. What is the mechanism of pulse oximetry? Why is it important to monitor arterial oxygen saturation? What levels of arterial oxygen saturation would you like to keep during surgery?

The mechanism of pulse oximetry is described in Chapter 2, section C.10 and Chapter 59, section A.5.

Safe anesthesia practice requires the monitoring of arterial oxygen saturation in all patients to prevent hypoxia. However, in infants of less than 44 to 50 weeks' gestation, it is also vital to guard against hyperoxia, which may cause ROP.

The arterial oxygen saturation should be kept between 86% and 92% (some say 85% to 95%).

Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:412-416.

Purohit DM, Ellison RC, Zierler S, et al. Risks of retrolental fibroplasia: experience with 3,025 premature infants. *Pediatrics*. 1985;76:339.

C.5. How would you maintain the patient's body temperature?

Hypothermia greatly increases the metabolic rate and oxygen consumption of preterm infants. The preterm infant is particularly susceptible to heat loss because of a large surface-tovolume ratio, lack of insulating fat, and a naturally flaccid and open posture. In addition, the preterm infant often has impaired thermal regulatory ability; therefore, all precautions must be taken to ensure normothermia. The patient may be transported to the operating room in a

battery-operated transport incubator if available. Otherwise, the infant should be covered with Saran Wrap and a warm blanket, and a cap should be put on his head to prevent heat loss. The operating room should be warmed to 35°C to 37°C (95°F to 98.6°F) and a servo-controlled infrared heater placed over the operating table. A water-circulating heating blanket should be put under the table sheet and kept at 37°C to 38°C (98.6°F to 100.4°F). All extremities should be wrapped in sheet wadding. All intravenous fluids and inspired gases should be warmed and humidified to help maintain the patient's body temperature. If the facility is available, then in the very low birth weight infants, the procedure can be done at the bedside with the appropriate equipment and using the ICU ventilator for airway management. This helps minimize the risks associated with transportation and also minimize the incidence of hypothermia.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:341-342.

C.6. How do the anesthetic requirements of the preterm infant differ from those of the adult?

Achieving proper anesthetic depth in the preterm infant presents a unique challenge to the anesthesiologist. Whereas anesthetic requirements (as determined by minimal alveolar concentration) are decreased in the preterm infant as compared with the adult, possibly due to immaturity of the central nervous system and to increase circulating concentrations of progesterone and *β*-endorphins. Cardiovascular sensitivity is greatly pronounced because of greater myocardial depression and a reduced peripheral response to catecholamines. Further, the baroreceptor reflex, often poorly developed in the preterm infant, is totally ablated by even light levels of inhalation anesthesia. Therefore, the preterm infant is extremely susceptible to anesthetic overdose, which produces cardiovascular depression leading to hypotension or cardiovascular collapse.

Unfortunately, an inadequate depth of anesthesia is also uniquely hazardous in the neonate. Because there is a lack of cerebral autoregulation, any systemic hypertension from inadequate depth of anesthesia may be transmitted directly to the cerebral circulation, resulting in intraventricular hemorrhage.

For these reasons, it is essential to carefully tailor anesthetic depth to surgical conditions, because the therapeutic margin between underdose and overdose is extremely narrow.

Coté C, Lerman J, Anderson B. *Coté and Lerman's A Practice of Anesthesia in Infants and Children* . 5th ed. Philadelphia, PA: Saunders/Elsevier; 2013:738-740.

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Gregory GA. The baroresponses of preterm infants during halothane anaesthesia. *Can Anaesth Soc J*. 1982;29:105-107.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:352.

Lou HC, Lassen PH, Friis-Hansen B. Impaired autoregulation of cerebral blood flow in the distressed newborn infant. *J Pediatr*. 1979;94:118.

C.7. What size endotracheal tube would you have used if the patient had not been intubated?

The larynx of a full-term neonate usually accommodates a 3.0- or 3.5-mm endotracheal tube, whereas infants weighing less than 3,500 g tolerate a 3.0-mm tube. In infants weighing less than 1,500 g, a 2.5-mm (internal diameter) tube is usually recommended. The endotracheal tube should be large enough to allow easy ventilation but small enough to permit leaking of gas between the tube and trachea when the lung is ventilated with 15 to 20 cm H_2O pressure. However, a higher leak pressure of 25 to 35 cm H_2O may be aimed for when high peak inspiratory pressures may be required during anesthesia, for example, during a thoracotomy or an upper laparotomy, or if the patient has decreased pulmonary compliance.

Coté C, Lerman J, Anderson B. *Coté and Lerman's A Practice of Anesthesia in Infants and Children* . 5th ed. Saunders/Elsevier; 2013:733-734.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:314-315.

C.8. How would you have induced anesthesia if the patient had not been intubated?

Preterm infants do need anesthesia for surgery. The patient should be preoxygenated with 100% oxygen, and ventilation should be controlled; otherwise, the preterm infant develops apnea and bradycardia. Anesthesia in the ICU is induced with fentanyl, 1 to 3 μg per kg. When the lid reflexes are lost, the infant is intubated after 0.05 to 0.1 mg per kg of pancuronium. After intubation, breath sounds should be checked bilaterally to ensure that the tube is properly positioned.

Alternatively, anesthesia may be induced in the operating room with an inhalation anesthetic such as sevoflurane followed by muscle relaxation with pancuronium or rocuronium before intubation.

Andropoulos D, Stayer S, Russell I, et al, eds. *Anesthesia for Congenital Heart Disease*. 2nd ed. West Sussex, United Kingdom: Wiley-Blackwell; 2010:376.

Robinson S, Gregory GA. Fentanyl-air-oxygen anesthesia for ligation of patent ductus arteriosus in preterm infants. *Anesth Analg*. 1981;60:331-334.

C.9. How would you maintain anesthesia?

Because preterm infants are extremely sensitive to cardiovascular depression from inhalation anesthetics, we prefer to use fentanyl with or without nitrous oxide for maintenance of anesthesia. Increments of fentanyl, 3 to 5 μg per kg, are titrated to maintain hemodynamic stability. A bolus injection of high-dose fentanyl, 30 to 50 μg per kg, often causes hypotension because the infant is usually dehydrated as a result of fluid restriction and diuretic therapy for congestive heart failure from PDA. Ketamine may be used alone or as a supplement to fentanyl-air-oxygen anesthesia.

Pancuronium, 0.1 mg per kg, is an attractive choice for muscle relaxation because it causes mild tachycardia and the infant's blood pressure is dependent on heart rate.

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Coté C, Lerman J, Anderson B. *Coté and Lerman's A Practice of Anesthesia in Infants and Children* . 5th ed. Philadelphia, PA: Saunders/Elsevier; 2013:738-740.

Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:412-416.

Robinson S, Gregory GA. Fentanyl-air-oxygen anesthesia for ligation of patent ductus arteriosus in preterm infants. *Anesth Analg*. 1981;60:331-334.

C.10. How would you ventilate the patient? What tidal volume, respiratory rates, and FIO_2 would you set for the infant?

Controlled ventilation should be employed because preterm infants do not breathe well under anesthesia. The patient may be ventilated by hand with a Jackson-Rees device. The technique allows instantaneous compensation for changes in pulmonary compliance and resistance, especially during thoracotomy. It also permits the use of PEEP. If extra hands are not available, mechanical ventilation, preferably with a pediatric bellows, may be used to ventilate the infant.

During spontaneous respiration, normal tidal volume is 7 mL per kg for all ages. However, the ventilator tidal volumes calculated on the basis of body weight for adult patients, such as 10 mL per kg, are not applicable for pediatric patients, especially small infants. A large amount of ventilator-delivered tidal volume is lost through the large compression volume of the anesthesia breathing circuit and the leak around the uncuffed endotracheal tube. For example, if the compression volume of the anesthesia ventilator is 4.5 mL per cm H_2O (a value typical for adult ventilators) and the ventilator is set to deliver a 100-mL tidal volume to a patient at 20 cm H_2O peak inspiratory pressure, 90 mL is lost to compression volume: Only 10 mL is delivered to the patient. In addition, if pulmonary and chest wall compliances change during anesthesia and surgery, the delivered tidal volume to the patient will also be changed. Therefore, it is wise to set tidal volume whatever necessary to achieve the desired inspiratory pressures, such as those used in the neonatal ICU before surgery. Usually the peak inspiratory pressures are set between 15 and 25 cm H_2O, depending on the patient's respiratory condition, to ensure adequate chest expansion.

The respiratory rates and inspiratory pressures are adjusted as needed to maintain the $PaCO_2$ between 35 and 40 mm Hg or the end-tidal CO_2 between 30 and 35 mm Hg. The FIO_2 is adjusted to keep the PaO_2 between 50 and 70 mm Hg or the arterial oxygen saturation between 87% and 92% (practically 90% to 95%).

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:340.

Robbins L, Crocker D, Smith RM. Tidal volume losses of volume-limited ventilators. *Anesth Analg*. 1967;46:428-431.

C.11. Discuss blood and fluid therapy in this preterm infant.

Fluid therapy should be aimed at correcting the preoperative deficit, providing maintenance fluid, and replacing intraoperative evaporative, third space, and blood loss.

Intraoperative blood loss must be carefully estimated by weighing the sponges and using small-calibrated suction bottles in plain view of the anesthesiologist. The preterm infant's blood volume is only 80 to 95 mL (85 to 100 mL per kg); therefore, even a 10-mL blood loss can be critical. Despite these precautions, estimation of blood loss is inevitably inaccurate because of the unmeasured loss in the drapes and tissues. For this reason, it is recommended that 125% to 150% of measured blood loss be replaced. Each milliliter of estimated blood loss is replaced with 3 mL of Ringer's lactate or 1 mL of 5% albumin in saline. If the hematocrit is low (<30%) to begin with, blood losses are replaced with packed RBC.

Maintenance fluids consisting of 5% dextrose in one-fourth strength normal saline are given at 4 mL/kg/hr, whereas evaporative and third-space losses are replaced with Ringer's lactate at 8 to 12 mL/kg/hr for abdominal or thoracic procedures. The adequacy of blood and fluid therapy may be ensured by stable blood pressure, normal central venous

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pressure (over 3 cm H_2O), and an adequate urine output of >0.75 mL/kg/hr and specific gravity of less than 1.010. In addition, the infant's fontanel should be above the inner table of the skull if there is no volume depletion.

Coté C, Lerman J, Anderson B. *Coté and Lerman's A Practice of Anesthesia in Infants and Children* . 5th ed. Philadelphia, PA: Saunders/Elsevier; 2013:165-170.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:352-354.

C.12. During dissection of the ductus arteriosus, the arterial oxygen saturation dropped from 92% to 80% and the heart rate decreased from 140 beats per minute to 80 beats per minute. What were the causes? How would you correct this situation?

Pediatric patients, especially preterm infants, develop hypoxemia quickly after hypoventilation because they have high metabolism (increased oxygen demand) and low FRC (decreased oxygen reserve). During dissection of the ductus arteriosus, the ipsilateral lung is retracted and compressed by the surgeon. Therefore, the pulmonary resistance increases and pulmonary compliance decreases. Consequently, the delivered tidal volume to the patient decreases and the gas leak around the endotracheal tube increases if the inspiratory pressures remain unchanged. Decreasing tidal volume causes hypoventilation, resulting in hypoxemia and CO_2 retention. In addition, compressing the lung tissue increases intrapulmonary shunt, which causes further hypoxemia. In pediatric patients, bradycardia is most commonly caused by hypoxemia. During dissection of the ductus arteriosus, surgical manipulation of the vagus nerve and lung tissue may initiate vagal reflex, with resultant bradycardia.

The infant should be manually ventilated with 100% oxygen to correct hypoxemia and bradycardia. If bradycardia persists, atropine, 0.01 to 0.02 mg per kg, should be given. The surgical manipulation should be stopped and the collapsed lung reexpanded. Blood loss or hypovolemia should also be corrected.

When the hemodynamic status and oxygenation are stabilized, the FIO_2 and respiratory pressures should be adjusted to ensure adequate ventilation and oxygenation.

D. Postoperative Management

D.1. Would you reverse the muscle relaxants and extubate the patient at the end of surgery?

No. Postoperative ventilatory support would be necessary for this preterm infant with RDS; therefore, reversal of muscle relaxation and extubation are not indicated.

Coté C, Lerman J, Anderson B. *Coté and Lerman's A Practice of Anesthesia in Infants and Children* . 5th ed. Philadelphia, PA: Saunders/Elsevier; 2013:742-743.

D.2. How can one minimize the risk of transporting the patient to the neonatal intensive care unit (ICU) after surgery?

The anesthesiologist's responsibilities do not end with the successful completion of the operative procedure. Removal of the surgical drapes must be done with caution to prevent inadvertent extubation or removal of the arterial or venous cannula. Transportation of the infant to the neonatal ICU is an extremely hazardous transition and requires watchful vigilance. Arrangements must be made in advance so that elevators are waiting and the nursery is ready to accept the patient. The anesthesiologist must accompany the child until satisfied that care has been appropriately transferred to the neonatal nursery staff.

The same monitors that were employed for surgery must be used in transport, including electrocardiogram and monitors for arterial blood pressure and oxygen saturation. Ventilation should be maintained by hand with a Jackson-Rees device or by a battery-operated transport ventilator, and the child should not be transported with 100% oxygen unless it was used for the operative procedure. A precordial stethoscope is especially helpful to monitor the adequacy of respiration and

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heart sounds. Finally, every effort to ensure thermal stability must be made, including the use of a heated Isolette (if possible), Saran Wrap, warm blankets, and a cap on the infant's head.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:488-489.

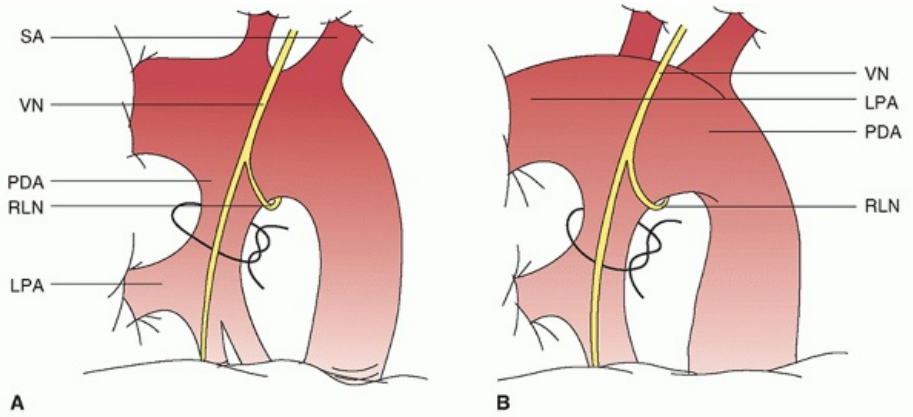


FIGURE 44.1 A. Anatomically atypical patent ductus arteriosus arising proximal to the left subclavian artery. **B.** Large patent ductus arteriosus sweeping into the descending aorta and appearing to be the arch. The ductus overlies the arch and hides it from view. A large distal left pulmonary artery is misinterpreted as the patent ductus (encircled by ligature). LPA, left pulmonary artery; PDA, patent ductus arteriosus; RLN, recurrent laryngeal nerve; SA, subclavian artery; VN, vagus nerve. (Adapted from Pontius RG, Danielson GK, Noonan JA, et al. Illusions leading to surgical closure to the distal left pulmonary artery instead of the ductus arteriosus. *J Thorac Cardiovasc Surg*. 1981;82:107-113.)

D.3. The patient's condition deteriorated postoperatively in the ICU. Physical examination revealed persistent cardiac murmur. What was the possible diagnosis?

It has been reported that a large ductus arteriosus arising from the aortic arch proximal to the subclavian artery creates the illusion of the arch, leading to surgical closure of the distal left pulmonary artery instead of ductus arteriosus (Fig. 44.1). A sign of successful PDA ligation is an increase in diastolic blood pressure from the elimination of pulmonary runoff during diastole. To help identify the ductus, some surgeons place a temporary clip on the what they believe is the ductus and observe whether the diastolic pressure increases correspondingly.

In this case, the ductus arteriosus was not ligated; therefore, the ductus murmur persisted. Inadvertent ligation of the distal left pulmonary artery resulted in pulmonary ischemia distal to the ligation. Meanwhile, the right lung was further flooded with the shunted blood through the unligated PDA. The resultant ventilation/perfusion maldistribution ([V with dot above]/[Q with dot above] abnormalities) caused further hypoxemia and CO_2 retention in this infant. The patient should be brought to the operating room for repair of the left pulmonary artery and ligation of the ductus arteriosus.

Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:414.

Pontius RG, Danielson GK, Noonan JA, et al. Illusions leading to surgical closure to the distal left pulmonary artery instead of the ductus arteriosus. *J Thorac Cardiovasc Surg*. 1981;82:107-113.

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Chapter 45
Bleeding Tonsils

Franklin B. Chiao

A 5-year-old boy with history of obstructive sleep apnea (OSA) has blood in his mouth after a tonsillectomy and adenoidectomy 4 hours ago. He appears pale and uncomfortable. His heart rate is about 140 beats per minute, his blood pressure is 66/30 mm Hg with a mean arterial pressure of 38 mm Hg, the pulse oximeter reads 99%, and his respiratory rate is 28 breaths per minute.

A. Medical Disease and Differential Diagnosis

1. What is in your differential diagnosis?
2. What are the development stages of tonsillar growth? What nerves innervate the tonsillar region? What is the vascular anatomy of the tonsils?
3. What are your immediate concerns if it is a bleeding tonsil?
4. Does age matter for risk of bleeding? What other risk factors are there?
5. What is the morbidity and mortality of post-tonsillectomy hemorrhage?

B. Preoperative Evaluation and Preparation

1. How will you assess this patient? What are important physical exam findings?
2. What additional steps would you take to assess and manage hemorrhage? Does the patient need an arterial or central venous line?
3. What anesthesia preparation should begin in the operating room for this patient?
4. What factors would influence your decision to use vasopressors?
5. Would you premedicate this patient?
6. Once the laboratory results are completed, how would they be interpreted?
7. What would you expect from the surgeon?
8. How do you address parental concerns about anesthesia-related neurotoxicity? What evidence is there for adverse impacts? What would you tell the parents about this?

C. Intraoperative Management

1. What is your induction plan? Would you perform a rapid sequence induction or mask inhalational induction?
2. How would one plan for suctioning the blood in the oropharynx?
3. What is your airway management plan? Should an experienced laryngoscopist be involved?
4. Once in the airway, there is poor visualization in the presence of blood in the oropharynx. What maneuvers may help identify the glottic opening?
5. What supplemental medications would you plan to use during the case?
6. Assuming the surgery is completed without any adverse events, what would be your extubation plan, if any, at this point?

D. Postoperative Management

1. Does this patient require an intensive care unit (ICU) setting?
2. How would you transport this patient?

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3. What are some potential postoperative complications? What if the patient had stridor and a hoarse cry?
4. What do surgeons often tell their patients before being discharged?

A. Medical Disease and Differential Diagnosis

A.1. What is in your differential diagnosis?

Blood in the oropharynx could have several etiologies. Given his recent tonsil surgery, postoperative bleeding from the surgical site is a major concern. Other etiologies include a uvular injury or postoperative hematemesis. Epistaxis may be a sign of nasopharyngeal trauma or the usual epistaxis in a patient with a history of nasal bleeding.

Salem A, Healy S, Pau H. Management of spontaneous tonsillar bleeding: review. *J Laryngol Otol*. 2010;124:470-473.

A.2. What are the development stages of tonsillar growth? What nerves innervate the tonsillar region? What is the vascular anatomy of the tonsils?

Tonsils grow rapidly until age 5 or 6 years. By puberty, they usually reach their maximum size of 10 to 15 mm by 20 to 25 mm. With aging, the reactive lymphoid tissue atrophies. The tonsillar area is innervated by branches of the maxillary and glossopharyngeal nerves.

Sources of bleeding can be arterial, venous, or involve vascular anomalies. The arterial blood supply comes from several branches of the external carotid artery. The main sources often consist of the ascending pharyngeal artery, descending palatine artery, ascending palatine artery, facial artery branches, and dorsal lingual artery. Venous return is to the peritonsillar plexus, the lingual vein, and the pharyngeal plexus.

Standring S, Borley NR, Collins P, et al, ed. *Gray's Anatomy: The Anatomical Basis of Clinical Practice* . 40th ed. Edinburgh, Scotland: Churchill Livingstone Elsevier; 2008:566-567.

A.3. What are your immediate concerns if it is a bleeding tonsil?

Post-tonsillectomy hemorrhage is a surgical emergency. Undue delay in treatment has resulted in catastrophic complications. There may be a limited initial vascular spasm and vasoconstriction from catecholamine release that reduces bleeding for a short time. If there is active bleeding, the surgeon must be alerted, and often the child must return to the operating room immediately. “Primary” bleeding occurs within 24 hours in about 1% of tonsillectomy patients, and secondary bleeding occurs in up to 4% of these patients and usually happens in the 2 weeks following surgery. Spontaneous hemorrhage is also possible. Peripheral vessels are usually the source, but erosion into vessels of the carotid sheath may occur.

The major anesthetic challenge is to secure the airway obscured by a blood-filled oropharynx in a hypovolemic and anemic patient.

Gardner JF. Sutures and disasters in tonsillectomy. *Arch Otolaryngol*. 1968;88:551-555.

Windfuhr JP, Chen YS, Remmert S. Hemorrhage following tonsillectomy and adenoidectomy in 15,218 patients. *Otolaryngol Head Neck Surg*. 2005;132(2):281-286.

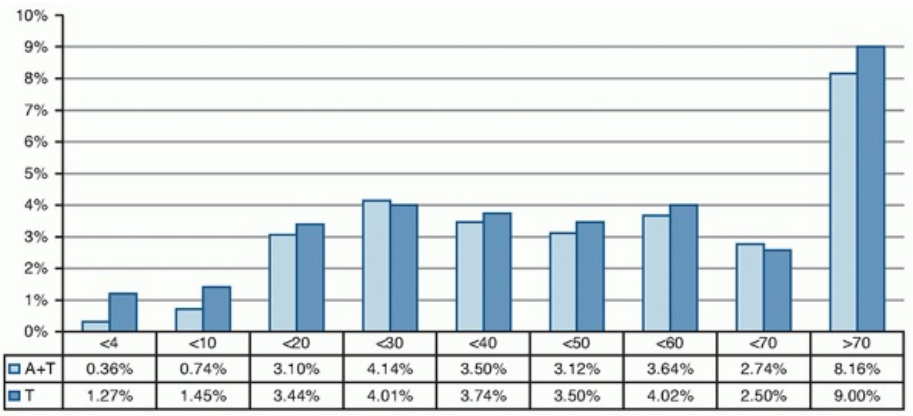
A.4. Does age matter for risk of bleeding? What other risk factors are there?

The incidence of post-tonsillectomy bleeding increases with age, particularly after age 10 years. Other risk factors include a history of recurrent tonsillitis, multiple bleeding episodes, and coagulopathies. There are cases of unsuspected vascular anomalies. It is not clear whether the choice of anesthetic technique for the initial tonsillectomy surgery makes any difference, such as awake versus deep extubation and endotracheal tube (ETT) versus laryngeal mask airway, in the incidence of postsurgical bleeding (Fig. 45.1).

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Tomkinson A, Harrison W, Owens D, et al. Risk factors for postoperative hemorrhage following tonsillectomy. *Laryngoscope*. 2011;121:279-288.



	<4	<10	<20	<30	<40	<50	<60	<70	>70
A+T	0.36%	0.74%	3.10%	4.14%	3.50%	3.12%	3.64%	2.74%	8.16%
T	1.27%	1.45%	3.44%	4.01%	3.74%	3.50%	4.02%	2.50%	9.00%

FIGURE 45.1 Postoperative hemorrhage: age distribution after tonsillectomy (T) and adenoidectomy with tonsillectomy (A+T). (From Windfuhr JP, Chen YS, Remmert S. Hemorrhage following tonsillectomy and adenoidectomy in 15,218 patients. *Otolaryngol Head Neck Surg*. 2005;132[2]:281-286, with permission.)

A.5. What is the morbidity and mortality of post-tonsillectomy hemorrhage?

Although most post-tonsillectomy bleeding is handled successfully, the potential for serious adverse outcomes including death from post-tonsillectomy bleeding cannot be understated. There are cases of emergent tracheotomies, hypoxic brain injury, and death from hemorrhage, aspiration, or airway obstruction. Autopsies confirmed these findings and have also found wound necrosis. One particular risk factor for mortality is a history of repeated bleeding episodes. Inpatient stay would seem to mitigate the risk, but when bleeding is brisk, there is sometimes still not enough time to return to the operating room. Post-adenoidectomy bleeding is also possible, but it is much more rare and milder.

Windfuhr JP. Lethal post-tonsillectomy hemorrhage. *Auris Nasus Larynx*. 2003;30:391-396.

Windfuhr JP, Schloendorff G, Sesterhenn AM, et al. A devastating outcome after adenoidectomy and tonsillectomy: ideas for improved prevention and management. *Otolaryngol Head Neck Surg*. 2009;140:191-196.

B. Preoperative Evaluation and Preparation

B.1. How will you assess this patient? What are important physical exam findings?

The key questions for the preoperative assessment are the following: Is the patient able to maintain his airway, is bleeding active, and is the patient conscious?

Hypovolemia, anemia, aspiration risk, and difficult laryngoscopy are major anesthetic concerns. Hypotension is a late sign of hypovolemic shock. Dizziness and orthostatic hypotension also indicate the need for more aggressive resuscitation. Given this patient's tachycardia and hypotension, he is probably hypovolemic.

Physical exam focuses on evaluating the airway and the patient's volume status. After examination of the airway, one should also look at a previous anesthetic record to see the intubation note. The presence of dry mucous membranes, poor skin turgor, or sunken orbits indicate volume depletion. Weighing of a diaper in babies or looking at urine output measurements helps assess fluid status as well.

Fields R, Gencorelli F, Litman R. Anesthetic management of the pediatric bleeding tonsil. *Paediatr Anaesth*.

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2010;20(11):982-986.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. Chichester, United Kingdom: Wiley-Blackwell; 2012:786.

B.2. What additional steps would you take to assess and manage hemorrhage? Does the patient need an arterial or central venous line?

An intravenous catheter must be placed preoperatively for fluid resuscitation, and blood for laboratory tests should be drawn. The team should start fluid resuscitation to replace blood loss. It is prudent to check hemoglobin, hematocrit, platelets, prothrombin time (PT)/international normalized ratio (INR), and partial thromboplastin time (PTT) values. If the hemoglobin level is low and/or the bleeding profuse, administration of packed red blood cells seems appropriate.

Although an arterial line and central venous line would help get blood for laboratory tests and assess volume status, there is often little time to place these, and their benefit is not evident in changing outcomes. If the patient has pulmonary hypertension from OSA or another major cardiac condition, an arterial line should be considered.

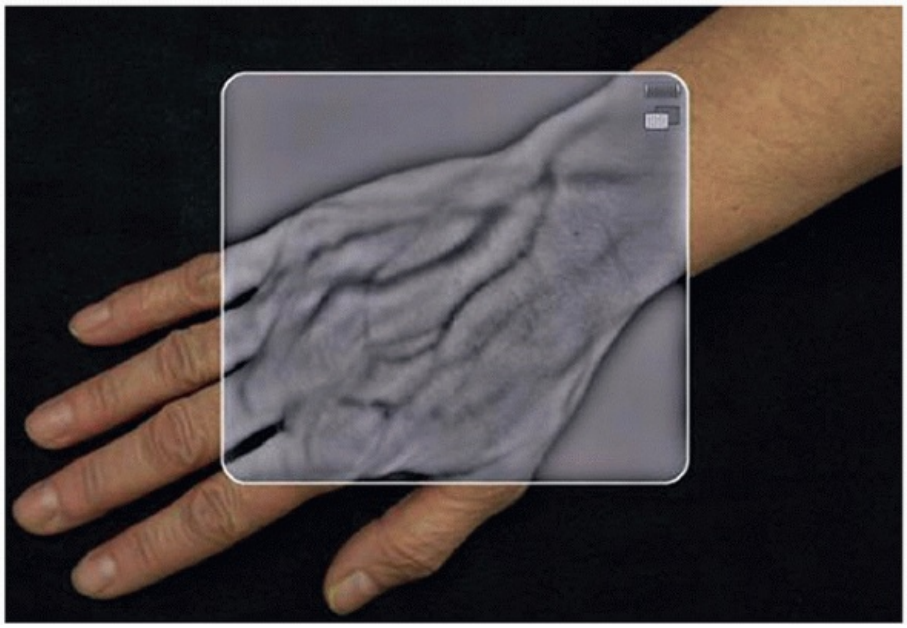
Randall DA, Hoffer ME. Complications of tonsillectomy and adenoidectomy. *Otolaryngol Head Neck Surg*. 1998;118(1):61-68.

Windfuhr JP, Schloendorff G, Sesterhenn AM, et al. A devastating outcome after adenoidectomy and tonsillectomy: ideas for improved prevention and management. *Otolaryngol Head Neck Surg*. 2009;140:191-196.

B.3. What anesthesia preparation should begin in the operating room for this patient?

Preparation will include airway and vascular access equipment, in addition to potential infusion pumps. One should set up two large-bore Yankauer suctions, styletted cuffed preformed oral RAE (Ring-Adair-Elwyn) or reinforced ETTs in three sizes, and two laryngoscope blades. One suction system may become blocked with clots. If a difficult intubation is suspected, the difficult airway cart and a video laryngoscope should be present. An intraosseous device and infrared vein-finding device (Fig. 45.2) should be available in case it is difficult to obtain intravenous access (Fig. 45.3). The blood transfusion tubing should be ready because the

bleeding can be brisk, and infusion pumps should be primed if the need for vasopressors is anticipated. The need for a massive transfusion is unlikely in most cases. Having an emesis basin available helps as well.



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FIGURE 45.2 Image of hand veins with the infrared vein technology (VueTek Veinsite). (From Chiao F, Resta-Flarer F, Lesser J, et al. Vein visualization: patient characteristic factors and the efficacy of a new infrared vein finder technology. *Br J Anaesth*. 2013;110[6]:966-971, with permission.)

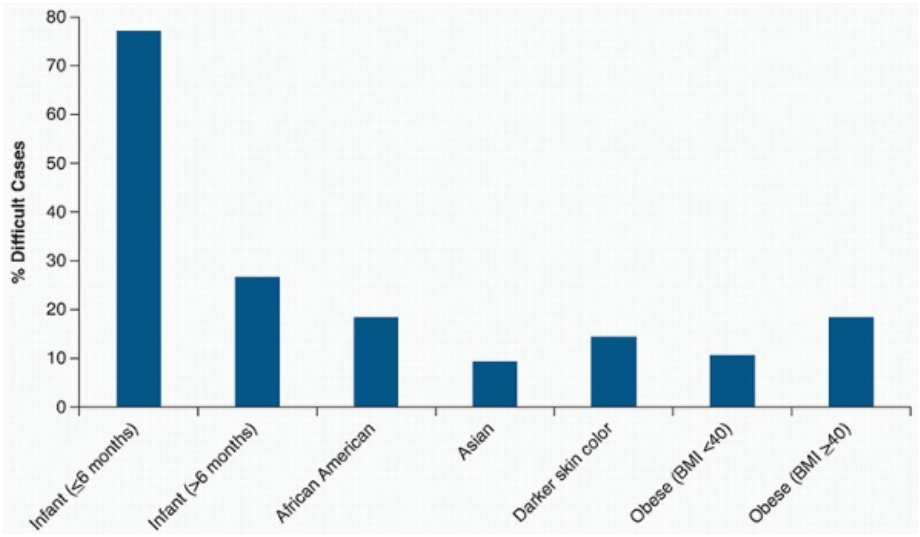


FIGURE 45.3 Percentage of difficult unassisted eyesight vein visualization cases within selected populations. BMI, body mass index. (From Chiao F, Resta-Flarer F, Lesser J, et al. Vein visualization: patient characteristic factors and the efficacy of a new infrared vein finder technology. *Br J Anaesth*. 2013;110[6]:966-971, with permission)

Chiao F, Resta-Flarer F, Lesser J, et al. Vein visualization: patient characteristic factors and the efficacy of a new infrared vein finder technology. *Br J Anaesth*. 2013;110(6):966-971.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. Chichester, United Kingdom: Wiley-Blackwell; 2012:786.

B.4. What factors would influence your decision to use vasopressors?

If the patient is hemodynamically unstable, a type and crossmatch should be done, and dopamine and epinephrine infusions should be available. A cardiac history, pulmonary hypertension, or the need to tightly manage the blood pressure would also indicate that vasopressors are helpful.

B.5. Would you premedicate this patient?

The decision to premedicate involves balancing the risk of a full stomach and aspiration versus the benefit of anxiolysis. This patient also has OSA, which makes him sensitive to opioids and prone to obstruction.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1359.

B.6. Once the laboratory results are completed, how would they be interpreted?

Depending on how hemoglobin is low, the administration of red blood cells may be warranted. If a coagulopathy exists, consider giving fresh frozen plasma (FFP) and/or platelets.

B.7. What would you expect from the surgeon?

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The surgeon will have a rigid bronchoscope and a tracheotomy set ready. The surgeon should be gowned and gloved with headlight on, and the scrub technician should also be ready before or as the patient enters the operating room.

Windfuhr JP, Schloendorff G, Sesterhenn AM, et al. A devastating outcome after adenoidectomy and tonsillectomy: ideas for improved prevention and management. *Otolaryngol Head Neck Surg*. 2009;140:191-196.

B.8. How do you address parental concerns about anesthesia-related neurotoxicity? What evidence is there for adverse impacts? What would you tell the parents about this?

The parents ask if this additional general anesthetic will cause “brain damage or cognitive problems.”

There have been several studies with respect to neurotoxicity over the past few years. In rodent studies, there is evidence of neuroapoptosis and long-term neurocognitive impairment. Subsequent studies conducted in monkeys also showed neurotoxicity. For ethical reasons, it is hard to have prospective trials in humans. There are some recent studies showing a weak association between childhood anesthetic exposure and neurocognitive outcome, so ruling out neurotoxicity in children is not easy. Extrapolating the animal data to humans for many reasons must be done cautiously.

The following consensus statement is endorsed by the International Anesthesia Research Society, U.S. Food and Drug Administration, the American Academy of Pediatrics, the Society for Pediatric Anesthesia, and the Society for Neuroscience in Anesthesiology and Critical Care:

> Each year, millions of young children require surgery and other procedures for serious or life-threatening medical conditions or to improve their quality of life. Anesthetic and sedative drugs are widely used to help ensure the safety, health, and comfort of children undergoing these procedures. However, increasing evidence from research studies suggests the benefits of these agents should be considered in the context of their potential to cause harmful effects.
>
> Previous research in young animals and children has raised concerns that exposure to commonly used anesthetics may produce adverse neurobehavioral effects. However, these studies had limitations that prevent experts from drawing conclusions on whether the harmful effects were due to the anesthesia or to other factors, including surgery, hospitalization, or pre- existing conditions. Furthermore, the findings in children have been mixed, with some studies of infants and young children undergoing anesthesia or sedation finding long-term deficits in learning and behavior, while others have not.
>
> Clearly, additional research is urgently needed to identify any possible risks to young children. In the absence of conclusive evidence, it would be unethical to withhold sedation and anesthesia when necessary. Instead, healthcare providers should do the following:

- Discuss with parents and other caretakers the risks and benefits of procedures requiring anesthetics or sedatives, as well as the known health risks of *not treating* certain conditions
- Stay informed of new developments in this area
- Recognize that current anesthetics and sedatives are necessary for infants and children who require surgery or other painful and stressful procedure

International Anesthesia Research Society. SmartTots releases consensus statement regarding anesthesia safety in children. http://smarttots.org/smarttots-releases-consensus-statement-regarding-anesthesia-safety-in-young-children/. October 13, 2015. Accessed October 20, 2015.

Jevtovic-Todorovic V. Pediatric anesthesia neurotoxicity: an overview of the 2011 SmartTots panel. *Anesth Analg*. 2011;113:965-968.

Nemergut ME, Aganga D, Flick RP. Anesthetic neurotoxicity: what to tell the parents? *Paediatr Anaesth*. 2014;24(1):120-126.

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C. Intraoperative Management

C.1. What is your induction plan? Would you perform a rapid sequence induction or mask inhalational induction?

Preoxygenation should proceed with consideration given to the left lateral position to drain blood from the mouth. These patients have a “full stomach,” so a rapid sequence induction is indicated. If the patient is hemodynamically stable, propofol may be used, but etomidate or ketamine should be considered if the patient is unstable. Be prepared for anesthesia-induced vasodilation and the subsequent hypotension. Either high-dose rocuronium or succinylcholine should be chosen depending on the risks of a slightly slower paralysis with rocuronium versus the benefit of avoiding side effects of succinylcholine. If succinylcholine is used, an anticholinergic, such as glycopyrrolate or atropine, should be ready to treat succinylcholineinduced bradycardia, which is more common in children. The high-dose nondepolarizing agent may paralyze the patient beyond the duration of the surgery. The surgeon must be present in the operating room at the time of induction.

Coté CJ, Lerman JL, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Saunders Elsevier; 2013:665-666.

C.2. How would one plan for suctioning the blood in the oropharynx?

As described earlier, there will be two large-bore suction catheters ready, but they should be used judiciously to avoid dislodging stable clots because disruption may cause the bleeding worsen. If suctioning needs to be done, it should be done with the Yankauer-type suction tips because they are rigid and can be directed into the midline to stay away from the tonsillar fossae. Once intubated, avoid suctioning the throat or trying to suction the stomach to prevent the risk of dislodging a clot and eliciting brisk uncontrolled bleeding. Once the bleeding is controlled, suctioning can be done under direct visualization.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. Chichester, United Kingdom: Wiley-Blackwell; 2012:786.

C.3. What is your airway management plan? Should an experienced laryngoscopist be involved?

A styletted, cuffed preformed oral RAE ETT, two laryngoscope blades, and, for known or anticipated difficult intubations, the difficult airway cart and video laryngoscope should be available. This is a situation where an experienced laryngoscopist should perform the direct laryngoscopy. Once intubated, secure the ETT well. The cuff will reduce the risk of aspiration and minimize gas leaks.

Weiss M, Dullenkopf A. Cuffed tracheal tubes in children: past, present and future. *Expert Rev Med Devices*. 2007;4:73-82.

C.4. Once in the airway, there is poor visualization in the presence of blood in the oropharynx. What maneuvers may help identify the glottic opening?

Gently pressing on the chest to simulate respiration can create air bubbles at the glottic opening to guide placement of the ETT.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. Chichester, United Kingdom: Wiley-Blackwell; 2012:786.

C.5. What supplemental medications would you plan to use during the case?

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Several supplemental medications are needed. Usually, antibiotics are not required. Regarding pain management, one can titrate in intravenous opioids, such as fentanyl or morphine. Cases can be as short as 20 minutes, so large doses of narcotics or use of nondepolarizing muscle relaxants can prolong emergence. For maintenance of anesthesia, inhalational agents are adequate. For nausea prophylaxis, antiemetics, such as ondansetron, should be given.

Lastly, dexamethasone is a helpful adjunct for analgesia, antiemesis, and reducing airway edema.

TABLE 45.1 Incidence and Timing of Hypoxemia in 475 Patients with Post-tonsillectomy Hemorrhage

Fifty moderate or severe oxyhemoglobin desaturation events and their relation to the clinical course

CLINICAL TIME POINT	MODERATE HYPOXEMINA[a]	SEVERE HYPOXEMIA[b]
Induction/Intubation	12	2
Intraoperative	6	1
Emergence/Extubation	22	6
Postanesthesia Care Unit	1	0

[a] Moderate hypoxemia was defined as SpO_2 <90%.

[b] Severe hypoxemia was defined as SpO_2 <80%.

From Fields R, Gencorelli F, Litman R. Anesthetic management of the pediatric bleeding tonsil. *Paediatr Anaesth*. 2010;20(11):982-986, with permission.

Baugh RF, Archer SM, Mitchell RB, et al. Clinical practice guideline: tonsillectomy in children. *Otolaryngol Head Neck Surg*. 2011;144(1 suppl):S1-S30.

C.6. Assuming the surgery is completed without any adverse events, what would be your extubation plan, if any, at this point?

Most hypoxic events occur on emergence and extubation, so careful attention is needed. The patient should be extubated when he is fully awake and in control of his laryngeal reflexes. Before extubation, the use of gastric suctioning after the surgery will help to reduce stomach contents.

Fields et al. looked at the incidence of respiratory and hemodynamic complications in children with a post-tonsillectomy hemorrhage and found that there was no significant morbidity or death in their study patients and that transient hypoxemia, unrelated to intubation difficulties, was the most common complication. Most of these hypoxemic events occurred during extubation or emergence (Table 45.1).

Cook-Sather SD, Liacouras CA, Previte JP, et al. Gastric fluid measurement by blind aspiration in paediatric patients: a gastroscopic evaluation. *Can J Anaesth*. 1997;44(2):168-172.

Fields R, Gencorelli F, Litman R. Anesthetic management of the pediatric bleeding tonsil. *Paediatr Anaesth*. 2010;20(11):982-986.

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Tsui BC, Wagner A, Cave D, et al. The incidence of laryngospasm with a “no touch” extubation technique after tonsillectomy and adenoidectomy. *Anesth Analg*. 2004;98:327-329.

D. Postoperative Management

D.1. Does this patient require an intensive care unit (ICU) setting?

The patient will usually go to the postanesthesia recovery unit, but direct admission to the ICU may be indicated in cases with large amounts of transfusions, a difficult airway, hemodynamic instability, or in patients with major comorbidities.

Lescanne E, Chiron B, Constant I, et al. Pediatric tonsillectomy: clinical practice guidelines. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2012;129:264-271.

Windfuhr JP. Lethal post-tonsillectomy hemorrhage. *Auris Nasus Larynx*. 2003;30:391-396.

D.2. How would you transport this patient?

The left or right lateral position often reduces airway obstruction. It is helpful for the doctor to place a hand on the patient's head as well to prevent patient injuries from adverse

movements during transport. Children are at higher risk than adults for emergence delirium. Having supplemental oxygen and emergency medications available would be prudent.

Randall DA, Hoffer ME. Complications of tonsillectomy and adenoidectomy. *Otolaryngol Head Neck Surg*. 1998;118(1):61-68.

Tsui BC, Wagner A, Cave D, et al, The incidence of laryngospasm with a “no touch” extubation technique after tonsillectomy and adenoidectomy. *Anesth Analg*. 2004;98:327-329.

D.3. What are some potential postoperative complications? What if the patient had stridor and a hoarse cry?

Fever, volume depletion, and prolonged emesis are the most common postoperative complications. Coagulopathy can manifest from large volumes of red blood cells transfusions. Rebleeding may occur and will need to be treated similarly. Upper airway complications, such as edema from suctioning/trauma, may require reintubation. Stridor can initially be treated with humidified oxygen, β_2-agonist nebulizer therapy, racemic epinephrine, and/or heliox.

Guida RA, Mattucci KF. Tonsillectomy and adenoidectomy: an inpatient or outpatient procedure? *Laryngoscope*. 1990;100(5):491-493.

Leach J, Manning S, Schaefer S. Comparison of two methods of tonsillectomy. *Laryngoscope*. 1993;103: 619-622.

D.4. What do surgeons often tell their patients before being discharged?

Instructions are usually given to patients about where to find the nearest emergency room, who to call, and how to get professional transportation/ambulance services in the event of rebleeding. Drinking and chewing are also emphasized. Pain is usually moderate and can be referred to the ears. Often, oral or rectal suppositories of acetaminophen and oxycodone are suggested for pain control. With OSA, there will be a heightened sensitivity to opioids.

Baugh RF, Archer SM, Mitchell RB, et al. Clinical practice guideline: tonsillectomy in children. *Otolaryngol Head Neck Surg*. 2011;144(1 suppl):S1-S30.

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Chapter 46
Brachial Plexus Block

Tiffany Tedore

William F. Urmey

A 72-year-old man presents after sustaining a fall and right proximal humeral fracture. The patient's history is remarkable for hypertension, several fainting episodes, and significant chronic obstructive pulmonary disease (COPD). He has a 30 pack-year cigarette smoking history. Recent pulmonary function tests 6 months before admission include a forced vital capacity (FVC) of 1.4 L (33% predicted). The patient's daily medications include atenolol and hydrochlorothiazide. Hydromorphone 1 mg was administered intravenously in the emergency room.

A. Medical Disease and Differential Diagnosis

1. What are the presenting problems in this patient?
2. What additional medical history would you want to obtain?
3. What implications does the use of atenolol have on the patient's coexisting medical condition?
4. Why is immobilization of the arm important following humeral fracture?
5. What nerve is at particular risk for injury from humeral fracture?

B. Preoperative Evaluation and Preparation

1. What testing would be helpful to elucidate the cause of this patient's fainting spells?
2. What premedication would you order?
3. What are the respiratory effects of benzodiazepines?

C. Intraoperative Management

1. What anesthetic technique would you use?
2. Describe the relevant anatomy of the brachial plexus.
3. What relevant anatomic structures in the neck and below the neck can be injured or injected accidentally during brachial plexus block?
4. What regional technique would you choose to block the brachial plexus in this patient?

5. What are the advantages and disadvantages of the following blocks?
   a. Interscalene block
   b. Supraclavicular block
   c. Infraclavicular block
   d. Axillary block
6. Describe the landmarks and procedures for nerve stimulator and ultrasound-guided interscalene block.
7. Describe the landmarks and procedures for nerve stimulator and ultrasound-guided supraclavicular block.
8. Describe the landmarks and procedures for nerve stimulator and ultrasound-guided infraclavicular block.
9. Describe the landmarks and procedures for nerve stimulator and ultrasound-guided axillary block.
10. The patient requests to have the brachial plexus block performed after you administer general anesthesia. Would you agree to this request?

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11. What relevant respiratory complications or side effects are you concerned about in this patient?
12. What is the incidence of hemidiaphragmatic paresis following interscalene brachial plexus block? Can this complication be avoided by lowering the volume or concentration of local anesthetic injected? By using ultrasound-guided supraclavicular block?
13. Describe the pulmonary function changes that occur after interscalene brachial plexus block.
14. What would you do if the patient complained of dyspnea after you performed an interscalene or supraclavicular block?
15. The surgeon prefers to perform the surgical procedure in the sitting position. What are the advantages and disadvantages of this position compared to the lateral position in this patient?
16. Which nerves are most commonly missed with axillary brachial plexus block? With interscalene block? With all brachial plexus blocks?
17. What is the expected duration of brachial plexus block with 40 mL of 1.5% mepivacaine with 5 μg per mL epinephrine?
18. What is the maximum safe dose of local anesthetic for brachial plexus block?

D. Postoperative Management

1. What regimen would you suggest for postoperative pain management?
2. In the postanesthesia care unit, the patient complains of dyspnea. How would you evaluate and manage this?
3. On the third postoperative day after removal of the brachial plexus catheter, the patient complains of persistent numbness and paresthesia in the ulnar nerve distribution. What would you tell the patient? How would you manage neurologic dysfunction after brachial plexus block that persists for 1 week?

A. Medical Disease and Differential Diagnosis

A.1. What are the presenting problems in this patient?

The patient is scheduled for urgent surgery for a proximal humeral fracture and may have some significant internal bleeding. Significant COPD, history of multiple fainting episodes in the past, and chronic hypertension are the presenting problems.

A.2. What additional medical history would you want to obtain?

It is important to know if the patient's fall was precipitated by a fainting episode or if the patient simply tripped or lost footing. The patient should be questioned whether any additional

trauma occurred at the time of the fall: Has the patient's history of fainting been evaluated in the past? Does the patient have any known cardiac disease? Does he have any history of stroke or carotid disease?

A.3. What implications does the use of atenolol have on the patient's coexisting medical condition?

The patient's use of atenolol may exacerbate COPD, especially if there is a reversible component of airway disease. It would be useful to determine whether the atenolol is being taken for the treatment of hypertension or syncope. Although uncontrolled and small controlled clinical trials have shown some benefit from the use of β-blockers, larger, long-term controlled trials have not supported their use for the treatment of reflex syncope. There is some evidence that β-blockers may be protective with regard to development of severe bradycardia or sudden asystole during surgical procedures performed in the “beach chair” or head-up position.

Liguori GA, Kahn RL, Gordon J, et al. The use of metoprolol and glycopyrrolate to prevent hypotensive/bradycardic events during shoulder arthroscopy in the sitting position under interscalene block. *Anesth Analg*. 1998;87:1320-1325.

Moya A, Sutton R, Ammirati F, et al. Guidelines for the diagnosis and management of syncope (version 2009). *Eur Heart J*. 2009;30:2631-2671.

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A.4. Why is immobilization of the arm important following humeral fracture?

Immobilization of the arm following humeral fracture is important to avoid injury to the brachial plexus or its terminal branches.

A.5. What nerve is at particular risk for injury from humeral fracture?

The radial nerve is at particular risk, especially with midshaft humeral fracture. Following proximal humeral fracture, the shoulder can be dislocated, and malpositioning can cause stretching or pressure on components of the brachial plexus. To this extent, it is important to document any preexisting neurologic findings on examination, especially if brachial plexus block is being considered.

B. Preoperative Evaluation and Preparation

B.1. What testing would be helpful to elucidate the cause of this patient's fainting spells?

Syncope is defined by a complete loss of consciousness that is of rapid onset and short duration, accompanied by loss of postural tone and a complete and spontaneous recovery. The major categories of syncope include reflex or neurally mediated syncope (vasovagal, situational, carotid sinus), orthostatic syncope (autonomic failure, drug-induced, hypovolemia), and cardiac syncope (arrhythmia, drug-induced, structural disease). Syncope is fairly common, affecting approximately 11% of the population. Vasovagal syncope is the most common cause, accounting for 21% of cases. Most affected patients experience a first episode between the ages of 10 and 30 years; only 5% of patients experience their first episode after age 40 years. The incidence of syncope increases with age, peaking after the age of 65 years.

The workup of syncope should include a detailed history and physical examination, including a measurement of orthostatic blood pressure and an electrocardiogram. An echocardiogram is indicated if the history or physical exam is suggestive of cardiac disease. Tilt-table testing or a neurologic workup may also be appropriate depending on the history and physical exam.

This patient had a prior evaluation that documented an abnormal response to head-up tilt-table testing during isoproterenol infusion and received a diagnosis of reflex (vasovagal) syncope. He has managed this conservatively with physical maneuvers (sitting, leg crossing) upon feeling faint and has not experienced a complete loss of consciousness for over 20 years.

da Silva RM. Syncope: epidemiology, etiology and prognosis. *Front Physiol*. 2014;5:471.

Moya A, Sutton R, Ammirati F, et al. Guidelines for the diagnosis and management of syncope (version 2009). *Eur Heart J*. 2009;30:2631-2671.

Soteriades ES, Evans JC, Larson MG, et al. Incidence and prognosis of syncope. *N Engl J Med*. 2002;347:878-885.

B.2. What premedication would you order?

No single premedication regimen has been shown to be consistently more effective than others. This patient has already received a recent significant intravenous dose of hydromorphone in the emergency room. If careful history rules out any significant problems or other drug intake, intravenous midazolam can be carefully titrated in the operating room while the patient is monitored with pulse oximetry in the presence of the anesthesia practitioner. Opiates should be avoided because the patient has already received intravenous hydromorphone.

B.3. What are the respiratory effects of benzodiazepines?

Although benzodiazepines almost certainly cause a dose-related, centrally mediated respiratory depression, overall respiratory depression is not nearly as profound as with the administration of intravenous opiates. Use of carefully titrated smaller therapeutic doses of midazolam is usually well tolerated, without significant respiratory depression. Use of benzodiazepines has been shown to elevate the seizure threshold during local anesthetic administration.

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Arcangeli A, Antonelli M, Mignani V, et al. Sedation in PACU: the role of benzodiazepines. *Curr Drug Targets*. 2005;6:745-748.

C. Intraoperative Management

C.1. What anesthetic technique would you use?

Both interscalene and supraclavicular brachial plexus blocks provide excellent operating conditions and allow for postoperative analgesia. Concomitant intravenous sedation and oxygen via nasal cannula may be appropriate, or laryngeal mask airway or endotracheal intubation may be preferred depending on the surgical positioning and access to the airway.

C.2. Describe the relevant anatomy of the brachial plexus.

The brachial plexus supplies the nerves to the upper limb. It is formed by the ventral primary divisions of the fifth to the eighth cervical and the first thoracic nerves, with possible contributions from the fourth cervical and second nerve thoracic roots. The roots join to form the superior, middle, and inferior trunks, which divide into anterior and posterior divisions (Fig. 46.1). The three posterior divisions form the posterior cord, whose major branches are the radial and the axillary nerves. The upper two anterior divisions form the lateral cord, whose major branches are the musculocutaneous nerve and the lateral root of the median nerve. The lowest anterior division forms the medial cord, which gives the medial root to the median nerve and terminates as the ulnar nerve. The sympathetic contributions to the brachial plexus are derived from the middle cervical ganglion and the stellate ganglion.

The brachial plexus begins at the level of the nerve roots, usually at C5-T1. It is at this level that the interscalene brachial plexus block, first described by Winnie, is performed. Injections at this level result in a block with central characteristics, much like a one-sided neuraxial block. Resulting sensory block at this level is characterized by a dermatomal pattern. If the block is incomplete, the typical cause is inadequate spread of local anesthetic to certain nerve roots. For example, the C8-T1 nerve roots are often spared during interscalene block anesthesia because local anesthetic distribution fails to include the lower, most caudal, nerve roots of the brachial plexus. As the brachial plexus courses more peripherally from the neck to the axilla, the nerve roots transform to trunks, divisions, and cords and finally form fully differentiated peripheral nerves. At the level of the axilla, where axillary block is performed, the plexus is composed of terminal nerves that include the median, radial, ulnar, and musculocutaneous nerves. At this level, an incomplete block typically spares sensory or motor blockade in the distribution of a given peripheral nerve, for example, the lateral antebrachial cutaneous nerve (the terminal sensory branch of the musculocutaneous nerve), which exits the surrounding fascia high in the brachial plexus. At this level, the nerves are spread out anatomically around the axillary artery, and depending upon the location of the needle tip during injection and the volume of local anesthetic, any of the four nerves could be spared. This has resulted in the description of multiple injection techniques for axillary block to ensure complete brachial plexus anesthesia.

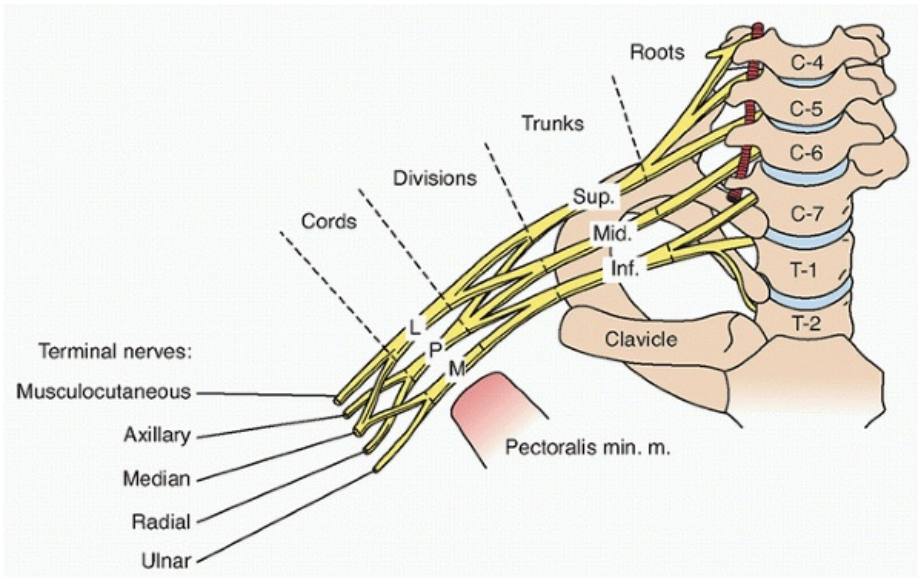


FIGURE 46.1 The brachial plexus. The roots join to form the superior (Sup), middle (Mid), and inferior (Inf) trunks,

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which divide into anterior and posterior divisions. L, lateral; M, medial; P, posterior.

At the level of the nerve roots or trunks, the brachial plexus is simply a neural plexus, being devoid of major consistently identifiable blood vessels. At this level, brachial plexus identification (i.e., needle tip location) relies on a neural response (paresthesia or motor response to electrical nerve stimulation) or direct imaging (e.g., using ultrasonographic guidance) of the neural tissue itself. At the level of the clavicle and first rib, the plexus picks up the subclavian artery, later to become the axillary artery. At this level or below, one can take advantage of the blood vessels (by palpation, Doppler flow guidance, or ultrasonographic guidance) to assist in the performance of brachial plexus block, and true perivascular techniques of brachial plexus block are the commonly preferred techniques.

Neal JM, Gerancher JC, Hebl JR, et al. Upper extremity regional anesthesia: essentials of our current understanding, 2008. *Reg Anesth Pain Med*. 2009;34:134-170.

Urmey WF. Pulmonary complications. In: Neal JM, Rathmell J, eds. *Complications in Regional Anesthesia and Pain Medicine*. Philadelphia, PA: Saunders; 2007:147-156.

Winnie AP. Interscalene brachial plexus block. *Anesth Analg*. 1970;49:455-466.

C.3. What relevant anatomic structures in the neck and below the neck can be injured or injected accidentally during brachial plexus block?

The brachial plexus in the neck has multiple significant anatomic relationships that include the phrenic nerve, subarachnoid space, epidural space, spinal cord, proximal nerve roots, vertebral artery, jugular veins, and the apex of the lung. Errant needle passes can hit any one of these, and in fact, there are published case reports of complications from needle injury or local anesthetic injection for each of these anatomic structures.

Below the neck, the major relevant structures are the blood vessels in the neurovascular plexus, which include the subclavian artery and vein, which more distally become the axillary artery and vein, as well as the parietal pleural, visceral pleural, and lung.

C.4. What regional technique would you choose to block the brachial plexus in this patient?

Interscalene block gives the most complete block for shoulder surgery and facilitates the placement of a catheter that can be used to extend the operative anesthesia or to administer prolonged postoperative analgesia if this is desired. The supraclavicular block has not historically been used for shoulder surgery due to the concern that it may not block the supraclavicular nerve

(C3-C4) and thus not provide anesthesia over the cape of the shoulder. Recent experience suggests that at higher volumes of local anesthetic (50 mL), supraclavicular block provides equivalent anesthetic conditions to interscalene block. The supraclavicular block may also have a decreased incidence of phrenic nerve blockade when compared to the interscalene block when lower volumes of local anesthetic (20 mL) are used, although this is not guaranteed. If coverage of the shoulder cape is a concern with the use of lower volumes of local anesthetic, the supraclavicular nerve can anesthetized separately with a superficial cervical plexus block.

Liu SS, Gordon MA, Shaw PM, et al. A prospective clinical registry of ultrasound-guided regional anesthesia for ambulatory shoulder surgery. *Anesth Analg*. 2010;111:617-623.

Neal JM, Gerancher JC, Hebl JR, et al. Upper extremity regional anesthesia: essentials of our current understanding, 2008. *Reg Anesth Pain Med*. 2009;34:134-170.

Renes SH, Spoormans HH, Gielen MJ, et al. Hemidiaphragmatic paresis can be avoided in ultrasound-guided supraclavicular brachial plexus block. *Reg Anesth Pain Med*. 2009;34:595-599.

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C.5. What are the advantages and disadvantages of the following blocks?

a. Interscalene block

b. Supraclavicular block

c. Infraclavicular block

d. Axillary block

Interscalene Block

One advantage of the interscalene block is a superficial location that makes it easily accessible by paresthesia, nerve stimulation, or ultrasonographic guidance techniques. Injection of an adequate volume of local anesthetic at the interscalene level results in reliably complete anesthesia or analgesia for surgery on or about the shoulder, including proximal humeral surgery. A single injection results in success rates approaching 100%. A catheter can be easily placed at this site. This block reliably covers the supraclavicular nerve (C3-C4), which supplies sensory innervation to the cape of the shoulder. Finally, the axillary nerve to the deltoid and the musculocutaneous nerve to the biceps brachialis derive from the C5-C6 nerve roots, and therefore, reliable relaxation of the deltoid and biceps muscles is guaranteed. This allows optimal surgical exposure and facilitates dislocation of the humeral head from the glenoid socket. If performed properly, it is impossible to cause a pneumothorax with an appropriate needle using this approach.

Disadvantages include the lack of blood vessels in the interscalene space that make perivascular techniques impossible. Close proximity of the phrenic nerve, or perhaps nerve root marginalization of those fibers contributing to phrenic nerve formation, has rarely resulted in injury to these structures and reported cases of permanent phrenic nerve palsy. Interscalene block with a volume of local anesthetic adequate for surgery results in 100% incidence of ipsilateral hemidiaphragmatic paresis.

Supraclavicular Block

The supraclavicular block is used for surgeries distal to and including the shoulder, although this block may spare the supraclavicular nerve (C3-C4) supplying sensation to the skin over the top of the shoulder. If being performed for shoulder surgery, this block may be supplemented with a superficial cervical plexus block. The supraclavicular block is most commonly performed using ultrasound guidance. It can also be performed with the subclavian perivascular or “plumb-bob” approaches. Advantages of ultrasound-guided supraclavicular block include superficial location of the artery and plexus that allow for easy imaging and perivascular blockade. Also, one is able to visualize two-dimensional local anesthetic distribution and can avoid inadvertent puncture or injection into the vessels. Disadvantages include the intimate proximity to the apex of the lung, which has resulted in case reports of pneumothorax following this block. Supraclavicular block is associated with a variable incidence of diaphragmatic paresis.

Infraclavicular Block

The infraclavicular block is used for procedures distal to the shoulder. It can be performed with nerve stimulation or ultrasound guidance. One advantage of the ultrasound-guided infraclavicular block is the visualization of the artery, which facilitates imaging for perivascular brachial plexus block. The block does not require positioning of the upper extremity. It is easy to place a catheter at a central location of the plexus via this approach. Disadvantages are

related to the depth of the plexus at this level. This may cause more discomfort during placement as the needle must pass through both the pectoralis major and minor muscles.

Axillary Block

The axillary block is utilized for anesthesia distal to the elbow. This block is characterized by the major advantage of the superficial location of the individual terminal branches of the brachial plexus. Thus, one can target the fully differentiated terminal nerves by using either nerve stimulation, paresthesia, or ultrasound-guided techniques. Disadvantages include the need to locate more than one nerve to guarantee successful brachial plexus block at this level. The musculocutaneous nerve is often located relatively distant to the other terminal nerves, lying within the body of the coracobrachialis muscle or between the coracobrachialis and biceps muscles and usually requires a separate injection.

Chan V. *A Practical Guide to Ultrasound Imaging for Regional Anesthesia: Part 2—Upper Limb Blocks. Version 1.1*. Toronto, Canada: Toronto Centre for Ultrasound Education; 2013:72-73.

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Macfarlane AJ, Perlas A, Chan V, et al. Eight ball, corner pocket ultrasound-guided supraclavicular block: avoiding a scratch. *Reg Anesth Pain Med*. 2008;33:502-504.

Neal JM, Moore JM, Kopacz DJ, et al. Quantitative analysis of respiratory, motor, and sensory function after supraclavicular block. *Anesth Analg*. 1998;86:1239-1244.

Renes SH, Spoormans HH, Gielen MJ, et al. Hemidiaphragmatic paresis can be avoided in ultrasound-guided supraclavicular brachial plexus block. *Reg Anesth Pain Med*. 2009;34:595-599.

Soares LG, Brull R, Lai J, et al. Eight ball, corner pocket: the optimal needle position for ultrasound-guided supraclavicular block. *Reg Anesth Pain Med*. 2007;32:94-95.

Urmey WF. Pulmonary complications. In: Neal JM, Rathmell J, eds. *Complications in Regional Anesthesia and Pain Medicine*. Philadelphia, PA: Saunders; 2007:147-156.

C.6. Describe the landmarks and procedures for nerve stimulator and ultrasound-guided interscalene block.

For interscalene block by electrical nerve stimulation, the patient's head is turned away from the side of the block at an approximately 45-degree angle with the surface of the bed or table. The interscalene groove (between the anterior and middle scalene muscles) is located by palpation just posterior to the lateral border of the sternocleidomastoid muscle. The electrically shielded stimulating needle is introduced in a dorsal, medial, and caudal direction until an appropriate motor response is elicited. Because of the orientation of the nerve roots in a cephalocaudad plane, a response from C5-C6 nerve roots is most frequently obtained first. C5-C6 motor response is characterized by deltoid, biceps, or brachioradialis muscle contractions. Reduction of electrical current amplitude below 0.5 mAmp at a pulse duration of 0.1 millisecond results in a success rate with single injection close to 100%.

For interscalene block by ultrasonographic guidance (Figs. 46.2, 46.3 and 46.4, Video 46.1), either an in-plane or out-of-plane approach can be used, depending on the experience and preference of the operator. For an in-plane approach, the needle is inserted in a posterolateral to anteromedial direction along the long axis of a high-frequency linear array transducer with the needle shaft and tip visualized. The middle and anterior scalene muscles should be visualized, and the hypoechoic nerve roots are usually stacked in a somewhat cephalocaudad arrangement. Injection should be made so that real-time spread of anesthetic can be visualized within the brachial plexus sheath spreading the cross-sectional nerve roots apart.

For an out-of-plane approach, the high-frequency linear array transducer may be placed just caudal to the conventional interscalene block injection point and just above the clavicle. The longitudinal axis of the transducer is oriented in a posterolateral to anteromedial direction, with the center of the probe overlying the interscalene space and the image of the nerve roots, which again will be hypoechoic in cross section. The needle is introduced in a slightly dorsal, medial, and caudal direction, as originally described in the conventional technique by Winnie. It is technically challenging to observe the needle tip when using the out-of-plane approach. Tissue movement as seen on the ultrasound image can be used to guide needle placement, as can intermittent injection of small volumes of local anesthetic. Nerve stimulation can also be used to confirm position of the needle tip within the brachial plexus.

Chan V. *A Practical Guide to Ultrasound Imaging for Regional Anesthesia: Part 2—Upper Limb Blocks. Version 1.1*. Toronto, Canada: Toronto Centre for Ultrasound Education; 2013:17-32.

Hadzic A, ed. *Textbook of Regional Anesthesia and Acute Pain Management* . New York: McGraw Hill; 2007:663-672.

Kapral S, Greher M, Huber G, et al. Ultrasonographic guidance improves the success rate of interscalene brachial plexus blockade. *Reg Anesth Pain Med*. 2008;33:253-258.

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Winnie AP. Interscalene brachial plexus block. *Anesth Analg*. 1970;49:455-466.

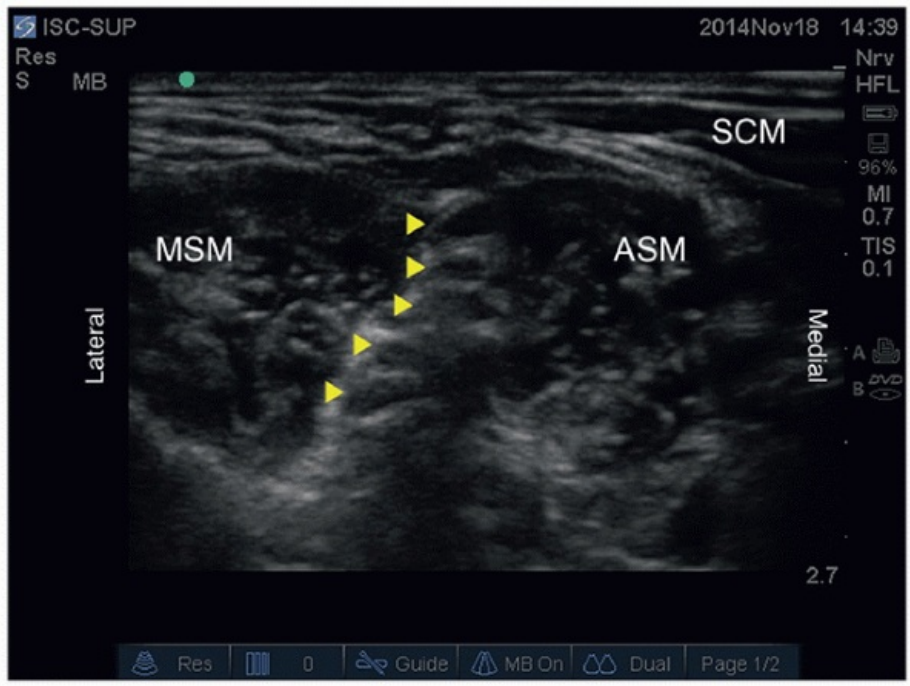


FIGURE 46.2 Ultrasound image of interscalene groove. The hypoechoic nerve roots of the brachial plexus *(yellow arrowheads)* can be seen between the anterior scalene muscle (ASM) and middle scalene muscle (MSM). SCM, sternocleidomastoid muscle.

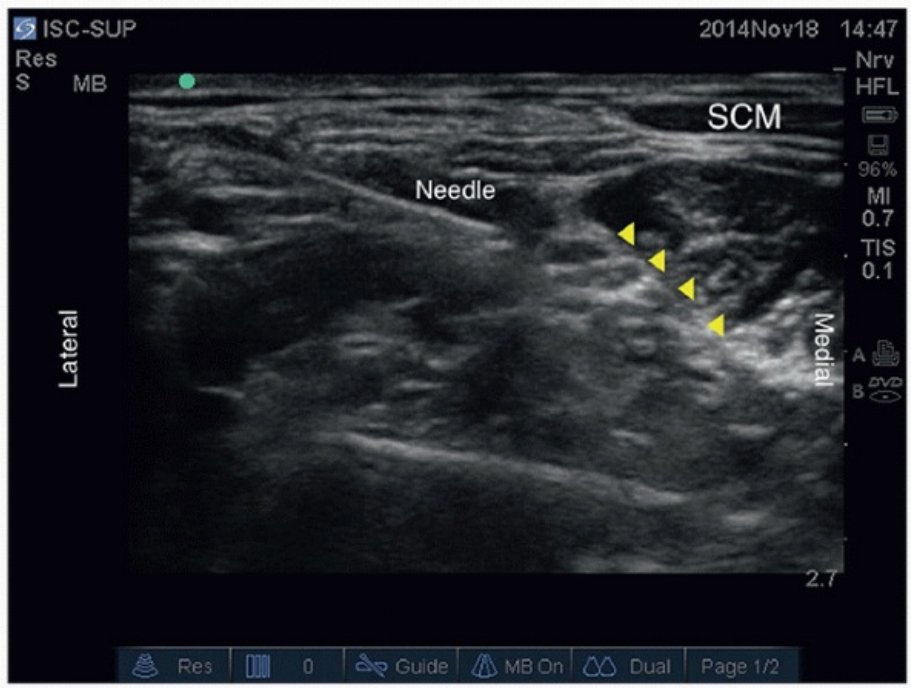


FIGURE 46.3 Ultrasound-guided interscalene block. The needle can be seen approaching the nerve roots *(yellow arrowheads)* in the interscalene groove from the lateral to medial direction. SCM, sternocleidomastoid muscle.

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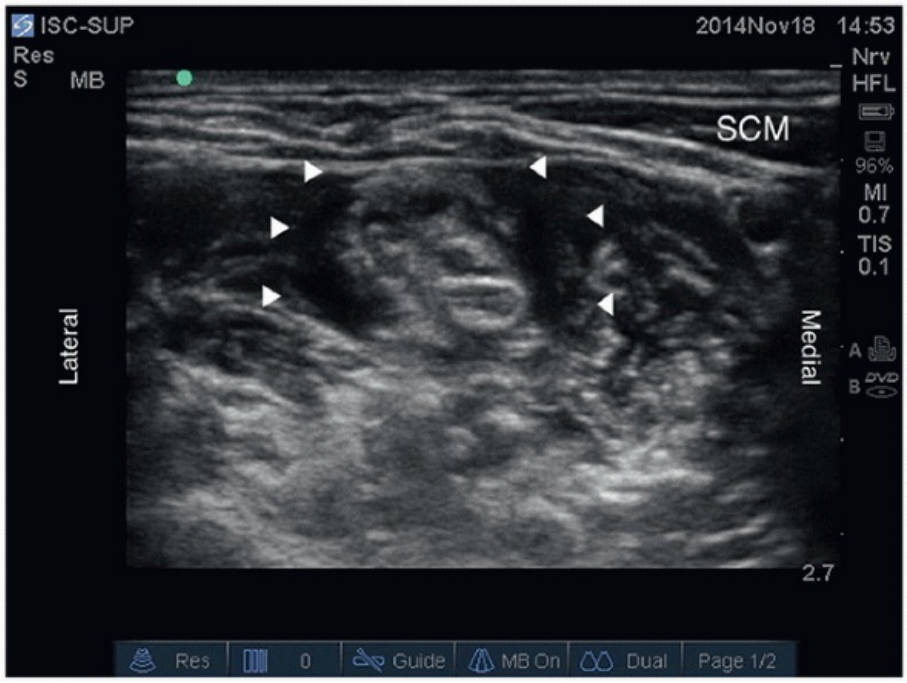


FIGURE 46.4 Ultrasound-guided interscalene block. Hypoechoic local anesthetic *(white arrowheads)* can be seen surrounding the brachial plexus in the interscalene groove. SCM, sternocleidomastoid muscle.

C.7. Describe the landmarks and procedures for nerve stimulator and ultrasound-guided supraclavicular block.

The divisions of the brachial plexus in the supraclavicular area are located cephaloposterior to the subclavian artery and superior to the first rib. Due to the high risk of subclavian artery puncture and pneumothorax with the perivascular and "plumb-bob" techniques, this block is predominately performed using ultrasound guidance. A high-frequency linear array transducer is placed just above and parallel to the clavicle in the supraclavicular fossa (Figs. 46.5 and 46.6). In the resulting ultrasound image, the plexus can be visualized superior and lateral to the subclavian artery and directly above the first rib. The dome of the lung can be seen medial to the first rib. An in-plane posterolateral to anteromedial technique is generally used, making sure that the needle tip and shaft are visualized throughout manipulation of the needle and that the pleura is clearly seen. Local anesthetic is deposited at the superior aspect of the plexus for proximal procedures (shoulder, humerus) and in the "eight ball, corner pocket" between the subclavian artery, first rib, and brachial plexus for distal procedures (forearm, hand).

Brown D, ed. *Atlas of Regional Anesthesia* . 4th ed. Philadelphia, PA: Saunders Elsevier; 2010:49-58.

Soares LG, Brull R, Lai J, et al. Eight ball, corner pocket: the optimal needle position for ultrasound-guided supraclavicular block. *Reg Anesth Pain Med*. 2007;32:94-95.

C.8. Describe the landmarks and procedures for nerve stimulator and ultrasound-guided infraclavicular block.

The infraclavicular block is performed at the cord level of the brachial plexus near the second portion of the axillary artery. For the nerve stimulator approach, the patient is placed supine

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with the arm to be blocked abducted 90 degrees at the elbow. The coracoid process is palpated, and the needle insertion site is located 2 cm medial and 2 cm caudad to the process. The needle is inserted in a vertical parasagittal plane until a distal upper extremity motor response is elicited. The needle may be redirected in a cephalocaudad arc if a response is not elicited on the initial attempt. The depth of the brachial plexus can vary from 3 to 10 cm depending on patient size.

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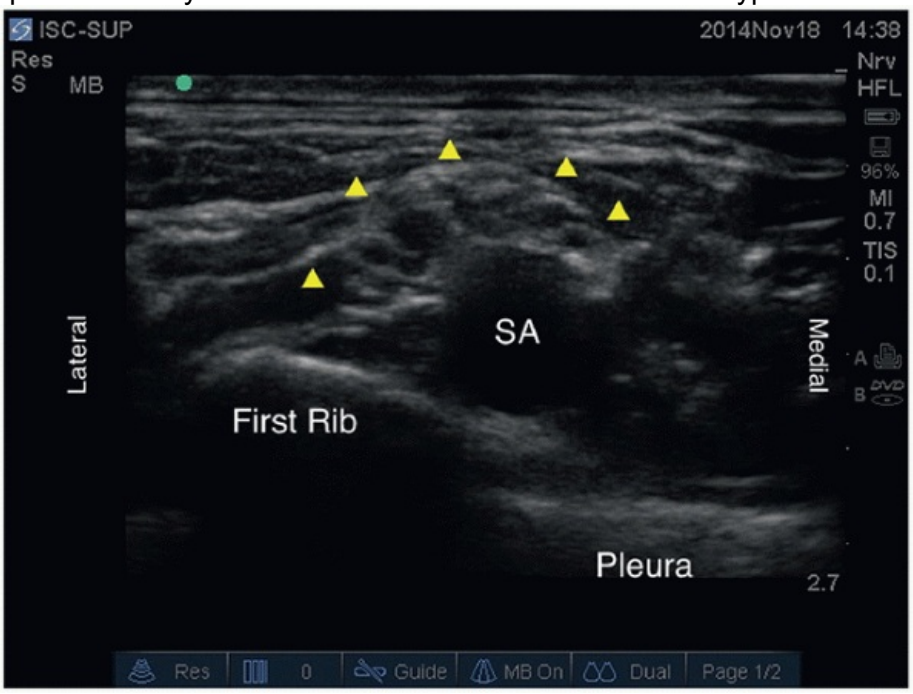


FIGURE 46.5 Ultrasound image of the supraclavicular fossa. The hypoechoic divisions of the brachial plexus *(yellow arrowheads)* can be seen superior and lateral to the subclavian artery (SA).

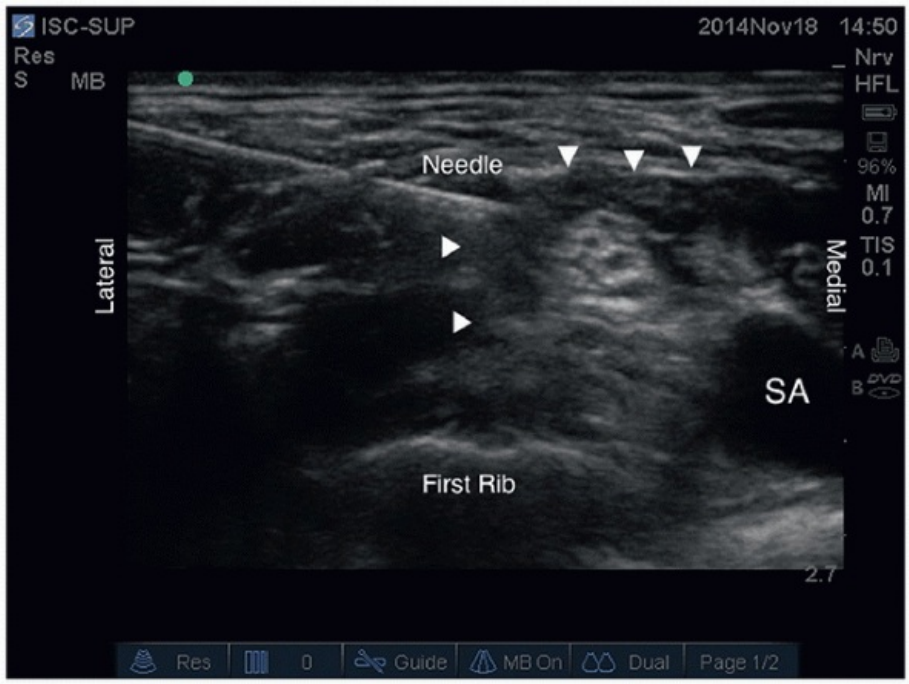


FIGURE 46.6 Ultrasound-guided supraclavicular block. The needle is positioned just superior and lateral to the brachial plexus. Hypoechoic local anesthetic *(white arrowheads)* can be seen surrounding the plexus. SA, subclavian artery.

The ultrasound-guided infraclavicular block (Fig. 46.7) is usually performed with the patient supine and with the arm either adducted at the side or abducted 90 degrees at the elbow. The ultrasound probe is placed in the deltopectoral groove just medial to the coracoid process. There is a large amount of variation in the precise location of the cords, but in this position, the lateral cord is most often located cephalad, the posterior cord posterior, and the medial cord caudad to the axillary artery. The medial cord may lie between the axillary artery and vein. Abduction of the arm to 90 degrees may improve visualization of the cords and will pull the clavicle down and away from the needle insertion site. A 10-cm needle is

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inserted in-plane and cephalad to the long axis of the probe, and the tip is positioned posterior to the axillary artery near the posterior cord. The steep insertion angle required and the depth of the brachial plexus at this level often result in poor visualization of the needle. The use of a small curvilinear probe and an echogenic needle may enhance needle visualization. The curvilinear probe allows greater room for needle entry and a wide sector view of the involved structures at the expense of reduced resolution when compared to a high-frequency linear probe. If all three cords are not easily identifiable, deposition of a ring of local anesthetic surrounding the axillary artery is associated with an effective block in 95% of cases. It may be necessary to reposition the needle and give multiple injections in order to surround all three cords.

Brown D, ed. *Atlas of Regional Anesthesia* . 4th ed. Philadelphia, PA: Saunders Elsevier; 2010:59-72.

Chan V. *A Practical Guide to Ultrasound Imaging for Regional Anesthesia: Part 2—Upper Limb Blocks. Version 1.1*. Toronto, Canada: Toronto Centre for Ultrasound Education; 2013:64-73.

Ootaki C, Hayashi H, Amano M. Ultrasound-guided infraclavicular brachial plexus block: an alternative technique to anatomical landmark-guided approaches. *Reg Anesth Pain Med*. 2000;25:600-604.

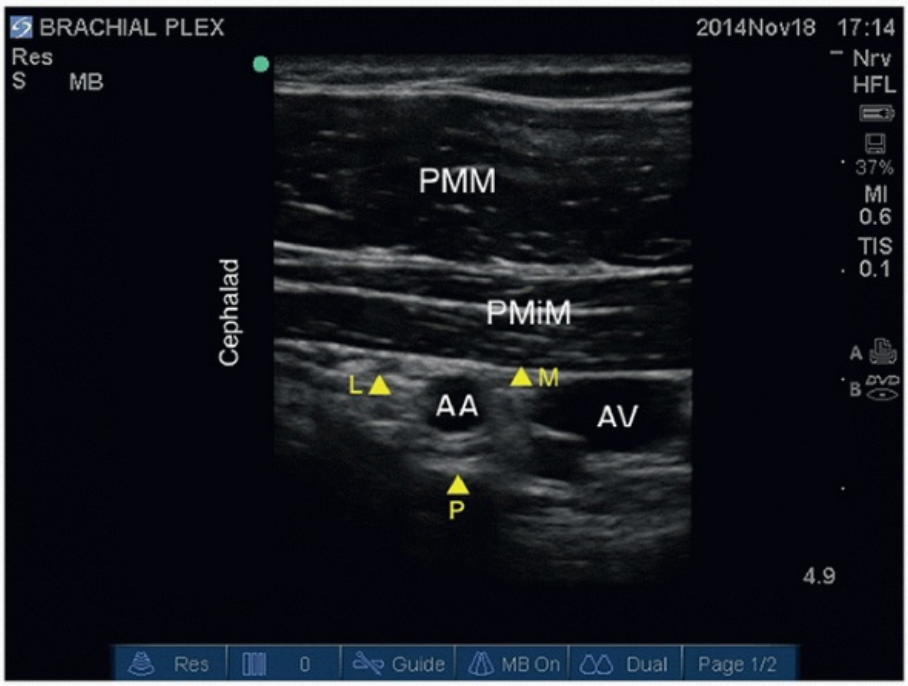


FIGURE 46.7 Ultrasound image of the infraclavicular region using a high-frequency linear probe. The lateral (L), posterior (P), and medial (M) cords can be seen surrounding the axillary artery (AA). AV, axillary vein; PMiM, pectoralis minor muscle; PMM, pectoralis major muscle.

C.9. Describe the landmarks and procedures for nerve stimulator and ultrasound-guided axillary block.

In the axilla, the median, ulnar, and radial nerves lie close to the axillary artery and are surrounded by the biceps, triceps, and coracobrachialis muscles. The radial nerve generally lies between the axillary artery and the humerus. The musculocutaneous nerve separates from the lateral cord proximal to the axilla and is often found between the biceps and coracobrachialis muscles.

For the nerve stimulator technique, the patient is positioned supine and the arm is abducted to 90 degrees and bent at the elbow. The patient's axillary artery is palpated, and a small-gauge electrically shielded stimulating needle is introduced just below the artery to elicit motor response from the radial nerve (deep to the artery) or ulnar nerve (medial to the artery; i.e., immediately below with the arm in this position). The needle is repositioned and advanced superficial to the artery for a median nerve motor response. Highest success rate correlates with at least two motor responses in which one response

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is from radial nerve stimulation. By insisting on current amplitude levels of 0.5 mAmp or below, at short pulse duration (0.1 millisecond), success rates in the 95% to 100% range can be expected.

The ultrasound-guided axillary block (Fig. 46.8) utilizes the same patient position as the nerve stimulator technique. The ultrasound probe is placed along the axillary crease in order to obtain a transverse view of the vessels and nerves. Care should be taken to identify the location of axillary veins, as even slight pressure from the ultrasound transducer can collapse these vessels and obscure their identification. The nerves will appear hyperechoic with a honeycomb-like texture and can be traced distally in the arm to confirm their identification. The block is usually performed in-plane with a 5-cm needle oriented from lateral to medial or out-of-plane with the needle oriented perpendicular to the long axis of the transducer. A shallow needle angle is utilized due to the superficial location of the nerves in the axilla and

generally results in a clear image of the needle. If an out-of-plane technique is used, injections of small amounts of local anesthetic during needle advancement can assist in identifying the location of the needle tip. If the individual radial, median, and ulnar nerves are difficult to identify, a perivascular ring of local anesthetic surrounding the axillary artery usually ensures a successful block of these nerves.

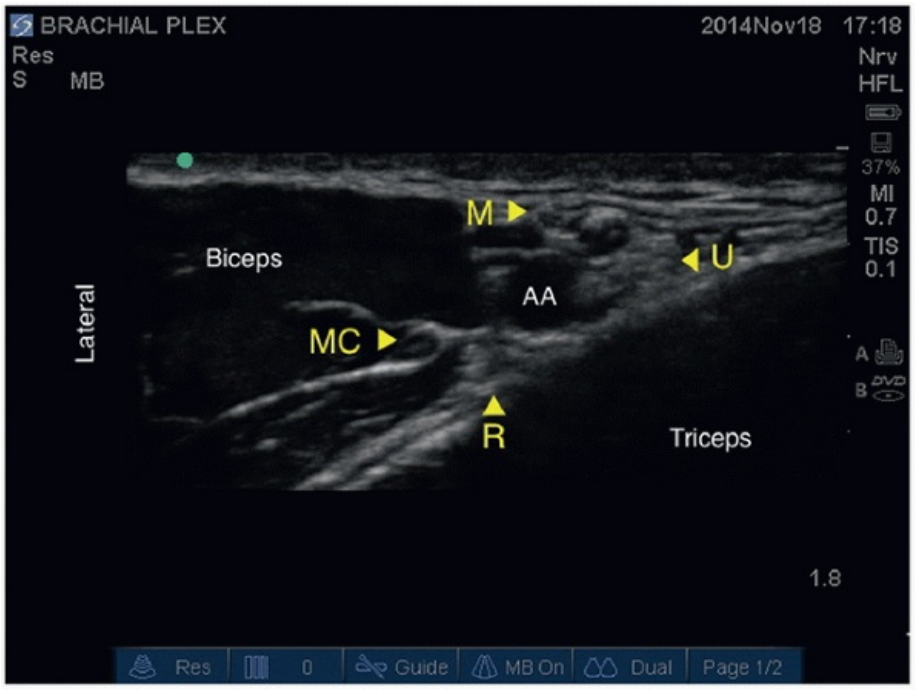


FIGURE 46.8 Ultrasound image of the axilla. The median (M), radial (R), and ulnar (U) nerves can be seen surrounding the axillary artery (AA). The musculocutaneous nerve (MC) lies between the body of the biceps and the coracobrachialis muscles.

Chan V. *A Practical Guide to Ultrasound Imaging for Regional Anesthesia: Part 2—Upper Limb Blocks. Version 1.1*. Toronto, Canada: Toronto Centre for Ultrasound Education; 2013:64-73.

Neal JM, Gerancher JC, Hebl JR, et al. Upper extremity regional anesthesia: essentials of our current understanding, 2008. *Reg Anesth Pain Med*. 2009;34:134-170.

C.10. The patient requests to have the brachial plexus block performed after you administer general anesthesia. Would you agree to this request?

In a landmark publication, Benumof reported four cases of permanent injury to the cervical spinal cord resulting from interscalene block performed during general anesthesia. Imaging of the cervical spinal cord showed vacuolization of the cord or the presence of a syrinx. Intraneural injection of local anesthetic under pressure has been found to spread along the longitudinal axis along the nerve during experimental studies. Thus, theoretically, injection into a proximal nerve root

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can spread and disrupt the cervical spinal cord.

Performance of regional anesthesia in the anesthetized patient does not allow the patient to report painful paresthesia or other sensations. Sudden severe pain on injection during peripheral nerve block is a time-honored signal that neural tissue is endangered and that the needle should be promptly withdrawn and repositioned. It has been shown that needle contact with the nerve is often not associated with the ability to elicit a motor response during electrical stimulation. Reports of accidental intraneural injection during ultrasonographic needle guidance have been published. Therefore, no available modality can ensure against this devastating complication. It is recommended that regional blocks not be performed in patients who are heavily sedated or following induction of general anesthesia. There are certain important exceptions to this rule, including children and adults who may suffer from dementia or developmental delay or for other reasons are unable to tolerate regional block under only minimal sedation.

Auroy Y, Benhamou D, Bargues L, et al. Major complications of regional anesthesia in France: The SOS Regional Anesthesia Hotline Service. *Anesthesiology*. 2002;97:1274-1280.

Benumof JL. Permanent loss of cervical spinal cord function associated with interscalene block performed under general anesthesia. *Anesthesiology*. 2000;93:1541-1544.

Hadzic A, Dilberovic F, Shah S, et al. Combination of intraneural injection and high injection pressure leads to fascicular injury and neurologic deficits in dogs. *Reg Anesth Pain Med*. 2004;29:417-423.

Neal J, Bernards C, Hadzic A, et al. ASRA practice advisory on neurologic complications in regional anesthesia and pain medicine. *Reg Anesth Pain Med*. 2008;33:404-415.

Urmey WF, Stanton J. Inability to consistently elicit a motor response following sensory paresthesia during interscalene block administration. *Anesthesiology*. 2002;96:552-554.

C.11. What relevant respiratory complications or side effects are you concerned about in this patient?

Ipsilateral hemidiaphragmatic paresis is a consistent side effect associated with interscalene block. It occurs with an incidence of 100%. It is also a variable side effect of supraclavicular block. This expected side effect takes on added importance if the patient has respiratory comorbidities, including contralateral phrenic or diaphragmatic pathology, severe chronic obstructive cardiopulmonary disease, neuromuscular disorders in which a 25% reduction in FVC would not be tolerated, or conditions that restrict ribcage motion such as ankylosing spondylitis. If these conditions are present, significant atelectasis or respiratory failure can occur. With proper technique and needle size, there is no possibility of causing a pneumothorax. Introduction of a catheter, nevertheless, could theoretically reach the apex of the lung.

Urmey WF, Talts KH, Sharrock NE. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. *Anesth Analg*. 1991;72:498-503.

C.12. What is the incidence of hemidiaphragmatic paresis following interscalene brachial plexus block? Can this complication be avoided by lowering the volume or concentration of local anesthetic injected? By using ultrasound-guided supraclavicular block?

Hemidiaphragmatic paresis occurs 100% of the time with interscalene block and cannot be avoided by reducing the volume of local anesthetic injected. Volumes as low as 5 mL (which is inadequate for surgical anesthesia) have been associated with a 45% incidence of hemidiaphragmatic paresis. Similarly, reductions in local anesthetic concentration do not avoid this side effect, with concentrations of bupivacaine as low as 0.125% being associated with 100% incidence of hemidiaphragmatic paresis. The use of ultrasound-guided supraclavicular blocks can reduce the incidence of hemidiaphragmatic paresis from 100% but will still be expected to be associated with a variable incidence. Blocks above the clavicle are associated with spread of local anesthetic into the cervical plexus. The mechanism for phrenic nerve paresis is motor blockade of the C3-C5 nerve roots before forming the phrenic nerve. The main nerve root contributing to

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formation to the phrenic nerve is the C4 nerve root. Any block causing sensory blockade of C5, C4, or C3 would be expected to have associated phrenic paresis. A recent publication suggests that with careful deposition of lower volumes of local anesthetic by ultrasonographic guidance, the incidence of hemidiaphragmatic paresis may indeed be avoided during supra clavicular block.

Renes SH, Spoormans HH, Gielen MJ, et al. Hemidiaphragmatic paresis can be avoided in ultrasound-guided supraclavicular brachial plexus block. *Reg Anesth Pain Med*. 2009;34:595-599.

Sinha SK, Abrams JH, Barnett JT, et al. Decreasing the local anesthetic volume from 20 to 10 mL for ultrasound-guided interscalene block at the cricoid level does not reduce the incidence of hemidiaphragmatic paresis. *Reg Anesth Pain Med*. 2011;36:17-20.

Urmey W, Gloeggler P. Pulmonary function changes during interscalene block: effects of decreasing local anesthetic injection volume. *Reg Anesth*. 1993;18:244-249.

Urmey WF, Talts KH, Sharrock NE. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. *Anesth Analg*. 1991;72:498-503.

C.13. Describe the pulmonary function changes that occur after interscalene brachial plexus block.

Pulmonary function (such as FVC and forced expiratory volume in 1 second) reductions of 25% to 30% occur routinely. These changes are usually complete within 15 minutes of completion of the injection. Increased upper rib cage expansion and ipsilateral paradoxical inward motion of the hemiabdomen have been reported. The combined effect of these changes is a reduced ability to cough and clear secretions, which may be poorly tolerated by a patient with severe COPD.

Urmey WF, McDonald M. Hemidiaphragmatic paresis during interscalene brachial plexus block: effects on pulmonary function and chest wall mechanics. *Anesth Analg*. 1992;74:352-357.

C.14. What would you do if the patient complained of dyspnea after you performed an interscalene or supraclavicular block?

The patient should be reassured and observed. Most patients complaining of dyspnea will have more than adequate pulmonary function for normal respiration. Symptoms of dyspnea may be relieved by placing the patient in the upright or sitting position as tolerated. This position optimizes diaphragmatic geometry and function and increases functional residual capacity. Auscultation often reveals diminished or silent breath sounds on the side of the block. Chest radiography may be obtained if pneumothorax is suspected. Application of a face mask to assess ventilation or end-tidal carbon dioxide may be done, and assisted or controlled ventilation can be used if necessary. Endotracheal intubation should be performed if clinically indicated.

C.15. The surgeon prefers to perform the surgical procedure in the sitting position. What are the advantages and disadvantages of this position compared to the lateral position in this patient?

As discussed earlier, the seated position optimizes chest wall mechanics. The sitting position also allows easier access to the airway and is more comfortable for the patient if sedation is preferred over general anesthesia. However, placing the patient in the seated position may be associated with hypotension or bradycardia. Severe bradycardia or asystole may occur. It is suggested that these events occur as a result of the Bezold-Jarisch reflex (paradoxical cardiac inhibition and bradycardia in response to decreased ventricular volume resulting from venous pooling in sitting position). Use of intravenous β-blockers may help to diminish the incidence of significant hypotension and bradycardia. The sitting position may be thought of as a variation of the tilt-table test. This patient would be at particular risk for developing intraoperative bradycardia in the sitting position because of the history of syncopal episodes and positive findings on the tilt test. Intraoperative bradycardia can be easily treated with small doses of intravenous epinephrine, ephedrine, atropine, and intravenous fluids. Vigilance and rapid response are of critical importance.

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The seated position has also been associated with case reports of stroke and neurologic deficit following shoulder surgery. There is some evidence to suggest improved cerebral perfusion when spontaneous, rather than positive pressure, ventilation is used for shoulder procedures in the upright position.

Gold BS, Weitz SR, Lurie KG. Intraoperative “syncope”: evaluation with tilt-table testing. *Anesthesiology*. 1992;76:635-637.

Kahn RL, Hargett MJ. Beta-adrenergic blockers and vasovagal episodes during shoulder surgery in the sitting position under interscalene block. *Anesth Analg*. 1999;88:378-381.

Liguori GA, Kahn RL, Gordon J, et al. The use of metoprolol and glycopyrrolate to prevent hypotensive/bradycardic events during shoulder arthroscopy in the sitting position under interscalene block. *Anesth Analg*. 1998;87:1320-1325.

Pohl A, Cullen DJ. Cerebral ischemia during shoulder surgery in the upright position: a case series. *J Clin Anesth*. 2005;17:463-469.

Tarkkila P, Isola J. A regression model for identifying patients at high risk of hypotension, bradycardia and nausea during spinal anesthesia. *Acta Anaesthesiol Scand*. 1992;36:554-558.

Weiner MM, Fischer GW, Rosenblatt MA. The beach-chair position and general anesthesia. *Reg Anesth Pain Med*. 2012;37:120.

Yadeau JT, Casciano M, Liu SS, et al. Stroke, regional anesthesia in the sitting position, and hypotension: a review of 4169 ambulatory surgery patients. *Reg Anesth Pain Med*. 2011;36:430-435.

C.16. Which nerves are most commonly missed with axillary brachial plexus block? With interscalene block? With all brachial plexus blocks?

Axillary brachial plexus block commonly misses the musculocutaneous nerve, which arises from C5-C6 nerve roots and exits the plexus above the axilla. The interscalene block commonly spares the ulnar nerve, which is formed by the C8-T1 nerve roots at the lower extent of the brachial plexus. The intercostobrachial nerve is a branch of the second thoracic nerve and is not anesthetized by brachial plexus blocks. A separate injection is required for procedures involving the medial upper arm or axilla, or if a tourniquet will be inflated for extended periods on the upper arm.

Lanz E, Theiss D, Jankovic D. The extent of blockade following various techniques of brachial plexus block. *Anesth Analg*. 1983;62:55-58.

Neal JM, Gerancher JC, Hebl JR, et al. Upper extremity regional anesthesia: essentials of our current understanding, 2008. *Reg Anesth Pain Med*. 2009;34:134-170.

C.17. What is the expected duration of brachial plexus block with 40 mL of 1.5% mepivacaine with 5 µg per mL epinephrine?

Such an injection typically lasts 4 to 5 hours for surgical anesthesia.

C.18. What is the maximum safe dose of local anesthetic for brachial plexus block?

There is no absolute maximum safe dose of local anesthetic. The brachial plexus is characterized by relatively low systemic absorption compared to that of other blocks, such as epidural or intercostal. Absorption of local anesthetic following regional anesthetic injection is site specific. The American Society of Regional Anesthesia and Pain Medicine has published guidelines for local anesthetic toxicity. One should be cognizant of the recent publications demonstrating the

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efficacy of intravenous infusion of lipid emulsion in reversing local anesthetic-induced cardiac toxicity in animals and in multiple case reports involving human patients. Background information as well as advice concerning resuscitation equipment and procedure, including recommended dosing of lipid emulsion, can be obtained by accessing lipidrescue.squarespace.com.

Neal JM, Bernards CM, Butterworth JF IV, et al. ASRA practice advisory on local anesthetic systemic toxicity. *Reg Anesth Pain Med*. 2010;35:152-161.

Neal JM, Mulroy MF, Weinberg GL. American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity: 2012 version. *Reg Anesth Pain Med*. 2012;37:16-18.

Rosenberg PH, Veering BT, Urmey WF. Maximum recommended doses of local anesthetics: a multifactorial concept. *Reg Anesth Pain Med*. 2004;29:564-575.

D. Postoperative Management

D.1. What regimen would you suggest for postoperative pain management?

Patient-controlled regional analgesia with a continuous infusion of local anesthetic is superior to intravenous patient-controlled analgesia for the treatment of pain after major shoulder surgery and also results in a faster time to discharge and increased patient satisfaction when used as part of a multimodal pain regimen. A supraclavicular or interscalene infusion of 0.2% ropivacaine at 4 to 8 mL per hour with patient administered boluses of 2 to 4 mL every 20 to 30 minutes is a good starting point. This can be combined with standing acetaminophen, cyclooxygenase-2 (COX-2) selective nonsteroidal anti-inflammatory drugs, and oral or intravenous opioids as needed.

Borgeat A, Tewes E, Biasca N, et al. Patient-controlled interscalene analgesia with ropivacaine after major shoulder surgery: PCIA vs PCA. *Br J Anaesth*. 1998;81:603-605.

Ilfeld BM, Vandenborne K, Duncan PW, et al. Ambulatory continuous interscalene nerve blocks decrease the time to discharge readiness after total shoulder arthroplasty: a randomized, triple-masked, placebo-controlled study. *Anesthesiology*. 2006;105:999-1007.

D.2. In the postanesthesia care unit, the patient complains of dyspnea. How would you evaluate and manage this?

The patient's vital signs should be monitored, including the oxygen saturation. Duration of hemidiaphragmatic paresis following brachial plexus block with mepivacaine or bupivacaine with added epinephrine lasts 3 to 4 hours or 9 to 18 hours, respectively. If a catheter has been placed, it should be checked via imaging to ascertain that it is not in the cervical plexus. Chest radiography should be performed to rule out pneumothorax or significant atelectasis. The patient should be supported by placement into the sitting position and ventilation assisted or controlled if necessary.

Urmey W, Gloeggler P. Effects of bupivacaine 0.5% compared with mepivacaine 1.5% used for interscalene brachial plexus block (abstract). *Reg Anesth*. 1992;17:13.

D.3. On the third postoperative day after removal of the brachial plexus catheter, the patient complains of persistent numbness and paresthesia in the ulnar nerve distribution. What would you tell the patient? How would you manage neurologic dysfunction after brachial plexus block that persists for 1 week?

Postoperative neurologic symptoms may be due to block, surgical, or patient-related factors. Causes unrelated to the brachial plexus block can include restrictive casts, compartment

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syndrome, or surgical causes such as tourniquet or traction injuries. The incidence of peripheral nerve injury after general anesthesia is approximately 0.04%. The incidence of blockrelated neurologic symptoms in the first several postoperative days ranges from 0.9 per 1,000 to 3 per 100 (0.18% to 3%). The incidence of symptoms lasting longer than 6 months ranges from 0.14 to 0.9 per 1,000 (0.014% to 0.09%).

It is appropriate to reassure the patient and tell him that these symptoms will likely resolve over time. If the symptoms persist for more than 1 week, a neurologist should be consulted to evaluate for neuropathy or brachial plexopathy. Electromyography (EMG) studies provide information on the location and degree of injury. It can take up to 4 weeks for an injury to cause sufficient Wallerian degeneration of axons to result in muscle denervation. EMG testing immediately after the injury can help to define any preexisting neurologic injury but should be repeated after 3 to 4 weeks. Serial testing can help to assess the evolution or recovery of the initial injury. Magnetic resonance imaging (MRI) is also considered a standard tool for the workup of neurologic injuries. It is especially suited to image the brachial plexus, where injuries often present with enhancement. The diagnostic ability of MRI is limited due to the fact that abnormalities seen on MRI can be nonspecific.

Aminoff MJ. Electrophysiologic testing for the diagnosis of peripheral nerve injuries. *Anesthesiology*. 2004;100:1298-1303.

Auroy Y, Benhamou D, Bargues L, et al. Major complications of regional anesthesia in France: The SOS Regional Anesthesia Hotline Service. *Anesthesiology*. 2002;97:1274-1280.

Barrington MJ, Morrison W, Sutherland T, et al. Case scenario: postoperative brachial plexopathy associated with infraclavicular brachial plexus blockade: localizing postoperative nerve injury. *Anesthesiology*. 2014;121:383-387.

Barrington MJ, Watts SA, Gledhill SR, et al. Preliminary results of the Australasian Regional Anaesthesia Collaboration: a prospective audit of more than 7000 peripheral nerve and plexus blocks for neurologic and other complications. *Reg Anesth Pain Med*. 2009;34:534-541.

Brull R, McCartney CJ, Chan VW, et al. Neurological complications after regional anesthesia: contemporary estimates of risk. *Anesth Analg*. 2007;104:965-974.

Sites BD, Taenzer AH, Herrick MD, et al. Incidence of local anesthetic systemic toxicity and postoperative neurologic symptoms associated with 12,668 ultrasound-guided nerve blocks: an analysis from a prospective clinical registry. *Reg Anesth Pain Med*. 2012;37:478-482.

Welch MG, Brummett CM, Welch TD, et al. Perioperative peripheral nerve injuries: a retrospective study of 380,680 cases during a 10-year period at a single institution. *Anesthesiology*. 2009;111:490-497.

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Chapter 47
Nerve Blocks of the Lower Extremity

Jeffrey Y. F. Ngeow

Roniel Weinberg

Danielle M. Gluck

A 60-year-old male was a pedestrian struck by a car while crossing a street. Upon arrival at the emergency room (ER), he had complaints of severe right lower extremity pain. His Glasgow Coma Score was 13 for slight confusion and eye opening to speech. His past medical history is significant for paroxysmal atrial fibrillation and chronic low back pain. Prior surgeries include a right anterior cruciate ligament (ACL) repair 4 years ago and an L4-S1 fusion. His medications include dabigatran (Pradaxa), methadone 15 mg every 6 hours, and oxycodone 15 to 30 mg every 6 hours as needed for breakthrough pain. The patient's vital signs reveal atrial fibrillation at a rate of 85 with blood pressure of 130/70 mm Hg. Head computed tomography (CT) scan in the ER reveals a small subdural hematoma, whereas plain film x-rays show a high right ankle fracture of the tibia and fibula, with laceration of the skin at both the medial and lateral aspects of the ankle. The consulting neurosurgical service has determined that the patient does not require immediate interventions and will be followed with close observation. The ER trauma team wants to take the patient in for open reduction and internal fixation (ORIF) of his ankle as soon as medical conditions allow.

A. Preoperative Evaluation

1. What is the Glasgow Coma Scale and its significance in this patient?
2. Should surgery be allowed to proceed in this patient who has a subdural bleed?
3. Does the patient's atrial fibrillation need to be addressed prior to surgery, and if so, how?

B. Preoperative Preparation

1. What is dabigatran (Pradaxa)? How is its effect measured? How far in advance of elective surgery should it be stopped? Can its effect be reversed?
2. What concerns do you have regarding neuraxial anesthesia in this patient who has a subdural hematoma?
3. What concerns do you have regarding neuraxial anesthesia in this patient who has prior back surgery?
4. The surgeon is willing to wait a few days prior to surgery while the swelling around the injury decreases. When would you feel comfortable proceeding with surgery in this patient?

C. Intraoperative Management

The patient presents to the operating room (OR) 72 hours after his injury. He was medically cleared for ORIF of his right ankle. You have decided to proceed with a regional nerve block anesthetic technique.

1. What two nerve plexuses need to be blocked in this case? What nerve roots contribute to each plexus? Name the major nerves that come from each plexus.
2. What is the innervation to the medial and lateral aspects of the ankle? What nerves need to be blocked for his surgery?

3. What nerves are blocked with an ankle block? Would you do an ankle block in this case?
4. Explain the posterior landmark technique to blocking the lumbar plexus. What motor response would be elicited with a nerve stimulator? At what stimulation level would you feel safe injecting the patient? Why not at a lower level of stimulation?
5. What is a fascia iliaca block (three-in-one block)?
6. Describe the different ultrasound approaches to blocking the saphenous nerve above the knee.

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7. What benefits might a saphenous nerve block above the knee provide compared to a femoral nerve block?
8. How would pain from a midthigh tourniquet dictate which peripheral nerve blocks to use in this patient? Describe the landmark technique of sciatic nerve block in the gluteal region. What is seen while performing an ultrasound technique to block the sciatic nerve?
9. Why does a popliteal nerve block have a high failure rate if performed too proximate to the popliteal fossa when using a landmark/nerve stimulator technique? Describe how this can be avoided when using ultrasound-based popliteal block.

D. Postoperative Pain Management

1. Describe compartment syndrome and how that risk would influence your postoperative plan for peripheral regional analgesia.
2. How would the addition of dexamethasone to your local anesthetic influence the duration of the blocks placed in the OR?
3. What is liposomal bupivacaine?
4. What benefit would a peripheral nerve catheter provide over a long-acting local anesthetic? Are there any downside?
5. You were able to perform a continuous spinal epidural (CSE) at L3-L4 and used 0.125% bupivacaine via epidural route for postoperative pain control. The patient reports that he is comfortable regarding both his back pain and his ankle pain. What benefit would continuing the patient's methadone confer in this case?
6. How can regional analgesia aid in fast-track postoperative care?

A. Preoperative Evaluation

A.1. What is the Glasgow Coma Scale and its significance in this patient?

The Glasgow Coma Scale (Score) was developed as a practical structured assessment of consciousness in patients following acute brain trauma. The scale, first described in 1974 and later revised in 1979, scores three different components of responsiveness for a score range of 3 to 15. The levels of response include eye opening (none, to pressure, to speech, spontaneous), verbal response (none, sounds, words, confused, oriented), and best motor response (none, extension, abnormal flexion, normal flexion or withdrawal, localizing, obeying commands), with the worse response receiving the lower number. Generally, scores of 13 to 15 signify mild head injury, 9 to 12 as moderate, and 8 and below as severe. Components of the scale and the overall score seem to strongly correlate to outcome after acute brain injury. A baseline score should be established upon patient presentation, with a revised and more predictive score upon stabilization of respiratory, circulatory, and metabolic abnormalities.

Teasdale G, Maas A, Lecky F, et al. The Glasgow Coma Scale at 40 years: standing the test of time. *Lancet Neurol*. 2014;13:844-854.

A.2. Should surgery be allowed to proceed in this patient who has a subdural bleed?

Although the patient suffered acute brain trauma and appears stable, he remains at risk for sudden deterioration secondary to increased hematoma formation or cerebral edema.

Following acute brain trauma, preservation of normal intracranial pressures and mean arterial pressures of more than 70 mm Hg is essential in decreasing poor outcomes. Subdural hematomas are the result of bleeding from bridging veins into the space between the dura and arachnoid. These can develop over the course of a few days and may often result from a seemingly benign injury or spontaneously. Patients will complain of headache and often appear drowsy or obtunded. The diagnosis is via CT scan, and the patient can be managed conservatively or with surgical evacuation. Assuming the patient's medical condition does not alter over the course of 24 to 48 hours, it would then be safe to proceed with repair of the ankle fracture.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Saunders/Elsevier; 2012:218-254.

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A.3. Does the patient's atrial fibrillation need to be addressed prior to surgery, and if so, how?

This patient has preexisting paroxysmal atrial fibrillation. Prior to surgery, he should be asked if he knows when his last episode of atrial fibrillation was, if he has symptoms when it is occurring, if he is typically rate controlled, if he was ever on medications for rate control, and if he has ever had a cardioversion or an ablation. Because these patients are more likely to have cardiac disease, a preoperative transthoracic echocardiogram in non-emergent cases is often helpful in evaluating cardiac and valvular functions. Although our patient's heart rate is controlled, consider the addition of a β-blocker or calcium channel blocker in non-rate-controlled patients, as tolerated by their blood pressure. In addition to inquiring about our patient's last dabigatran (Pradaxa) use, discuss with the surgical team the plan for possible perioperative anticoagulation.

Cornia P, Wong C, eds. *The Perioperative Medicine Consult Handbook*. New York: Springer; 2013:57-66.

B. Preoperative Preparation

B.1. What is dabigatran (Pradaxa)? How is its effect measured? How far in advance of elective surgery should it be stopped? Can its effect be reversed?

Often, patients with atrial fibrillation will take an oral anticoagulant to reduce their risk of stroke. Dabigatran etexilate (Pradaxa) is a direct thrombin (factor IIa) inhibitor that is among a group of new oral anticoagulants. Although they are generally easier to manage than warfarin and do not require laboratory monitoring, they do not have specific reversal agents. Thrombin activates factors V, VIII, and IX; helps convert fibrinogen to fibrin; and stimulates platelet aggregation. Dabigatran inhibits both free and clot-bound thrombin. It is a prodrug that is hydrolyzed by serum esterases to its active form. Peak plasma level is within 1.5 to 3 hours of administration, and its half-life is 14 to 17 hours in healthy patients and up to 28 hours in patients with end-stage renal disease. Eighty percent of the medication is excreted unchanged via the kidneys. In patients with normal renal function, the medication should be stopped 24 hours prior to low-risk surgery and 48 hours prior to high-risk surgery. These time intervals are extended up to four times depending on the patient's renal impairment. In patients not at high risk for thrombosis and with normal creatinine clearance, it may be appropriate to wait four to six half-life intervals from cessation of dabigatran prior to neuraxial injection and removal of epidural catheters.

The Hemoclot direct thrombin inhibitor assay, Ecarin clotting time, and Ecarin chromogenic assay serve as more sensitive quantitative testing for dabigatran activity, whereas a normal activated partial thromboplastin time (aPTT) and thrombin time would suggest lack of significant dabigatran activity. There is no specific reversal agent for excessive bleeding in patients on dabigatran. Recombinant factor VIIa, four-factor prothrombin complex concentrate (PCC), three-factor PCC concentrate, and activated PCC have been suggested for this purpose. A direct dabigatran antibody is under development. In addition, gastric lavage with activated charcoal within 2 hours of administration can be attempted. Ultimately, dialysis will remove the anticoagulant effects of Pradaxa.

An antidote to dabigatran was developed in Germany. This uses the concept of fragment antigen binding (Fab). The drug idarucizumab has already earned the designation of U.S. Food and Drug Administration's (FDA) “breakthrough” drug and is on fast-track review.

Benzon HT, Avram MJ, Green D, et al. New oral anticoagulants and regional anaesthesia. *Br J Anaesth*. 2013;111(suppl 1):i96-i113.

Fawole A, Daw HA, Crowther MA. Practical management of bleeding due to the anticoagulants dabigatran, rivaroxaban, and apixaban. *Cleve Clin J Med*. 2013;80:443-451.

Schiele F, Ryn van J, Canada K, et al. A specific antidote to dabigatran: functional and structural characterization. *Blood*. 2013;121(18):3554-3562.

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B.2. What concerns do you have regarding neuraxial anesthesia in this patient who has a subdural hematoma?

The development of subdural hematoma associated with postdural puncture headache or low CSF pressure is likely similar to development of hematoma following trauma, which is caused by sheering of bridging veins, which are generally at their thinnest point in the subdural space. A review documented 46 cases of subdural hematoma, which developed following intentional dural puncture during spinal procedures or unintentional violation of the dura mater during epidural catheter placement. Given that this patient has already developed a subdural hematoma, neuraxial anesthesia would need to be undertaken with great care, and if done, a spinal should be avoided in favor of an epidural technique.

Zeidan A, Farhat O, Maaliki H, et al. Does postdural puncture headache left untreated lead to subdural hematoma? Case report and review of the literature. *Int J Obstet Anesth*. 2006;15:50-58.

B.3. What concerns do you have regarding neuraxial anesthesia in this patient who has prior back surgery?

Neuraxial anesthesia should be considered with caution in this patient with a history of a lumbar fusion at L4-S1. Neuraxial anesthesia can be challenging in this patient population due to abnormalities of the usual landmarks, scar formation, presence of hardware, and bone grafts. These patients are at higher risk for false loss of resistance, inability to access the epidural or subarachnoid space, patchy and failed blocks, unintentional dural puncture, and traumatic needle placement. In a retrospective review of 937 patients with a history of spinal stenosis and/or lumbar disc disease, Hebl et al. showed that prior spinal surgery in 207 of the patients did not affect block success rate or frequency of complications. However, of the 207 patients, only 5 had prior spinal fusion. Care should be taken to confirm that the fusion is at the level that the patient reports. In addition, ultrasound can be helpful in determining the best interspace, correct level, midline, and epidural space depth.

Hebl JR, Horlocker TT, Kopp SL, et al. Neuraxial blockade in patients with preexisting spinal stenosis, lumbar disk disease, or prior spine surgery: efficacy and neurologic complications. *Anesth Analg*. 2010;111(6):1511-1519.

Vercauteren M, Waets P, Pitkänen M, et al. Neuraxial techniques in patients with pre-existing back impairment or prior spine interventions: a topical review with special reference to obstetrics. *Acta Anaesthesiol Scand*. 2011;55:910-917.

B.4. The surgeon is willing to wait a few days prior to surgery while the swelling around the injury decreases. When would you feel comfortable proceeding with surgery in this patient?

Because this patient does not have any renal insufficiency, the half-life of dabigatran is approximately 14 to 17 hours. After assessing the patient's current medical status and prior medical history, an anesthetic plan of general, regional, or neuraxial can be considered. If choosing an anesthetic plan of neuraxial anesthesia or one involving deep regional blocks, it is preferable to wait 3 to 4 days, which is 4 to 6 dabigatran half-life intervals. Otherwise, if his atrial fibrillation is stable with preserved cardiac function, and no changes in mental status or deterioration secondary to his subdural hematoma, surgery can proceed within 24 to 48 hours.

Fawole A, Daw HA, Crowther MA. Practical management of bleeding due to the anticoagulants dabigatran, rivaroxaban, and apixaban. *Cleve Clin J Med*. 2013;80:443-451.

C. Intraoperative Management

The patient presents to the OR 72 hours after his injury. He was medically cleared for ORIF of his right ankle. You have decided to proceed with a regional nerve block anesthetic technique.

C.1. What two nerve plexuses need to be blocked in this case? What nerve roots contribute to each plexus? Name the major nerves that come

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from each plexus.

Peripheral regional anesthesia for almost all major orthopedic surgery of the lower extremity involves blocking the whole or branches of both the lumbar and the lumbosacral plexuses. In broad terms, the lumbar plexus innervates the ventral aspect of the lower extremity, whereas the sacral plexus innervates the dorsal aspect. The lumbar plexus is made up of the ventral rami of L1-L3, part of L4, and, in 50% of patients, a branch from T12. The plexus is located within the psoas muscle, anterior to the transverse processes of the lumbar vertebra. The plexus gives off the iliohypogastric (T12-L1), ilioinguinal (L1), genitofemoral (L1-L2), lateral femoral cutaneous (L2-L3), femoral (L2-L4), and obturator nerves (L2-L4).

The lumbosacral trunk is formed from ventral rami of L4 and L5 and the anterior branch of S1. The sacral plexus is composed of the union of the lumbosacral trunk with S1-S3 and occasionally S4. The sciatic nerve contains the tibial nerve, which is made up of the anterior divisions of the ventral rami of L4, L5, and S1-S3 and the common peroneal nerve, which is made of the dorsal branches of the same nerve roots. The sciatic nerve splits into the tibial and common peroneal nerves in the popliteal fossa. The common peroneal nerve branches into the superficial and deep tibial nerves. The tibial nerve branches into the medial plantar, calcaneal, and sural (with contribution from communicating superficial peroneal branches) nerves. Other nerves from the lumbosacral plexus include the superior gluteal (L4-S1), inferior gluteal (L5-S2), posterior femoral cutaneous (S1-S3), piriformis (S1-S2), obturator internus (L5, S1-S2), and quadratus femoris (L4-L5, S1).

Brown D, ed. *Atlas of Regional Anesthesia* . 4th ed. Philadelphia, PA: Saunders/Elsevier; 2010:89-96.

Hadzic A, ed. *Hadzic's Peripheral Nerve Blocks and Anatomy for Ultrasound-Guided Regional Anesthesia* . 2nd ed. New York: McGraw-Hill Professional; 2012:217-248.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:1721-1751.

Narouze SN, ed. *Atlas of Ultrasound-Guided Procedures in Interventional Pain Management*. New York: Springer; 2011:240-258.

C.2. What is the innervation to the medial and lateral aspects of the ankle? What nerves need to be blocked for his surgery?

Below the knee, the saphenous nerve provides innervation to the medial aspect of the lower extremity. The lateral aspect is innervated by the common peroneal nerve, with the tibial nerve providing innervation in the posterior aspect. The superficial peroneal nerve innervates the dorsal aspect of the foot, whereas the deep peroneal nerve provides innervation to the deep dorsal structures and the web space between the first and second digits. The sural nerve innervates the lateral aspect of the foot, whereas the calcaneal and medial plantar nerves innervate the plantar aspect of the foot.

In our case, to provide effective surgical anesthetic peripheral nerve blockade, both the medial and lateral aspects of the ankle would need to be anesthetized. Thus, the tibial, common peroneal, and the saphenous branch of the femoral nerve would require surgical blockade.

Brown D, ed. *Atlas of Regional Anesthesia* . 4th ed. Philadelphia, PA: Saunders/Elsevier; 2010:135-138.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:1721-1751.

Narouze SN, ed. *Atlas of Ultrasound-Guided Procedures in Interventional Pain Management*. New York: Springer; 2011:240-258.

C.3. What nerves are blocked with an ankle block? Would you do an ankle block in this case?

The posterior tibial, deep and superficial peroneal, and sural and saphenous nerves require blockade for anesthesia of the foot. Typically, an ankle block is performed at the level of the medial and lateral malleoli. The posterior tibial nerve is blocked by inserting a fine needle along

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the medial aspect of the Achilles tendon at the level of the medial malleolus and advanced until the posterior tibia/medial malleolus is contacted (Fig. 47.1). Three to 5 mL of local anesthetic is deposited superficial to the periosteum. The deep peroneal nerve at the ankle lies deep between the tendons of the tibialis anterior and the extensor hallucis longus (EHL). These tendons are identified by asking the patient to dorsiflex the big toe (EHL) and the ankle (tibialis anterior) (Fig. 47.2). Another 2 to 3 mL of local anesthetic can be deposited here just superficial to the periosteum. The needle can be redirected to block the branches of the superficial peroneal and saphenous nerves by making a subcutaneous ring across the dorsum of the foot using 3 to 5 mL of the anesthetic solution. The sural nerve can be blocked by inserting a needle lateral to the Achilles tendon at the level of the lateral malleolus. The needle is advanced until the periosteum is contacted and another 3 to 5 mL of local anesthetic is deposited superficial to the periosteum.

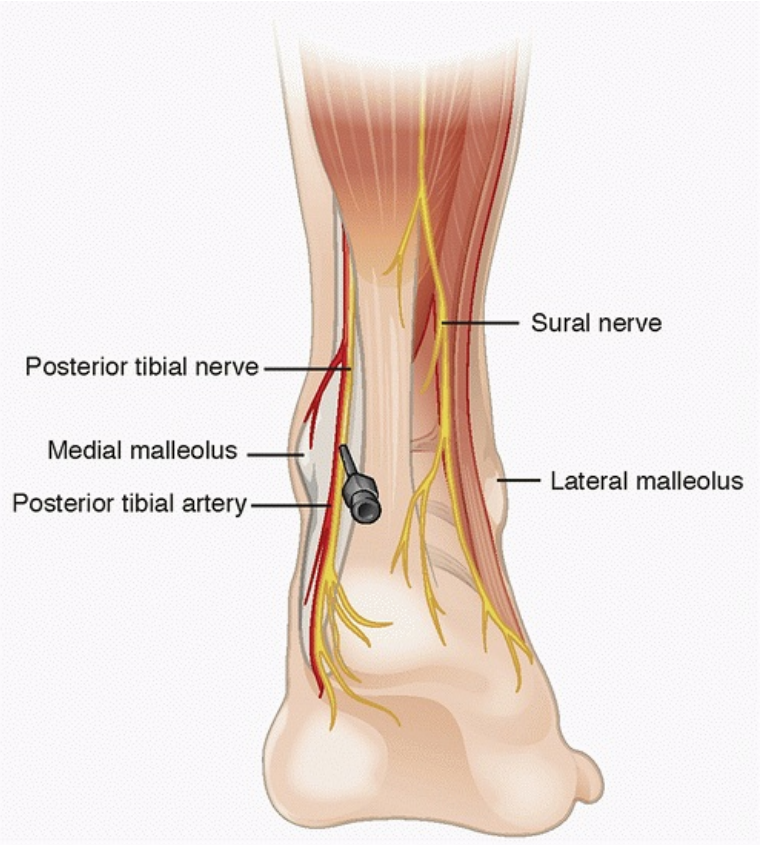


FIGURE 47.1 The posterior tibial nerve block.

Our patient would require anesthesia cephalad to the level of the malleoli, given that he has sustained a high ankle fracture. Thus, an ankle block would likely not provide adequate surgical anesthesia and should not be employed as the primary anesthetic in this case.

Brown D, ed. *Atlas of Regional Anesthesia* . 4th ed. Philadelphia, PA: Saunders/Elsevier; 2010:135-138. Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:1721-1751.

C.4. Explain the posterior landmark technique to blocking the lumbar plexus. What motor response would be elicited with a nerve stimulator? At what stimulation level would you feel safe injecting the patient? Why not at a lower level of stimulation?

The posterior approach to the lumbar plexus block, also known as a psoas compartment block, is performed by injecting 20 to 40 mL of local anesthetic in a lumbar paravertebral location. For this injection, the patient should be in the lateral decubitus position. The classic approach was described by Winnie at the L4 level using a paresthesia technique that can be modified with the use of a nerve stimulator. The point of puncture is at the intersection of the intercristal line (line joining the iliac crests) and a caudad-cephalad line that passes through the posterior superior iliac spine (PSIS) and is parallel to the spinous processes. If the lumbar plexus is not located, the needle should be directed more medially. Mannion et al.

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recommended a medial needle redirection of no more than 15 degrees to reduce the risk of bilateral spread. Capdevila et al. described a modification of this approach by using a point of puncture at the lateral two-thirds of the distance between the spinous process and the PSIS and 1 cm above the intercristal line. The needle should be advanced in a perpendicular plane and contact made with the L4 transverse process. The needle should then be redirected caudally, until a quadriceps femoris twitch is obtained, usually at the depth of another 18 mm.

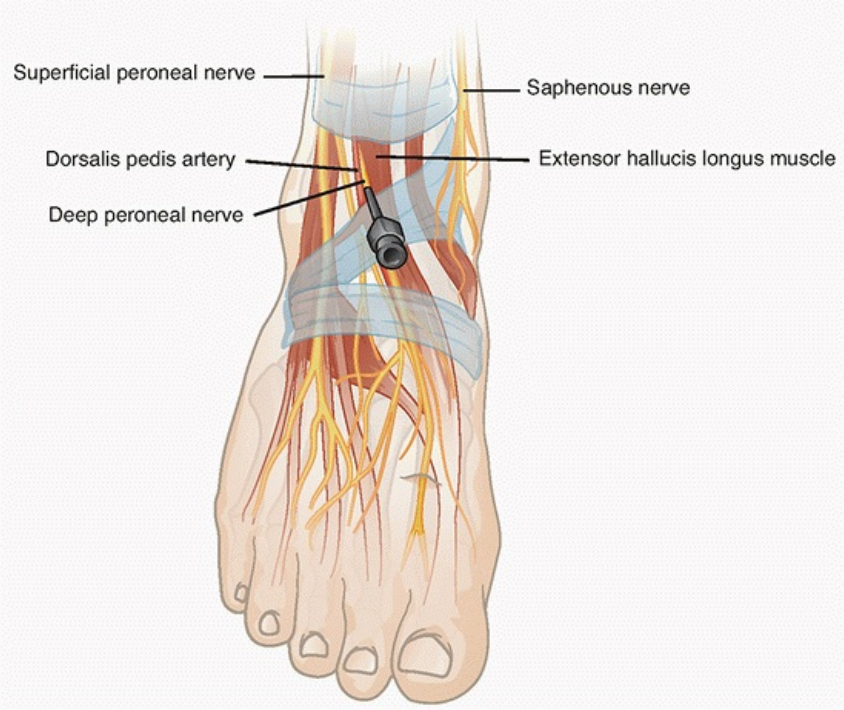


FIGURE 47.2 The deep peroneal nerve block.

Although spinal anesthesia, intravascular injections, incorrect catheter placement, and renal and psoas hematoma have all been reported, the most common complication of a lumbar plexus block is epidural and bilateral spread. Motor stimulation should be elicited between 0.5 and 1.0 mA, as twitches evoked at lower currents may indicate needle placement in a dural sleeve, which might increase the risk of epidural or spinal spread.

Capdevila X, Coimbra C, Choquet O. Approaches to the lumbar plexus: success, risks, and outcome. *Reg Anesth Pain Med*. 2005;30(2):150-162.

Capdevila X, Macaire P, Dadure C, et al. Continuous psoas compartment block for postoperative analgesia after total hip arthroplasty: new landmarks, technical guidelines, and clinical evaluation. *Anesth Analg*. 2002;94:1606-1613.

Hadzic A, ed. *Hadzic's Peripheral Nerve Blocks and Anatomy for Ultrasound-Guided Regional Anesthesia* . 2nd ed. New York: McGraw-Hill Professional; 2012:217-228.

Mannion S, O'Callaghan S, Walsh M, et al. In with the new, out with the old? Comparison of two approaches for psoas compartment block. *Anesth Analg*. 2005;101:259-264.

Winnie AP, Ramamurthy S, Durrani Z, et al. Plexus blocks for lower extremity surgery: new answers to old problems. *Anesthesiol Rev.* 1974;1:11-6.

C.5. What is a fascia iliaca block (three-in-one block)?

The femoral, lateral femoral cutaneous, and obturator nerves can be blocked separately (Fig. 47.3). The three-in-one

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block is a large-volume paravascular block, first described by Winnie et al., intended as an anterior approach to block all three nerves with one needle. To perform this block, a needle is inserted lateral to the femoral artery, caudad to the inguinal ligament. The needle is advanced in a cephalad direction until a femoral paresthesia, or stimulation occurs,

or a perineural needle location is visualized via ultrasound scan. Local anesthetic is injected while the distal femoral sheath is compressed digitally. Unfortunately, the obturator nerve is not blocked reliably using this approach. A cadaver study failed to show a continuous femoral nerve fascial sheath that would allow spread from the inguinal region to the lumbar plexus.

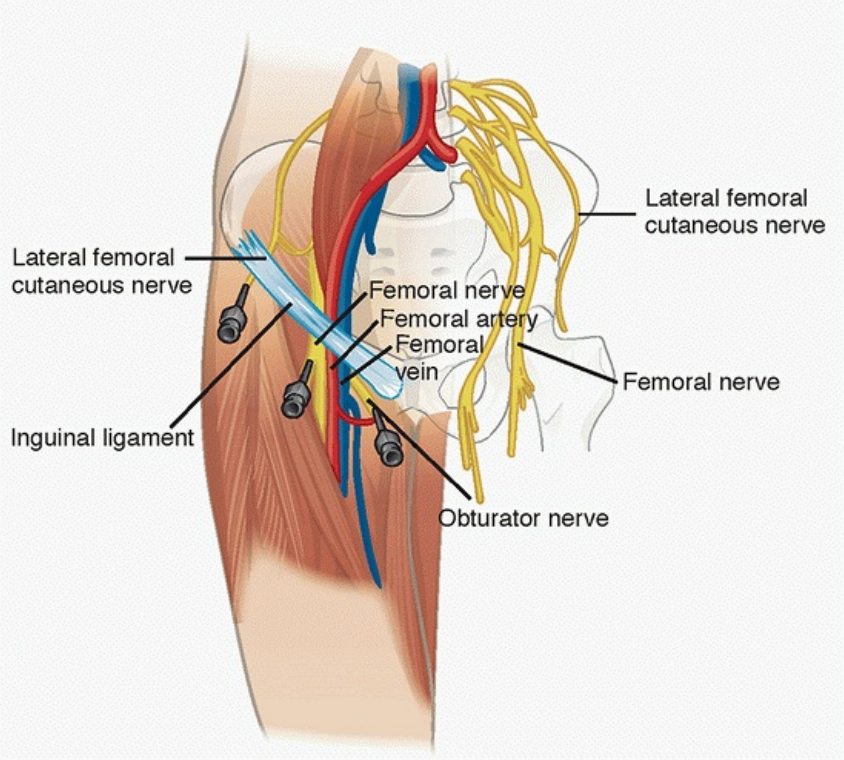


FIGURE 47.3 The femoral nerve block, lateral femoral cutaneous nerve block, and obturator nerve block.

Dalens et al. described a fascia iliaca block in children. The external iliac vessels run anterior to the fascia, whereas the nerves of the lumbar plexus run posterior to it. The fascia iliaca is continuous with the posterior aspect of the inguinal ligament. The fascia passes behind the femoral vessels and laterally attaches to the anterior superior iliac spine. It is covered by the fascia lata and forms the top of a fat-filled space called the lacuna musculorum (lateral to the lacuna vasorum; the femoral vessels sheath). A line, mimicking the inguinal ligament, is drawn from the pubic bone to the anterior superior iliac spine. The puncture site is 0.5 cm caudal to a point at the lateral two-thirds of that line. The anesthetic is injected on the second “give” or loss of resistance, with pressure caudad to the needle. Although Dalens et al. showed a 90% success rate of sensory blockade of the three main nerves of the lumbar plexus in pediatric patients, Capdevila et al. was only able to show a 34% success rate in adults. Dolan et al. described using ultrasound guidance to identify the fascia iliaca, guide needle placement just below it, and show medial and lateral flow of the local anesthetic below the fascia iliaca (Fig. 47.4, Video 47.1). Complete sensory block of the anterior, medial, and lateral aspects of the thigh increased from 47% with loss of resistance technique to 82% with the ultrasound-guided technique.

Awad IT, Duggan EM. Posterior lumbar plexus block: anatomy, approaches, and techniques. *Reg Anesth Pain Med*. 2005;30(2):143-149.

Brown D, ed. *Atlas of Regional Anesthesia* . 4th ed. Philadelphia, PA: Saunders/Elsevier; 2010:97-99.

Dalens B, Vanneuville G, Tanguy A. Comparison of the fascia iliaca compartment block with the 3-in-1 block in children. *Anesth Analg*. 1989;69:705-713.

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Dolan J, Williams A, Murney E, et al. Ultrasound guided fascia iliaca block: a comparison with the loss of resistance technique. *Reg Anesth Pain Med*. 2008;33(6):526-531.

Morau D, Lopez S, Biboulet P, et al. Comparison of continuous 3-in-1 and fascia iliaca compartment blocks for postoperative analgesia: feasibility, catheter migration, distribution of sensory block, and analgesic efficacy. *Reg Anesth Pain Med*. 2003;28(4):309-314.

Winnie AP, Ramamurthy S, Durrani Z. The inguinal paravascular technique of lumbar plexus anesthesia: the "3-in-1 block." *Anesth Analg.* 1973;52:989-96.

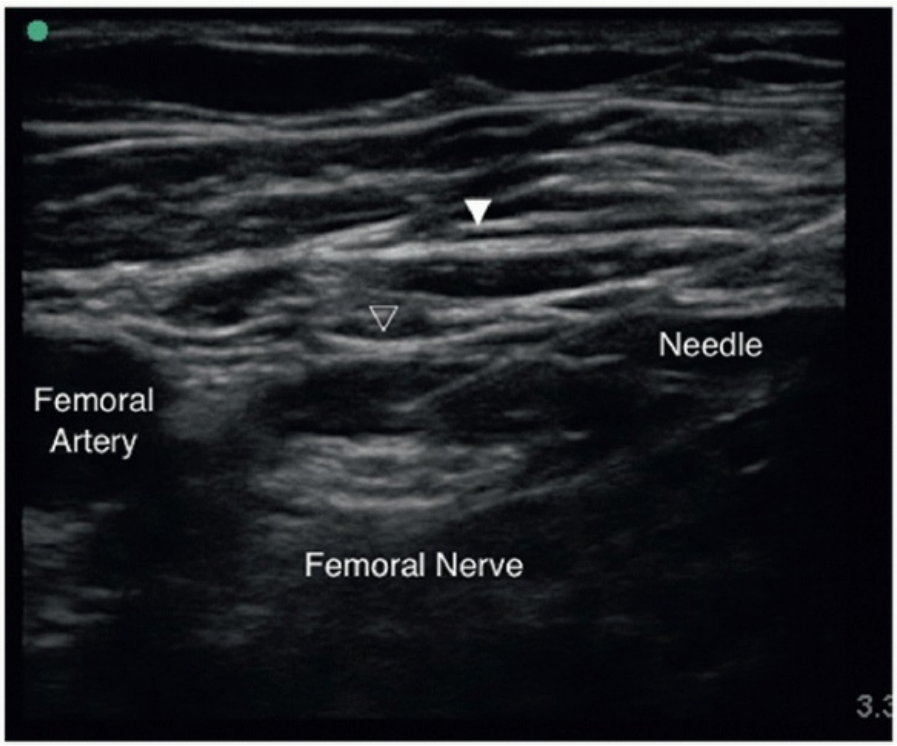


FIGURE 47.4 Perineural femoral nerve block. Fascia lata indicated by *solid triangle*, and fascia iliaca by *blank triangle.*

C.6. Describe the different ultrasound approaches to blocking the saphenous nerve above the knee.

The saphenous nerve is a sensory branch of the femoral nerve, which when blocked in combination with a sciatic nerve block, provides anesthesia for surgeries distal to the knee. Traditionally, this nerve was blocked via a subcutaneous wheel of local anesthetics from the medial aspect of the tibial tuberosity to the anterior aspect of the tibia. The nerve lays lateral to the femoral artery while exiting the femoral triangle and then crosses over the roof of the adductor canal (subsartorial canal) and lays medial to the artery at the distal aspect of the adductor canal. The canal is bound anterolaterally by the vastus medialis muscle, anteriorly by the sartorius muscle, and posteromedially by the adductor magnus muscle. The saphenous nerve emerges from the adductor canal with the saphenous branch of the descending genicular artery and divides into the infrapatellar and sartorial branches. The sartorial branch courses through the fascia between the sartorius and gracilis muscles and emerges subcutaneously below the knee. Studies have proven ultrasound techniques to be quite reliable and effective in blocking this nerve, as the saphenous nerve emerges from the adductor canal. Just above the level of the knee, the nerve can be blocked between the sartorius and gracilis muscles in close proximity to the saphenous branch of the descending genicular artery. Krombach and Gray described blocking the saphenous nerve about 5 to 7 cm proximal to the popliteal crease, in the vastoadductor membrane (facial plane adjacent to the vastus medialis) deep to the sartorius muscle (Figs. 47.5 and 47.6, Video 47.2). Manickam et al. described blocking the saphenous nerve more

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proximally, in the distal adductor canal deep to the sartorius and anteromedial to the femoral artery.

Horn JL, Pitsch T, Salinas F, et al. Anatomic basis to the ultrasound-guided approach for saphenous nerve blockade. *Reg Anesth Pain Med*. 2009;34(5):486-489.

Krombach J, Gray AT. Sonography for saphenous nerve block near the adductor canal. *Reg Anesth Pain Med*. 2007;32(4):369-370.

Manickam B, Perlas A, Duggan E, et al. Feasibility and efficacy of ultrasound-guided block of the saphenous nerve in the adductor canal. *Reg Anesth Pain Med*. 2009;34(6):578-580.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:1751-1766.

Saranteas T, Anagnostis G, Paraskeuopoulos T, et al. Anatomy and clinical implications of the ultrasoundguided subsartorial saphenous nerve block. *Reg Anesth Pain Med*. 2011;36(4):399-402.

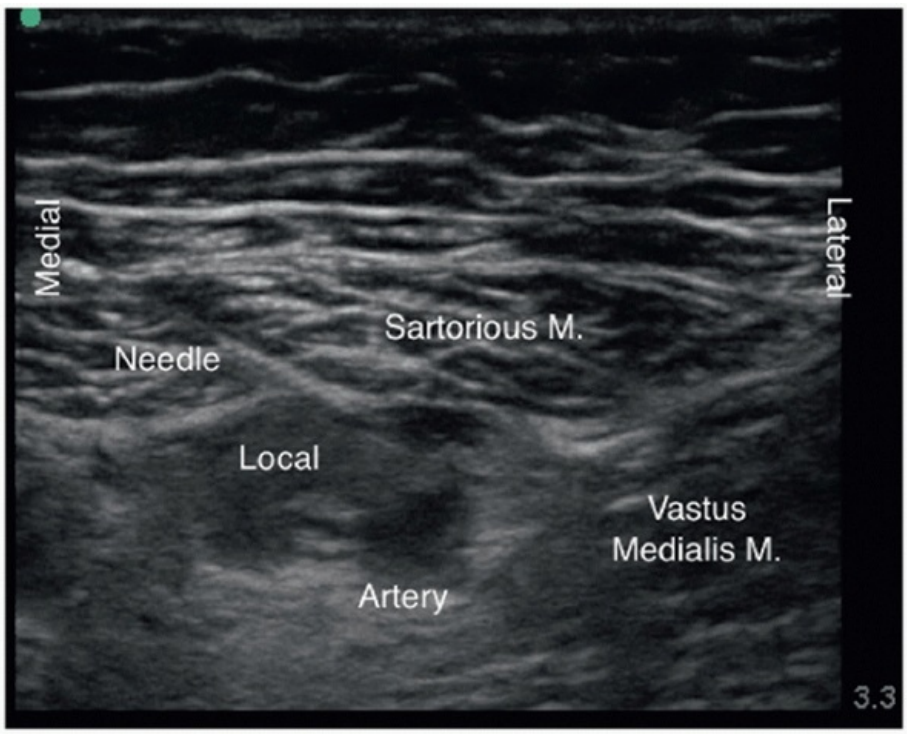


FIGURE 47.5 Post-periarterial saphenous nerve injection in the adductor canal.

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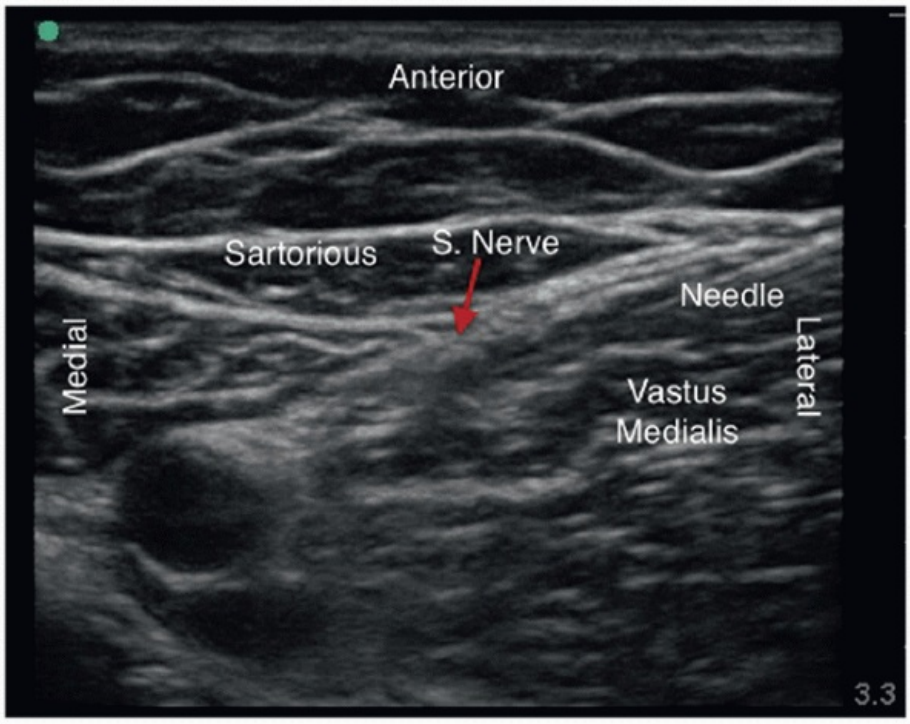


FIGURE 47.6 Saphenous nerve block: view of the lower adductor canal. Notice the sartorius muscle moving medially.

C.7. What benefits might a saphenous nerve block above the knee provide compared to a femoral nerve block?

Femoral and saphenous nerve blocks have been shown to provide effective analgesia at the level of the knee and below. However, as a femoral nerve block provides analgesia to all the branches of the femoral nerve, it confers significant motor blockade to the quadriceps and has been associated with a small risk of falls during postoperative ambulation. Ideally, in cases where early ambulation and mobilization is desired, such as “fast-track” joint replacements, an analgesic block with motor preservation would be advantageous. In a group of healthy volunteers, Jaeger et al. demonstrated that a saphenous nerve block in the adductor canal reduced quadriceps strength 8% from baseline, whereas a femoral nerve block caused a 49% reduction from baseline. Although 100% could mobilize after a saphenous nerve block, only about 50% could mobilize following a femoral nerve block. Kim et al. demonstrated that at 6 to 8 hours after total knee arthroplasty, adductor canal block compared to femoral nerve block provided equivalent analgesia but with significant sparing of quadriceps motor blockade. Grevstad et al. showed that compared to a femoral nerve block placed after total knee arthroplasty, an adductor canal/saphenous nerve block improved quadriceps muscle strength. A possible basis for improved strength is that analgesia decreases centrally mediated inhibition of voluntary muscle contraction. Although a midthigh saphenous nerve block in the adductor canal will often spread to the nerve to the vastus medialis (sensory and motor), there would be less reduction in quadriceps muscle strength compared to a femoral nerve block.

Grevstad U, Mathiesen O, Valentiner LS, et al. Effect of adductor canal block versus femoral nerve block on quadriceps strength, mobilization, and pain after total knee arthroplasty: a randomized, blinded study. *Reg Anesth Pain Med*. 2015;40(1):3-10.

Jaeger P, Nielsen ZJ, Henningsen MH, et al. Adductor canal block versus femoral nerve block and quadriceps strength: a randomized, double-blind, placebo-controlled, crossover study in healthy volunteers. *Anesthesiology*. 2013;118:409-415.

Kim DH, Lin Y, Goytizolo EA, et al. Adductor canal block versus femoral nerve block for total knee arthroplasty: a prospective, randomized, controlled trial. *Anesthesiology*. 2014;120:540-550.

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C.8. How would pain from a midthigh tourniquet dictate which peripheral nerve blocks to use in this patient? Describe the landmark technique of sciatic nerve block in the gluteal region. What is seen while performing an ultrasound technique to block the sciatic nerve?

A midthigh tourniquet will have implications in determining what blocks should be performed for lower extremity surgery. Although a tourniquet is used to decrease intraoperative blood loss, it occasionally has the unintended consequence of causing considerable pain in the thigh. The tourniquet is wrapped entirely around the leg and can affect both the femoral and sciatic nerves. Thus, it is important to block these nerves more proximal than at the adductor canal or the popliteal fossa. The mechanism of tourniquet pain is more than just secondary to pressure from the tourniquet and involves both unmyelinated C fibers and myelinated A fibers. The C fibers are more resistant to local anesthetics, so when either neuraxial anesthesia or regional block begins to wear off, or if it is incomplete to begin with, the C fibers begin to conduct through the nerve and the typical dull pain is felt. This dull pain can still be detected even with an “adequate” sensory block of the A fibers. This is not the case with general anesthesia which offers a decreased chance of tourniquet pain.

To perform a transgluteal sciatic nerve block with the landmark technique, the patient should be positioned in the lateral decubitus position with the leg to be blocked uppermost and flexed at the hip and knee. The landmarks are the greater trochanter and the PSIS. The distance between the two is measured, and the skin at 4 cm distal to the midpoint is marked as the insertion site (Fig. 47.7). Once this site is located and the skin is prepped,

the block needle is introduced at 90 degrees to the skin. Using a nerve stimulator, muscle twitches of the gluteal muscles are initially seen, and with further advancement, hamstring or calf twitches are seen. Ideally, the twitch remains at about 0.2 to 0.5 mA, indicating appropriate closeness to the nerve. When negative aspiration is confirmed, the local anesthetic of choice can then be injected.

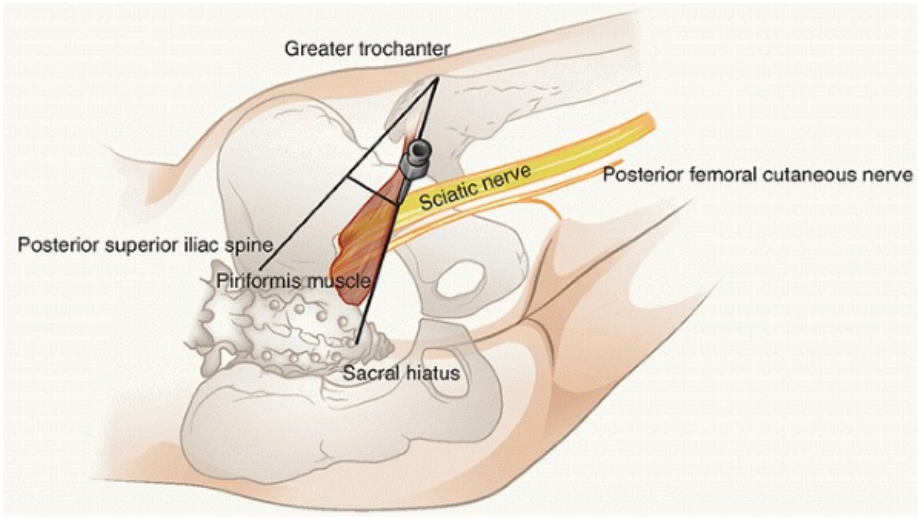


FIGURE 47.7 Sciatic nerve block, the Labat approach.

When utilizing the ultrasound technique and a subgluteal approach, the nerve can be visualized between the ischial tuberosity and the greater trochanter. The patient is positioned either in the prone or lateral decubitus position; again, the leg and knee are flexed. Once the skin is cleaned, the curved transducer probe is placed over the skin. The nerve will be visualized between the two osseous structures, frequently described as being in a “hammock” under the gluteus muscle. The local anesthetic solution will usually push the nerve away and actually improve the visualization of the nerve.

Hadzic A, ed. *Hadzic's Peripheral Nerve Blocks and Anatomy for Ultrasound-Guided Regional Anesthesia* . 2nd ed. New York: McGraw-Hill Professional; 2012:229-248.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:1721-1751.

Sharma JP, Salhotra R. Tourniquets in orthopedic surgery. *Indian J Orthop*. 2012;46(4):377-383.

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C.9. Why does a popliteal nerve block have a high failure rate if performed too proximate to the popliteal fossa when using a landmark/nerve stimulator technique? Describe how this can be avoided when using ultrasound-based popliteal block.

The landmark technique for performing a popliteal fossa block involves delineating the biceps femoris tendon, the semitendinosus and semimembranosus tendons, as well as the popliteal fossa crease. Needle insertion is at a point 7 cm above the popliteal crease at the midpoint between the lateral and medial tendons (Fig. 47.8, Video 47.3). Although this technique will work for a large majority of patients, a high failure rate does occur as a significant portion of the population has variant anatomy where the division of the sciatic nerve into the common peroneal nerve and the tibial nerve occurs more proximal to the level of the needle insertion point (Fig. 47.9). Thus, an incomplete blockade could occur as only one branch of the sciatic nerve is effectively blocked. The use of an ultrasound-guided technique allows for visualization of the nerve and the exact location of the division, helping to prevent such failure.

Adibatti M, Sangeetha V. Study on variant anatomy of sciatic nerve. *J Clin Diagn Res*. 2014;8(8):ACO7-ACO9.

Hadzic A, ed. *Hadzic's Peripheral Nerve Blocks and Anatomy for Ultrasound-Guided Regional Anesthesia* . 2nd ed. New York: McGraw-Hill Professional; 2012:249-266.

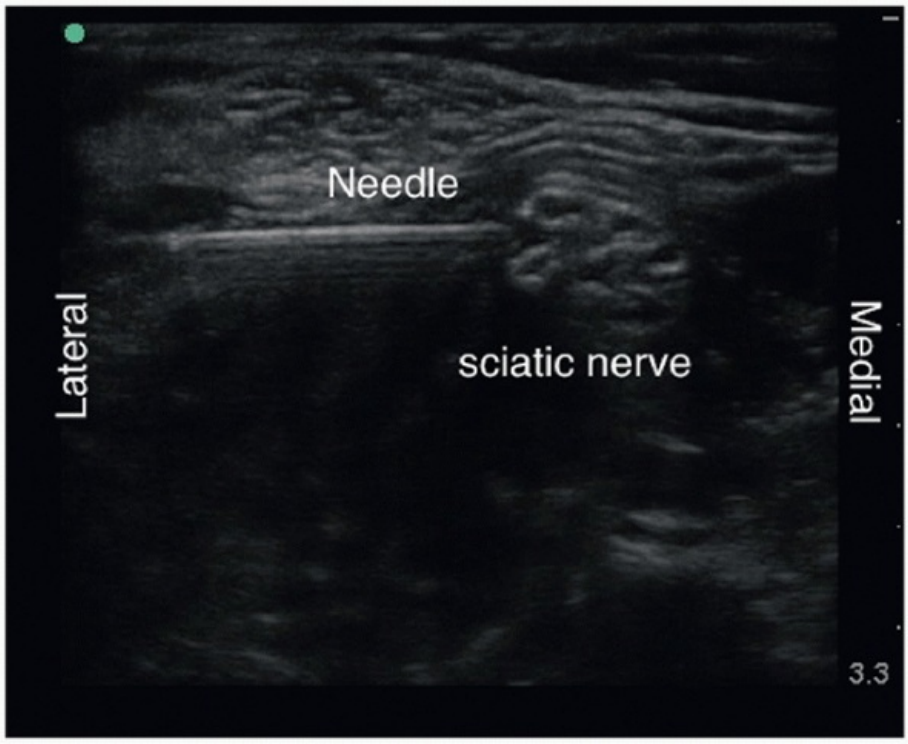


FIGURE 47.8 Popliteal fossa block just proximal to bifurcation.

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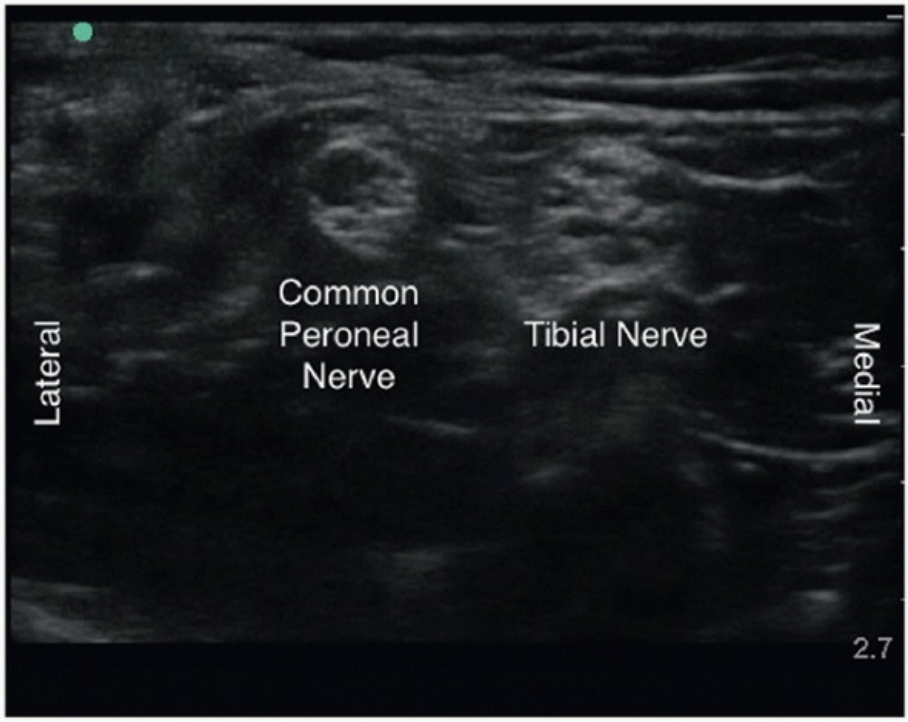


FIGURE 47.9 Popliteal fossa block showing local anesthetic surrounding nerves distal to nerve bifurcation.

D. Postoperative Pain Management

D.1. Describe compartment syndrome and how that risk would influence your postoperative plan for peripheral regional analgesia.

Compartment syndrome develops when there is an increase in pressure within a fixed compartment. Patients often have a collection of signs and symptoms including pain out of proportion to the injury, paresthesias, pallor, decreased sensation, and weakness, as well as the late finding of paralysis. It is typically seen after trauma, especially long bone fractures, and specifically after any injury that increases the volume of a compartment of limited size. Tibial fractures are the most common cause, with 1% to 10% incidence. The pathophysiology has been described as cellular anoxia due to blood flow in injured area not meeting the metabolic demands of local tissue, resulting in swelling and obstruction to venous outflow. This then further decreases the arteriovenous gradient.

The use of regional anesthesia in patients at risk for compartment syndrome remains controversial. Theoretically, neuraxial blockade will prevent recognition of an acute compartment syndrome. However, recent case reports have shown that signs and symptoms of acute compartment syndrome were present in patients given high concentrations of local anesthetic for neuraxial analgesia but that the significance of the symptoms were not appropriately recognized. Similar case reports have demonstrated that patients with dense motor and sensory blocks who are later diagnosed with acute compartment syndrome are still able to report severe pain in the distribution of the peripheral nerve block.

One should consider the risks of compartment syndrome, the exact location of the fracture, positioning during surgery, and the benefits of a regional anesthetic in this patient, taking into account his chronic pain issues.

Elliot KG, Johnstone AJ. Diagnosing acute compartment syndrome. *J Bone Joint Surg Br*. 2003;85:625-632.

Kucera TJ, Boezaart AP. Regional anesthesia does not consistently block ischemic pain: two further cases and a review of the literature. *Pain Med*. 2014;15:316-319.

Mannion S, Capdevila X. Acute compartment syndrome and the role of regional anesthesia. *Int Anesthesiol Clin*. 2010;48(4):85-105.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:2423-2478.

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D.2. How would the addition of dexamethasone to your local anesthetic influence the duration of the blocks placed in the OR?

The addition of dexamethasone to local anesthetic for peripheral nerve blockade has been shown to increase the duration of blockade. When dexamethasone is added to bupivacaine or ropivacaine 0.5%, the duration of sensory block increases from approximately 12 to 24 hours. However, giving an equivalent dose of intravascular dexamethasone has also been shown to prolong the duration of the sensory block to 24 hours. When reviewed by meta-analysis, the use of dexamethasone as a perineural adjuvant has also been shown to decrease postoperative opioid consumption.

De Oliveira GS Jr, Castro Alves LJ, Nader A, et al. Perineural dexamethasone to improve postoperative analgesia with peripheral nerve blocks: a meta-analysis of randomized control trials. *Pain Res Treat*. 2014;2014:179029.

Desmet M, Braems H, Reynvoet M, et al. I.V. and perineural dexamethasone are equivalent in increasing the analgesic duration of a single-shot interscalene block with ropivacaine for shoulder surgery: a prospective, randomized, placebo-controlled study. *Br J Anaesth*. 2013;111(3):445-452.

D.3. What is liposomal bupivacaine?

Liposomal bupivacaine is a slow release form of the local anesthetic bupivacaine that has FDA approval to be used for local infiltration to decrease postoperative pain. Each liposome has internal chambers with encapsulated bupivacaine that is released over an extended period of time. Some studies reported a duration of blockade of up to 72 hours as part of a peripheral or neuraxial technique, giving promise that this agent can be a potential substitute for the peripheral catheter. However, currently, liposomal bupivacaine is only approved for local infiltration, although studies are ongoing to determine the safety and efficacy of its use in neuraxial and peripheral nerve blockade.

Ilfeld B. Liposome bupivacaine in peripheral nerve blocks and epidural injections to manage postoperative pain. *Expert Opin Pharmacother*. 2013;14(17):2421-2431.

Skolnik A, Gan T. New formulation of bupivacaine for the treatment of postoperative pain: liposomal bupivacaine and SABER-Bupivacaine. *Expert Opin Pharmacother*. 2014;15(11):1535-1542.

D.4. What benefit would a peripheral nerve catheter provide over a long-acting local anesthetic? Are there any downside?

Peripheral nerve catheters are a proven method for prolonging postoperative pain control with decreased intravenous or oral narcotic use and hence their related side effects. The catheter also provides patients with the ability to control their own pain management. As compared with long-lasting single-shot injections with additives, a catheter technique could provide analgesia beyond the first 24 hours, which is essentially the limit of duration of a single-shot block. Some limitations to the placement of peripheral nerve catheters include the risk of infection, technical challenges inherent in their placement, and the need for anesthesiologists and other staff to manage them. Other risks of peripheral catheters include damage to the nerve itself from direct contact or nerve entrapment, damage to nearby structures, and intravascular placement and migration.

Ilfeld BM, Morey TE, Wright TW, et al. Continuous interscalene brachial plexus block for postoperative pain control at home: a randomized, double-blinded, placebo-controlled study. *Anesth Analg*. 2003;96(4):1089-1095.

Merritt CK, Mariano ER, Kaye AD, et al. Peripheral nerve catheters and local anesthetic infiltration in perioperative analgesia. *Best Pract Res Clin Anaesthesiol*. 2014;28(1):41-57.

D.5. You were able to perform a continuous spinal epidural (CSE) at L3-L4 and used 0.125% bupivacaine via epidural route for postoperative pain

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control. The patient reports that he is comfortable regarding both his back pain and his ankle pain. What benefit would continuing the patient's methadone confer in this case?

The use of chronic opioid regimens for patients suffering from chronic nonmalignant pain has increased dramatically over the past two decades. Acute postoperative pain control in patients who are taking maintenance opioids for addiction and dependence presents a challenge for health care providers. Studies have shown that these patients require opioid doses that are multiple of those patients not exposed to opioids chronically. Aside from tolerance to opioids, these patients often exhibit increased pain to surgical stimuli, when compared to an opioid-naive population. This may be secondary to increased anxiety and depression, the development of opioid-induced hyperalgesia, and changes in the endogenous opioid system. Multimodal analgesia, including regional techniques and nonopioid adjuvants, such as ketamine, nonsteroidal anti-inflammatory drugs, and acetaminophen, greatly aids in controlling the pain postoperatively. Nonetheless, continuation of maintenance opioids (50% to 100%) is essential in avoiding withdrawal symptoms. Approaches to maintaining opioid levels include continuation of the same preoperative opioid and route, changing the route of administration while continuing the same opioid, or using an equianalgesic conversion to a different opioid. In addition, patients should generally receive their usual dose of opioids prior to surgery. Withdrawal from methadone may present 12 to 24 hours after the last doses, whereas withdrawal from medications such as morphine may fall within 6 to 18 hours. Withdrawal syndrome can present with agitation, diaphoresis, hypertension, diarrhea, nausea, emesis, abdominal cramps, and even seizures.

Hadi I, Morley-Forster PK, Dain S, et al. Brief review: perioperative management of the patient with chronic non-cancer pain. *Can J Anaesth*. 2006;53:1190-1199.

Mehta V, Langford R. Acute pain management for opioid dependent patients. *Anaesthesia*. 2006;61:269-276.
Richebé P, Beaulieu P. Perioperative pain management in the patient treated with opioids: continuing professional development. *Can J Anaesth*. 2009;56:969-981.

D.6. How can regional analgesia aid in fast-track postoperative care?

Fast-track programs are used to help decrease morbidity by decreasing perioperative hospitalization. Both neuraxial and peripheral blockade can be utilized as an effective modality to aid the fast-track programs. Regional anesthesia can attenuate the inflammatory, endocrine,

and metabolic responses to surgical stress, which can decrease perioperative complications. It also tempers the shivering response, which can potentially prolong postanesthetic care unit stays. Regional techniques can be used to minimize inhalational agents, muscle relaxants, and opioids with a resultant earlier awakening from general anesthesia or complete avoidance of general anesthesia. In addition, there is often earlier return of bowel function and a decreased risk of deep vein thrombosis. Specifically, for lower extremity surgery, regional anesthesia can improve patient satisfaction with decreasing time to home readiness, opioid consumption, pain scores, time to ambulation, and postoperative nausea and vomiting.

Carli F, Kehlet H, Baldini G, et al. Evidence basis for regional anesthesia in multidisciplinary fast-track surgical care pathways. *Reg Anesth Pain Med*. 2011;36(1):63-72.

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Chapter 48
Complex Regional Pain Syndromes

Sudhir A. Diwan
Vinod Malhotra
Neel D. Mehta
Mohammad M. Piracha

A 35-year-old woman complains of diffuse burning pain in the left arm and hand for the last 6 months. She recalls spraining her left wrist while playing volleyball. Her left hand feels colder than the right, and her fingertips are blue. She is a recently divorced high-profile executive.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis of pain in this patient?
2. What is complex regional pain syndrome (CRPS)?
3. What are the two types of CRPS?
4. What are the diagnostic criteria for CRPS? What is the incidence of this disease?
5. Define allodynia, hyperalgesia, hyperesthesia, and dysesthesia.
6. What are the associated stages of CRPS?
7. What are the possible etiologies of CRPS?
8. Explain the pathophysiology of the development of CRPS.
9. Define sympathetically maintained pain (SMP) and sympathetically independent pain (SIP).
10. How does CRPS differ from neuralgia?
11. What is central pain? How will you differentiate central pain from CRPS?
12. Is the social history of this patient relevant to the development of chronic pain syndrome?

B. Pain Management

1. How will you work up CRPS type I and II?
2. Describe the sympathetic nerve supply to the arm?
3. Where is the stellate ganglion located?
4. What are the anatomic landmarks used in the stellate ganglion block?
5. What are the clinical signs of stellate ganglion block?
6. What is Horner syndrome?
7. After a stellate ganglion block, this patient reports no significant change in the degree of pain despite developing Horner syndrome. Is the pain psychogenic in this patient?
8. What types of nerve fibers are interrupted in stellate ganglion block?
9. What is a differential block?
10. What are the two major classes of local anesthetics? Describe the major differences in their clinical pharmacology.

11. What factors determine the onset, potency, and duration of a local anesthetic block?
12. How does the addition of epinephrine to commercially available premixed solutions affect the efficacy of local

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anesthetics?

13. How will you treat this patient?
14. What is the pharmacologic management of CRPS?
15. What is the role of intravenous regional block (Bier method) in diagnosis and treatment of CRPS?
16. Compare and contrast the mechanism of actions of ketamine and methadone.
17. What roles does ketamine infusion play in the treatment of CRPS?
18. What is the role of spinal cord stimulation (SCS) and surgical sympathectomy?

C. Complications

1. What are the complications of stellate ganglion block?
2. What is the systemic toxicity of local anesthetics?
3. How do you treat the systemic toxicity of local anesthetic drugs?

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis of pain in this patient?

Pain accompanied by burning and temperature change in this patient is most likely due to CRPS. The differential diagnosis may also include the following:

1. Peripheral neuropathy
2. Soft tissue injury
3. Vascular insufficiency (Raynaud disease)
4. Nerve entrapment syndrome (carpal tunnel syndrome)
5. Brachial plexopathy

Over the years, CRPS has been referred to as *reflex sympathetic dystrophy* (RSD), causalgia, SMP, and chronic peripheral pain syndrome. The term *CRPS* was introduced in 1994 by the International Association for the Study of Pain subcommittee on taxonomy. It is subdivided into CRPS type I (formerly described as *RSD*) and CRPS type II (formerly described as *causalgia*).

Jänig W, Stanton Hicks M, eds. *Progress in Pain Research and Management*. Seattle, WA: IASP Press; 1996:79-92. *Reflex Sympathetic Dystrophy: A Reappraisal*; vol 6.

Merskey H, Bogduk N, eds. Relatively generalized syndromes. In: *Classification of Chronic Pain*. 2nd ed. Seattle, WA: IASP Press; 1994:39-56.

Stanton-Hicks M, Jänig W, Hassenburch S, et al. Reflex sympathetic dystrophy: changing concepts and taxonomy. *Pain*. 1995;63:127-133.

A.2. What is complex regional pain syndrome (CRPS)?

CRPS is characterized by pain associated with sensory, autonomic, trophic, and motor abnormalities. CRPS is triggered by *noxious stimuli* (type I) or by *nerve injury* (type II). It is not limited to the distribution of a single peripheral nerve and is disproportionate to the inciting event.

RSD, causalgia, algodystrophy, Sudeck atrophy, and various other conditions are all grouped under CRPS. This diagnosis better describes the wide range of clinical signs and symptoms and the complexity of the pathophysiology responsible for the clinical picture.

Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurol*. 2011;10:637-648.

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Merskey H, Bogduk N, eds. Relatively generalized syndromes. In: *Classification of Chronic Pain*. 2nd ed. Seattle, WA: IASP Press; 1994:39-56.

Stanton-Hicks M, Jänig W, Hassenburch S, et al. Reflex sympathetic dystrophy: changing concepts and taxonomy. *Pain*. 1995;63:127-133.

A.3. What are the two types of CRPS?

CRPS-I is defined as a clinical syndrome triggered by a *noxious stimulus* that is not limited to the distribution of a single peripheral nerve; no nerve lesion can be identified. CRPS-II is defined as a clinical syndrome that is due to a *nerve injury* and is mostly limited to the distribution of the injured nerve. The diagnostic criteria are the same for CRPS-I and II.

Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurol*. 2011;10:637-648.

Stanton-Hicks MD, Burton AW, Bruehl SP, et al. An updated interdisciplinary clinical pathway for CRPS: report of an expert panel. *Pain Pract*. 2000;2(1):1-16.

A.4. What are the diagnostic criteria for CRPS? What is the incidence of this disease?

The diagnosis of CRPS can be made in the following context: a history of trauma to the affected area associated with pain that is disproportionate to the inciting event plus one or more of the following as defined by either the Orlando criteria or a modified version referred to as the Budapest criteria.

- Abnormal function of the sympathetic nervous system (vasomotor changes, skin color changes)
- Swelling
- Movement disorder
- Changes in tissue growth (dystrophy and atrophy)
- Sensory disturbances (hyperalgesia or allodynia)

The main features include pain that is continuous, burning in nature, independent of type and severity of injury, and not limited to a dermatomal distribution. Patients may complain of allodynia, dysesthesia, or hyperalgesia. Movement or stress exacerbates pain. Edema is usually present. Abnormal sudomotor activity, limb discoloration, and local temperature changes are common but inconsistent.

It affects between 200,000 and 1.2 million Americans. This syndrome may follow as many as 5% of all traumatic injuries with the arms being affected in approximately 60% of cases and the legs about 40%.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:314-331.

Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurol*. 2011;10:637-648.

A.5. Define allodynia, hyperalgesia, hyperesthesia, and dysesthesia.

- *Allodynia*: pain caused by a stimulus that normally does not provoke pain (i.e., touching with a cotton swab)
- *Hyperalgesia*: an increased response to a stimulus that is normally painful (i.e., increased response to pinprick)
- *Hyperesthesia*: increased sensitivity to a stimulus either due to a diminished threshold or an increased response to stimuli that are normally recognized. Hyperesthesia includes both allodynia and hyperalgesia.

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- *Dysesthesia*: an abnormal sensation that is unpleasant to the patient. It may be either spontaneous or evoked (i.e., lumbar radiculopathy).

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:314-331.

A.6. What are the associated stages of CRPS?

Stage I

- Onset of severe pain limited to the site of injury
- Increased sensitivity of skin to touch and light pressure (hyperesthesia)

- Localized swelling
- Muscle cramps
- Stiffness and limited mobility

At the onset, the skin is usually warm, red, and dry; then it may change to blue (cyanotic) in appearance and become cold and sweaty.

- Increased sweating (hyperhidrosis)
- In mild cases, this stage lasts a few weeks and then subsides spontaneously or responds rapidly to treatment.

Stage II

- Pain becomes even more severe and more diffuse.
- Swelling tends to spread and it may change from a soft to hard (brawny) type.
- Hair may become coarse then scant; nails may grow faster and become brittle, cracked, and heavily grooved.
- Spotty wasting of bone (osteoporosis) occurs early but may become severe and diffuse.
- Muscle wasting begins.

Stage III

- Marked wasting of tissue (atrophic) eventually becomes irreversible.
- For many patients, the pain becomes intractable and may involve the entire limb.
- A small percentage of patients have developed generalized RSD, affecting the entire body.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain.* 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:314-331.

A.7. What are the possible etiologies of CRPS?

CRPS may follow relatively minor trauma with or without nerve injury. Causes leading to CRPS include the following:

- Injuries to peripheral tissues (e.g., fractures, dislocations, and postoperative state)
- Inflammatory conditions (e.g., fasciitis, tendonitis, bursitis, and arthritis)
- Immobilization as a result of injury or cast application
- Peripheral nerve injury resulting from direct compression or ischemia (e.g., brachial plexopathy, postherpetic neuralgia, and nerve root injury)
- Central nervous system insults (e.g., head injury, ischemia, and brain tumor)
- Spinal cord lesions

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- Idiopathic

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:314-331.

A.8. Explain the pathophysiology of the development of CRPS.

Several hypotheses have been postulated, but none can explain all the findings and the varying responses to treatment in these patients. These hypotheses include the following:

- Abnormal discharges in sympathetic and nociceptive afferents produced by trauma
- Sensitization of peripheral sensory receptors produced by sympathetic hyperactivity
- Formation of ephapses (artificial synapses) after peripheral nerve injury
- Spontaneous neuronal ectopy at the site of demyelination or axonal injury
- Central reorganization of pain processing (central sensitization)

More than one sequence of events likely take place in a patient, giving rise to a mixed clinical picture. A dynamic change in the physiology and structure of central pain projecting neurons mediated through the *N*-methyl-D-aspartate (NMDA) receptor. Injury initiates and maintains a state of central sensitization in the central pain pathways, resulting in a lower threshold to fire pain transmission neurons and an increase in their receptive fields. This may involve disinhibition of spinal and trigeminal nociceptive neurons. This often

precedes thermal and mechanical allodynia and spontaneous pain. Finally, the psychological component and neuromodulation cannot be discernibly separated.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis, MO: Mosby; 2008:427-431.

Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurol*. 2011;10:637-648.

McMahon SB, Koltzenburg M, Tracey I, et al, eds. *Wall and Melzack's Textbook of Pain*. 6th ed. New York: Churchill Livingstone; 2013:961-977.

A.9. Define sympathetically maintained pain (SMP) and sympathetically independent pain (SIP).

The pain that is maintained by sympathetic innervation or circulating catecholamines is defined as SMP. It describes a pain mechanism, not a clinical syndrome. Therefore, by definition, patients with CRPS who report pain relief after a sympathetic block (e.g., stellate ganglion block) have SMP. Conversely, pain conditions that show features of sympathetic overactivity, yet fail to respond to sympathetic blocks, are described as SIP.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:314-331.

A.10. How does CRPS differ from neuralgia?

The chronic pain seen in neuralgia is usually paroxysmal in nature and follows the distribution of nerve. The pain is sharp and shooting without associated vasomotor or sudomotor changes. The chronic pain syndrome of CRPS is a sustained, diffuse, burning pain that is independent of nerve distribution and is associated with vasomotor and sudomotor changes, edema, allodynia or hyperalgesia, and changes in skin color.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby;

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2013:346-360.

A.11. What is central pain? How will you differentiate central pain from CRPS?

Central pain is regional pain initiated or caused by a primary lesion or dysfunction in the central nervous system; it is usually associated with abnormal sensitivity to temperature and to noxious stimulus. Central pain, also referred to as *deafferentation pain*, is a difficult pain syndrome to treat because the pathophysiology is not well understood. Regional pain not relieved by peripheral nerve blocks, either sympathetic or somatic, is more likely to be central pain. Central pain may be associated with various neurologic symptoms and signs such as monoparesis, hemiparesis, or paraparesis. Central pain conditions typically include partial or complete loss of sensation, involvement of spinothalamic functions, and development of hypersensitivity in body parts that have loss normal somatosensory feedback as a result of a central nevous system lesion.

Abram SE, Haddox JD, eds. *The Pain Clinic Manual*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2000:253-259.

McMahon SB, Koltzenburg M, Tracey I, et al, eds. *Wall and Melzack's Textbook of Pain* . 6th ed. New York: Churchill Livingstone; 2013:990-1002.

A.12. Is the social history of this patient relevant to the development of chronic pain syndrome?

In patients with CRPS, the disproportionate pain and dysfunction and the absence of clear pathogenesis and pathophysiology have led to examination of potential psychological etiology. Also noted is the fact that as the CRPS progresses, patients' personality measures such as Minnesota Multiphasic Personality Inventory (MMPI) profiles tend to resemble those of patients experiencing chronic pain and psychological distress as evidenced by hypochondriasis, depression, and hysteria scales. Certainly, stress has been implicated in increasing sympathetic outflow. The literature suggests that the presence of psychological disorders, particularly anxiety and depression, may predispose the patient to the development of CRPS. However, a large

case-control study reported no differences in psychological variables between those with CRPS and those without CRPS after controlling for age, sex, and trauma. Furthermore, anxiety and stress can augment nociception, and therefore, antidepressive treatments can be useful.

de Mos M, Huygen FJ, Dieleman JP, et al. Medical history and the onset of complex regional pain syndrome (CRPS). *Pain*. 2008;139:458-466.

Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurol*. 2011;10:637-648.

McMahon SB, Koltzenburg M, Tracey I, et al, eds. *Wall and Melzack's Textbook of Pain* . 6th ed. New York: Churchill Livingstone; 2013:990-1002.

B. Pain Management

B.1. How will you work up CRPS type I and II?

CRPS is diagnosed clinically with a detailed history and physical examination. Because it is a clinical diagnosis of exclusion, other specific conditions that could account for the degree of pain and dysfunction must be ruled out. Objective signs are variable but almost universally include loss of function of the affected part due to pain. Allodynia and hyperalgesia are extremely common. Change in temperature and sweating may vary depending on the stage of the disease. Several diagnostic studies may aid in the diagnosis of CRPS but are seldom pathognomonic.

A quantitative sweat test may show excessive sweating, and thermography may demonstrate abnormal heat regulation

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and disparity in temperature between affected and normal regions. Radiologic studies may reveal patchy osteoporosis in early stages. Triple-phase bone scintigraphy using technetium-99m may show increased periarticular uptake in the affected extremity illustrated by unilateral hyperperfusion in the perfusion and blood pool phases. Negative triple-phase bone scan results do not rule out CRPS. Thermographic, radiologic, or scintigraphic findings can be nonspecific and should be correlated with the clinical findings. Positive diagnostic sympathetic blocks can confirm the sympathetically mediated component of CRPS.

McMahon SB, Koltzenburg M, Tracey I, et al, eds. *Wall and Melzack's Textbook of Pain* . 6th ed. New York: Churchill Livingstone; 2013:990-1002.

B.2. Describe the sympathetic nerve supply to the arm?

The preganglionic sympathetic outflow to the upper extremity is derived from T2-T9. These fibers synapse with postganglionic neurons in the stellate ganglion. Therefore, a stellate ganglion block interrupts sympathetic outflow to the upper extremity.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346-360.

B.3. Where is the stellate ganglion located?

The stellate ganglion is formed by the fusion of the inferior cervical and the first thoracic ganglia. It usually measures 2.5 cm × 1.5 cm × 0.5 cm and lies between the base of the transverse process of the seventh cervical vertebra and the neck of the first rib. It is situated behind the carotid sheath, ventral to the longus colli muscle, behind the vertebral artery, and lateral to the body of the vertebra. The vertebral, subclavian, inferior thyroid, and the first intercostals arteries are in close proximity to the ganglion and so is the recurrent laryngeal nerve. The left pleura is 1 to 2 cm below it, whereas the right pleura is in closer proximity.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346-360.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1721-1751.

B.4. What are the anatomic landmarks used in the stellate ganglion block?

The landmarks used in the stellate ganglion block are the jugular notch of the sternum, the sternocleidomastoid muscle, the cricoid cartilage, and Chassaignac tubercle. In a supine

patient with the neck extended, a mark placed approximately 3.5 cm from the midline along the jugular notch and the same distance above the clavicle should overlie the transverse process of the seventh vertebra and the medial border of the sternocleidomastoid muscle. This marking is further confirmed by palpating the cricoid cartilage, which lies at the level of the sixth cervical vertebra, and the anterior tubercle on the vertebral transverse process, which is the most prominent tubercle in the neck (Chassaignac tubercle).

Benzon H, Rathmell JP, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346-360.

B.5. What are the clinical signs of stellate ganglion block?

A stellate ganglion block results in the following ipsilateral signs:

- *Eye*: ptosis, narrowing of the palpebral fissure, miosis, enophthalmos, conjunctival injection, and lacrimation

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- *Face and neck*: anhidrosis, elevated local temperature, and nasal stuffiness
- *Arm*: increased temperature and plethysmographic evidence of improved cutaneous blood flow

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1721-1751.

B.6. What is Horner syndrome?

Horner syndrome is a clinical entity characterized by ptosis, miosis, anhidrosis, and enophthalmos. It is usually seen with disease processes involving the cervical sympathetics and is the classic signs of a successful stellate ganglion block.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1721-1751.

B.7. After a stellate ganglion block, this patient reports no significant change in the degree of pain despite developing Horner syndrome. Is the pain psychogenic in this patient?

Not necessarily. The Horner syndrome indicates only the interruption of sympathetic supply to the head and neck. Unless it is accompanied by objective changes in the arm, it does not indicate a sympathetic nerve block of the upper extremity. Further, SMP will respond to sympathectomy, whereas SIP will not.

McMahon SB, Koltzenburg M, Tracey I, et al, eds. *Wall and Melzack's Textbook of Pain* . 6th ed. New York: Churchill Livingstone; 2013:990-1002.

B.8. What types of nerve fibers are interrupted in stellate ganglion block?

The stellate ganglion block results in interruption of the preganglionic, thinly myelinated type B fibers, as well as the postganglionic, unmyelinated type C fibers.

Casale R, Glynn CJ, Buonocore M. Autonomic variations after stellate ganglion block: are they evidence of an autonomic afference? *Funct Neurol*. 1990;5:245-246.

B.9. What is a differential block?

The variable effects of local anesthetics on fibers performing different functions are termed a *differential block*. The diagnostic distinction can be made by selectively blocking the function of these nerve fibers. The mechanism that results in a differential block is best explained by fiber size and myelination because these factors determine different sensitivities of nerve fibers to local anesthetics. By using different concentrations of local anesthetic, sympathetic and somatic fibers can be selectively blocked. A differential block may be helpful in differentiating somatic versus sympathetic pain and peripheral versus central pain.

Cousins MJ, Carr DB, Horlocker TT, et al, eds. *Cousins & Bridenbaugh's Neural Blockade*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:838-840.

B.10. What are the two major classes of local anesthetics? Describe the major differences in their clinical pharmacology.

The two major classes of clinically employed local anesthetics are esters and amides. The esters are hydrolyzed in the plasma by pseudocholinesterase; the amides are biotransformed in the liver. Although infrequent, local anesthetic toxicity is encountered more commonly in the ester group because of the para-aminobenzoic acid moiety. True allergic reactions to amides are rare and in most instances are caused by the preservatives in the solution. Each of the two groups of local anesthetics contains drugs with varying degrees of rate of onset, duration of neural blockade, potency, and toxicity.

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Benzon H, Rathmell JP, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346-360.

B.11. What factors determine the onset, potency, and duration of a local anesthetic block?

- Onset correlates with pK_a.
- Potency correlates with lipid solubility.
- Duration correlates with degree of protein binding.

The commonly used local anesthetics are weakly basic tertiary amines that are lipid soluble and unstable in water. They are prepared as acidic salts because the ionized form, which is soluble in water, is stable. Therefore, the aqueous solution contains the ionized (cation) form of the local anesthetic in dissociation equilibrium with the unionized (free base) form depending on the pH of the medium.

$$\underset{\text{Cation}}{R \equiv NH^+} \rightleftharpoons \underset{\text{Base}}{R \equiv N} + H^+$$

When injected into the body, the relative rise in pH will allow the local anesthetic to convert to the uncharged base. The free base, being lipid soluble, will diffuse across the neural membrane and is responsible for neural blockade. With the exception of procaine and chloroprocaine, the commonly employed local anesthetics are highly protein-bound and are therefore longer acting (Table 48.1).

Benzon H, Rathmell JP, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346-360.

B.12. How does the addition of epinephrine to commercially available premixed solutions affect the efficacy of local anesthetics?

The addition of epinephrine to a local anesthetic increases the duration and intensity of a block. However, in commercially available premixed solutions containing epinephrine,

antioxidants are added to preserve epinephrine, and the result is a lower buffered pH level of the solution. This lowering of the pH level can result in decreased efficacy of the local anesthetic. Best results are achieved by adding the desired concentration of epinephrine to the local anesthetic solution just before injection.

TABLE 48.1 Physiochemical Properties of Commonly Used Local Anesthetics

LOCAL ANESTHETIC	pK_a	PROTEIN BINDING (%)
Esters		
Procaine	8.9	5.8
Chloroprocaine	8.7	—
Tetracaine	8.5	75.6
Amides		

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Lidocaine	7.9	64.3
Mepivacaine	7.6	77.5
Bupivacaine	8.1	95.6
Etidocaine	7.7	94.0

Benzon H, Rathmell JP, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346-360.

B.13. How will you treat this patient?

Early diagnosis and aggressive physical therapy with pharmacologic control of pain form the basis of the treatment of CRPS. Physical therapy is widely recommended and accepted as a first line of treatment. The treatment of CRPS will differ depending on whether the pain is SMP or SIP. A series of sympathetic blocks has been shown effective in treating SMP of CRPS. A multidisciplinary approach including physiotherapy and symptom-specific psycho-logical treatments (e.g., biofeedback and hypnosis) may be beneficial. Many patients have a component of both SMP and SIP, and a combination of sympathectomy and analgesic treatment is recommended. However, no single treatment is consistently successful. Therefore, the treatment plan should be individualized.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:314-331.

McMahon SB, Koltzenburg M, Tracey I, et al, eds. *Wall and Melzack's Textbook of Pain*. 6th ed. New York: Churchill Livingstone; 2013:990-1002.

B.14. What is the pharmacologic management of CRPS?

SMP of CRPS is treated with the drugs that deplete norepinephrine from the sympathetic nerve terminals. Oral sympatholytic agents include phenoxybenzamine, prazosin, and terazosin. Topical clonidine, a selective α_2-agonist, has been successfully used to treat SMP. Tricyclic antidepressants have been effective in approximately half the number of patients and have been recommended as first-line agents. Other drugs that have been successfully used to treat CRPS are anticonvulsants (e.g., gabapentin, pregabalin, carbamazepine, and topiramate), local anesthetics such as lidocaine and mexiletine, calcitonin, corticosteroids, and high-dose opioids. Anecdotal reports suggest that methadone (opioid with anti-NMDA receptor effect) has been more effective than other opioids. Long-term intrathecal morphine has been reported to produce analgesic effects in CRPS. Nonsteroidal anti-inflammatory drugs have also been used successfully.

Abram SE, Haddox JD, eds. *The Pain Clinic Manual*. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:177-184.

Becker WJ, Ablett DP, Harris CJ, et al. Long-term treatment of intractable reflex sympathetic dystrophy with intrathecal morphine. *Can J Neurol Sci*. 1995;22:153-159.

B.15. What is the role of intravenous regional block (Bier method) in diagnosis and treatment of CRPS?

Intravenous regional block (Bier method) with guanethidine, reserpine, bretylium, and phentolamine has been used to achieve temporary sympatholytic effect and relieve SMP of CRPS. Intravenous guanethidine and reserpine have been reported to relieve pain in more than 50% of patients as compared with a control group in one study. However, guanethidine and reserpine are not commercially available in the United States. The combination of bretylium and lidocaine is more effective than lidocaine alone. α-Adrenergic blockade with intravenous phentolamine is a sensitive test

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to identify patients with SMP. Phentolamine has been used as a predictor agent before more invasive sympathetic blocks.

Blanchard J, Ramamurthy S, Walsh N, et al. Intravenous regional sympatholysis: a double-blind comparison guanethidine, reserpine, and normal saline. *J Pain Symptom Manage*. 1990;5:357-361.

Hord AH, Rooks MD, Stephens BO, et al. Intravenous regional bretylium and lidocaine for the treatment of reflex sympathetic dystrophy: a randomized double-blind study. *Anesth Analg*. 1992;74:818-821.

Raja SN, Treede RD, Davis KD, et al. Systemic alpha-adrenergic blockade with phentolamine: a diagnostic test for sympathetically maintained pain. *Anesthesiology*. 1991;74:691-698.

B.16. Compare and contrast the mechanism of actions of ketamine and methadone.

Methadone is a strong, long-acting opioid analgesic, whereas ketamine is a dissociative anesthetic. Methadone is used as an opioid but has mild NMDA receptor antagonist properties— the only strong opioid that has this quality. Ketamine is used in oral preparations, intravenous delivery systems, in skin preparations, and other delivery methods including being compounded in various percentages. These medications can block NMDA glutamate receptors and decrease the windup pain and central sensitization typical of chronic intractable pain. Windup causes an amplification of the incoming pain signal at the level of seconddegree neurons in the dorsal horn of the spinal cord. By blocking these receptors, not only is windup pain decreased but also tolerance to opioid medications can also be decreased. Ketamine has the added effect of blocking sodium channels.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346-360.

Chizh, BA. Low dose ketamine: a therapeutic and research tool to explore N-methyl-D-aspartate (NMDA) receptor-mediated plasticity in pain pathways. *J Psychopharmacol*. 2007;21(3):259-271.

B.17. What roles does ketamine infusion play in the treatment of CRPS?

Although ketamine may have more than one mechanism of action, the basis for using it to treat CRPS may reside in its strong ability to block NMDA receptors. Ketamine is the only potent NMDA-blocking drug currently available for clinical use. An appropriately prolonged infusion of ketamine appears to maintain a level of ketamine in the central nervous system long enough to reverse the effects of the sensitization process and associated pain.

Currently, three methods of ketamine administration have been used for treatment, including an outpatient low-dose ketamine administration, a low-dose awake inpatient technique, and a ketamine “coma” technique, which is a controversial treatment not currently allowed in the United States. While studies are continuing, ketamine therapy has been shown to be effective for relief of pain CRPS-I; to date, no adverse cognitive effects of extended ketamine infusion treatment have occurred. Side effects, however, can occur in the high-dose setting; the infusion can be associated with significant risks including chronic catheterization, the need for parenteral nutrition, and endotracheal intubation. The outpatient therapy requires the patient to return for a 10-day period of time and often losses effectiveness after 6 to 12 weeks.

Goldberg ME, Torjman MC, Schwartzman RJ, et al. Pharmacodynamic profiles of ketamine (R)- and (S)- with 5-day inpatient infusion for the treatment of complex regional pain syndrome. *Pain Physician*. 2010;13(4):379-387.

Kiefer RT, Rohr P, Ploppa A, et al. Complete recovery from intractable complex regional pain syndrome, CRPS-type I, following anesthetic ketamine and midazolam. *Pain Pract*. 2007;7:147-150.

B.18. What is the role of spinal cord stimulation (SCS) and surgical

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sympathectomy?

Surgical, chemical, or radiofrequency sympathectomy produces short-term pain relief, but long-term results are poor and inconsistent. Delayed failure of sympathectomy may be due to regeneration of ipsilateral nerves or reinnervation from the contralateral sympathetic nerves. SCS is an effective treatment for the pain of CRPS, including recurrent pain after surgical or radiofrequency sympatholysis. Epidural SCS is a simple procedure and carries low morbidity.

Kumar K, Nath RK, Toth C. Spinal cord stimulation is effective in the management of reflex sympathetic dystrophy. *Neurosurgery*. 1997;40(3):503-508.

Rocco AG. Radiofrequency lumbar sympatholysis. The evolution of a technique for managing sympathetically maintained pain. *Reg Anesth*. 1995;20(1):3-12.

C. Complications

C.1. What are the complications of stellate ganglion block?

Although complications appear infrequently, the more common complications of stellate ganglion block are as follows:

- Intra-arterial injection: seizure and hematoma
- Recurrent laryngeal nerve paralysis: hoarseness of voice

- Brachial plexus block: motor weakness
- Accidental epidural or subarachnoid injection
- Esophageal injury
- Pneumothorax: respiratory distress

To avoid complications, aspiration of the needle should be performed before, during, and after administration of local anesthetics to look for (1) air, (2) blood, and (3) cerebrospinal fluid.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346-360.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1721-1751.

C.2. What is the systemic toxicity of local anesthetics?

The systemic toxic effects of local anesthetics are related to drug levels in blood, and they are manifested mainly in the central nervous system and the cardiovascular system. As a rule, the central nervous system effects precede the cardiovascular toxic manifestations.

Central Nervous System Effects

Central nervous system effects include light-headedness, dizziness, tinnitus, visual disturbances, drowsiness, disorientation, slurred speech, muscle twitching, generalized grand mal seizures, and electroencephalographic changes. The blood levels of local anesthetics associated with central nervous system changes in humans are as follows:

- Procaine: 20 μg per mL
- Lidocaine, mepivacaine, and prilocaine: 5 to 10 μg per mL
- Tetracaine, bupivacaine, and etidocaine: 1.5 to 4 μg per mL
- Lowering the $PaCO_2$ by hyperventilation decreases the convulsive threshold dose of a local anesthetic drug.

Cardiovascular Effects

Ventricular arrhythmias are reported with intravenous bupivacaine only. Cardiac resuscitation is extremely difficult in patients with bupivacaine-induced cardiac arrhythmias. Ropivacaine is less toxic than bupivacaine but more toxic than lidocaine. The mechanism of enhanced cardiotoxicity in pregnant patients is not well understood; nevertheless, 0.75% bupivacaine is no longer recommended in pregnant patients in the United States (Table 48.2).

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Benzon H, Rathmell JP, Wu CL, et al, eds. *Raj's Practical Management* of Pain. 5th ed. St. Louis, MO: Mosby; 2013:346-360.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1028-1054.

TABLE 48.2 Cardiovascular Effects of Lidocaine

BLOOD LEVEL LIDOCAINE (μg/mL)	ELECTROCARDIOGRAPHIC CHANGES	HEMODYNAMIC EFFECTS
<5	—	—
5-10	↑ PR interval	↓ Myocardial contraction
	↑ QRS duration	↓ Cardiac output
	Sinus bradycardia	Vasodilatation
>10	↑ PR interval	↓ Myocardial contraction
	↑ QRS duration	↓ Cardiac output
	Sinus bradycardia	Circulatory collapse
	Atrioventricular block	
	Asystole	

↑, increase; ↓, decrease.

C.3. How do you treat the systemic toxicity of local anesthetic drugs?

The principles of treatment include the following:

- Secure and maintain the airway.
- Ensure adequate oxygenation and ventilation.
- Treat hypotension and bradycardia promptly.

For patients in cardiac arrest or with severe, refractory arrhythmias, intravenous fat emulsions should be given. The suggested bolus dose is 1.5 mL per kg of 20% fat emulsion (Intralipid) over 1 minute followed by a continuous infusion at 0.25 mL/kg/min. If there is no clinical improvement, the bolus dose should be repeated and the infusion should be increased to 0.5 mL/kg/min. The infusion should be continued for at least 10 minutes after hemodynamic stability is restored but discontinued within an hour.

- Perform immediate cardiopulmonary resuscitation for profound cardiovascular collapse.
- Perform electrical cardioversion for ventricular tachycardia or fibrillation.
- Control seizures with the following:

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- Diazepam, 0.1 to 0.2 mg per kg, intravenously
- Thiopental sodium, 1 to 2 mg per kg, intravenously

Benzon H, Rathmell JP, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346-360.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1684-1720.

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Chapter 49
Cancer Pain

Sudhir A. Diwan
Shakil Ahmed
Sadiah Siddiqui
Neel D. Mehta

A 44-year-old man was referred to the pain clinic for evaluation and management of abdominal pain. He was recently diagnosed with adenocarcinoma of the pancreas with retroperitoneal lymph nodes in the para-aortic region. His pain is localized in the epigastric region and is worse during the night and decreased during the day. He is taking controlled-release morphine sulfate (MS Contin), 100 mg orally every 8 hours, and morphine sulfate, 30 mg orally every 3 hours as needed, for breakthrough pain. The patient reports inadequate pain control, nausea, vomiting, and constipation.

A. Medical Disease and Differential Diagnosis

1. What is the definition of pain?
2. How significant is the problem of pain in patients with cancer?
3. What are the components of cancer pain?
4. How does the pain contribute to the suffering of patients with cancer?
5. How do psychological factors affect pain in patients with cancer?
6. What are the causes of pain in patients with cancer?
7. How do you classify pain in patients with cancer?
8. What are the characteristics of pancreatic cancer pain?
9. How do you assess pain in patients with cancer?
10. What is the differential diagnosis of abdominal pain?

B. Pharmacologic Treatment of Pain

1. What is the World Health Organization stepladder approach for cancer pain management?
2. Which class of drugs does morphine sulfate belong to?
3. What is the difference between morphine and synthetic opioids?
4. How does mixed opioid agonist/antagonist differ from opioid agonist?
5. Describe the role of methadone in the management of cancer pain.
6. What are the advantages and disadvantages of methadone?
7. What is the mechanism of action of opioids?
8. What are the side effects of opioid therapy?
9. Define tolerance and physical dependence.
10. How would you treat the side effects of opioid therapy?
11. What is tramadol?
12. When would you consider adjuvant analgesics as part of the treatment plan?

13. The patient and his family are worried about addiction. How would you approach this problem?

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14. Describe different routes of opioid administration.
15. Describe advantages and complications of patient-controlled analgesia (PCA). What is minimum effective analgesic concentration (MEAC)?
16. What is meperidine? How is it different from other opioids?
17. What is rotation of opioids? When would you consider rotation of opioids?

C. Interventional Pain Management

1. Describe the role of peripheral nerve blocks in cancer pain management.
2. Describe the role of celiac plexus block in cancer pain management.
3. What are the complications of celiac plexus block?
4. Would you consider neuraxial opioid infusion in this patient? Discuss complications of this procedure.
5. Which medications can be used intrathecally? What is ziconotide?
6. What is a Personal Therapy Manager (PTM) and what role does it play in neuraxial pain relief?
7. Would you consider neuraxial neurolysis in this patient to manage his pain? Discuss advantages and disadvantages of these blocks.
8. Which neuroablative procedures can be considered in the terminal stage of pancreatic cancer?
9. Describe the role of radiation therapy in cancer pain.

D. Nonpharmacologic Management

1. What are the various nonpharmacologic techniques of cancer pain management?
2. What physical modalities have been successfully tried in cancer pain management?
3. Describe the role of neuromodulation in cancer pain management.
4. What psychological techniques have been promoted for comfort care and pain relief?
5. What are distraction and reframing techniques? What is the role of hypnosis in cancer pain management?

A. Medical Disease and Differential Diagnosis

A.1. What is the definition of pain?

According to the International Association of the Study of Pain, pain is defined as “an unpleasant, sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.”

International Association for the Study of Pain. IASP taxonomy. Updated August 6, 2014. http://www.iasp-pain.org. Accessed May 23, 2015.

Merskey H, Bogduk N, eds. *Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms*. 2nd ed. Seattle: IASP Press; 1994:210.

A.2. How significant is the problem of pain in patients with cancer?

A total of 1,658,370 new cancer cases and 589,430 cancer deaths are projected to occur in the United States in 2015. It is estimated that 48,960 men and women will be diagnosed with pancreatic cancer and 40,560 will die of the disease. Thirty percent of the patients with cancer have pain at the time of diagnosis, and 65% to 85% of patients with cancer have pain at advanced stages. Thirty-six percent have pain severe enough to impair their ability to function.

Vainio and Auvinen studied 1,840 patients with advanced cancer and found 24% with no pain, 24% with mild pain, 30% with moderate pain, and 21% with severe pain. Daut and Cleeland

found pain to be an early symptom of cancer in 48% to 50% of patients with cancer of breasts, ovary, prostate, colon, and

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rectum, and in 20% of patients with uterus and cervical cancer.

Bruera ED, Portenoy RK, eds. *Cancer Pain: Assessment and Management*. 2nd ed. New York: Cambridge University Press; 2010:37-53.

Daut RL, Cleeland CS. The prevalence and severity of pain in cancer. *Cancer*. 1982;50:1913-1918.

Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin*. 2015;65(1):5-29.

Vainio A, Auvinen A. Prevalence of symptoms among patients with advanced cancer: an international collaborative study. *J Pain Symptom Manage*. 1996;12(1):3-10.

A.3. What are the components of cancer pain?

The components of cancer pain are sensory, affective, and psychological.

The sensory components could be nociceptive pain elicited by activation of sensory nerve endings by mechanical, chemical, radioactive, or thermal energy. It is often associated with ongoing tissue damage and may be of somatic or visceral origin. Somatic pain may be superficial, well localized, sharp, pricking, burning or deep diffused, dull, and aching. Visceral pain is usually diffuse, referred to body surface, and has a sickening quality to it.

Neuropathic pain is due to pathologic change in the discharge properties of the neurons because of invasion, compression, or damage caused by various cancer treatment modalities. It is typically described as burning, lancinating, painful numbness, or itching sensations. Phantom pain is a pain referred to the amputated part of the body. Psychological pain is usually due to fear, anxiety, depression, existential questions, anger, social and financial issues, social support, and the impact the pain has on the family and caregivers. Most cancer patients report more than one site of pain.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:537-559.

Zaza C, Baine N. Cancer pain and psychosocial factors: a critical review of the literature. *J Pain Symptom Manage*. 2002;24:526-542.

A.4. How does the pain contribute to the suffering of patients with cancer?

Sustained pain on its own can create complex, enduring, unpleasant emotional suffering by its ability to create awareness of the perceived threat to one's life. It causes helplessness in the face of the inevitability of demise as well as exhaustion of hope. Patients with cancer usually identify pain as an indicator of disease progression. Suffering may be attributable to many factors besides physical complaints. Psychological factors include financial issues, lack of social support, loss of job or social position in society, loss of independence, effect on family and friends, social isolation, and fear of death.

Spiegel D, Giese-Davis J. Depression and cancer pain: mechanisms and disease progression. *Biol Psychiatry*. 2003;54:269-282.

A.5. How do psychological factors affect pain in patients with cancer?

The ultimate perception of pain depends on the nociceptive stimulus and psychological fear, anger, anxiety, or depression. Twenty-five percent of patients with cancer meet criteria for major depressive syndromes at some point in their illness, with an overall prevalence of 53% in hospitalized patients with cancer. Psychological factors may significantly exacerbate pain. The psychological suffering is associated with the disease and the imminence of death.

Symptoms usually include anxiety, restlessness and irritability, sleep disorders, obsessive thinking, slowness in motor responses, and hopelessness. Psychological suffering was most typically manifested in depression, which most of the patients suffer during the initial stages of the disease, when the disease metastasize, and when they are in a particularly poor condition. These factors affect overall pain behavior and suffering. General deterioration causes them to withdraw

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into their home or the hospital.

Hyphantis T, Tomenson B, Paika V, et al. Somatization is associated with physical health-related quality of life independent of anxiety and depression in cancer, glaucoma and rheumatological disorders. *Qual Life Res*. 2009;18(8):1029-1042.

Spiegel D, Giese-Davis J. Depression and cancer pain: mechanisms and disease progression. *Biol Psychiatry*. 2003;54:269-282.

A.6. What are the causes of pain in patients with cancer?

Pain in patients with cancer may be due to (1) presence and progression of the tumor itself, for example, bone involvement, viscus obstruction, and nerve compression; (2) indirect effect of the tumor, for example, metabolic imbalance, infection, and venous or lymphatic obstruction; (3) consequence of cancer treatment, such as chemotherapy, radiation therapy, or surgery; or (4) unrelated mechanisms such as migraine and myofascial pain.

Localized invasion of peripancreatic structures most commonly causes back pain, which stems from tumor invasion of the splanchnic plexus, common bile duct obstruction, retroperitoneum, or pancreatitis. This pain is described as severe, gnawing, epigastric, upper abdominal radiating to the middle of the back, worse on lying down and improved with upright position.

Grond et al. found in a prospective study of 2,266 patients with cancer that 30% had one pain syndrome, 39% had two pain syndromes, 31% had three pain syndromes, 85% by the cancer itself (bone, 35%; soft tissue, 45%; and visceral, 34%), and 17% by anticancer treatment.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:537-559.

Grond S, Zech D, Diefenbach C, et al. Assessment of cancer pain: a prospective evaluation in 2266 cancer patients referred to a pain service. *Pain*. 1996;64:107-114.

Mantyh P. Bone cancer pain: causes, consequences, and therapeutic opportunities. *Pain*. 2013;154(suppl 1):S54-S62.

A.7. How do you classify pain in patients with cancer?

Pain, in patients with cancer, may be classified on the basis of the following:

- Duration: acute or chronic
- Intensity and severity: visual analog score; numeric pain score; and verbal: mild, moderate, severe, or worst possible pain
- Pathophysiology and mechanism: nociceptive or neuropathic; tumor infiltration of nerves; infiltration of soft tissue or hollow organs, serosa, solid organ necrosis; and destruction of bone
- Individual type and stage of disease: pancreatic, ovarian, prostatic, breast, or lung
- Pattern of pain: incidental pain related to an event or activity; spontaneous pain unrelated to an event or activity and end-of-dose failure
- Pain syndromes: tumor invasion of bone, nerves, spinal cord, viscera, blood vessels, postsurgical, and postchemotherapy and postradiation therapy pain

The pancreatic carcinoma usually presents with vague symptoms of anorexia, weight loss, abdominal discomfort, new-onset diabetes mellitus, or thrombophlebitis. The vague nature of symptoms may result in delay of diagnosis.

Boland EG, Mulvey MR, Bennett MI. Classification of neuropathic pain in cancer patients. *Curr Opin Support Palliat*

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Care. 2015;9(2):112-115.

Caraceni A, Weinstein S. Classification of cancer pain syndromes. *Oncology (Williston Park)*. 2001;15:1627-1640.

Ochoa JL. Neuropathic pain: redefinition and a grading system for clinical and research purposes. *Neurology*. 2009;72(14):1282-1283.

A.8. What are the characteristics of pancreatic cancer pain?

About 30% to 60% of patients present with pain, and 80% of the patients with advanced cancer complain of pain. Pain is diffuse epigastric radiating to the back that is increased on lying down and improved on sitting.

Bruera ED, Portenoy RK, eds. *Cancer Pain: Assessment and Management*. 2nd ed. New York: Cambridge University Press; 2010:37-53.

Evans DB, Pisters PWT, Abbruzzese JL, eds. *Pancreatic Cancer*. New York: Springer-Verlag; 2002:223-233.

A.9. How do you assess pain in patients with cancer?

A stepwise approach is required for the assessment of pain. It includes history, physical examination, and data collection ending with clinical diagnosis. It helps the clinician achieve goals of providing pain relief. Assessment involves identifying features of pain, such as location, intensity, quality, timing, exacerbating/relieving factors, response to previous analgesics,

and disease-modifying treatments; effects of pain on daily activities and psychological state; associated symptoms; complete physical examination; and laboratory data and imaging.

Bruera ED, Portenoy RK, eds. *Cancer Pain: Assessment and Management*. 2nd ed. New York: Cambridge University Press; 2010:89-105.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:537-559

A.10. What is the differential diagnosis of abdominal pain?

Although abdominal pain may arise from different intraperitoneal structures, the retroperitoneal organs can cause similar pain symptoms. Location and radiation of the pain can give important clues to make the diagnosis. Retroperitoneal structures present with dull or sharp back pain that is increased on lying down and relieved on sitting hunched up. Abdominal tumors are frequently characterized by colicky pain associated with nausea that is worse after eating. Abdominal pain may be referred to distant areas like shoulder, neck, or back depending on the organ involved. Tumors of the small bowel or large bowel may present with symptoms of obstruction (e.g., abdominal distention, nausea, and bilious vomiting) or hematemesis or melena. Other common causes of abdominal pain include omental metastasis, volvulus of intestine, infectious peritonitis, radiation enteritis, and peritoneal carcinomatosis. Mesenteric ischemia presents with diffuse pain that is increased with meals and weight loss.

Nonmalignant causes of abdominal pain such as appendicitis, cholecystitis, and pancreatitis can occur in patients with cancer coincidentally and may complicate the diagnostic process. Opioid analgesics may not be used in these patients because they may exacerbate symptoms of colicky pain (due to spasm of sphincter of Oddi), nausea, vomiting, paralytic ileus, and constipation.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:537-559.

B. Pharmacologic Treatment of Pain

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B.1. What is the World Health Organization stepladder approach for cancer pain management?

The World Health Organization advocated a stepladder approach to manage cancer pain exclusively with oral medications depending on the pain intensity and to some extent the pain mechanism (Fig. 49.1).

Step 1. Manage the pain by nonopioid medications with or without adjuvants.

Step 2. If pain is persisting or increasing, add weak opioids to nonopioid analgesics and adjuvants.

Step 3. Strong opioids are used with nonopioid analgesics and adjuvants until the patient achieves complete analgesia.

Step 4. A new fourth step has been recommended for treatment of crises or persistent chronic pain, and this includes transforaminal epidural steroid injections, lumbar percutaneous adhesiolysis and neurolysis, and other interventional procedures.

Noninvasive routes of drug delivery should be maintained as long as possible because of its simplicity, convenience, and cost.

Azevedo São Leão Ferreira K, Kimura M, Jacobsen-Teixeira M. The WHO analgesic ladder for cancer pain control, twenty years of use. How much pain relief does one get from using it? *Support Care Cancer*. 2006;14(11):1086-1093.

Pazdur R, Wagman L, Camphausen KA, et al, eds. *Cancer Management: A Multidisciplinary Approach* . 12th ed. Philadelphia, PA: F.A. Davis Company; 2010:731-746.

Vargas-Schaffer G. Is the WHO ladder still valid? Twenty-four years of experience. *Can Fam Physician*. 2010;56(6):514-517.

World Health Organization. *Traitement de la douleur cancéreuse*. Geneva, Switzerland: World Health Organization; 1997.

World Health Organization. WHO's cancer pain ladder for adults. http://www.who.int/cancer/palliative/painladder/en/. Accessed June 30, 2015.

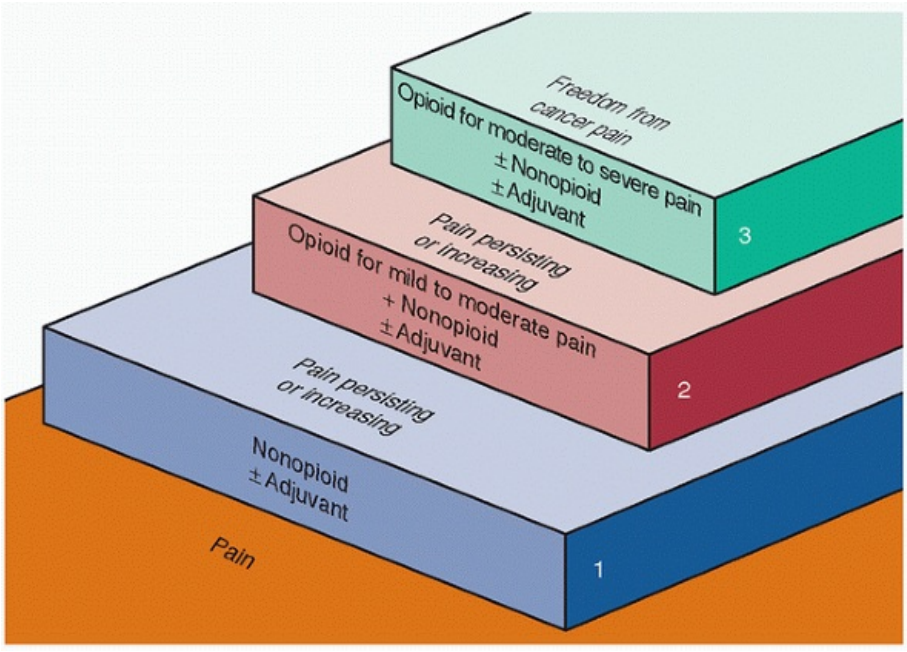


FIGURE 49.1 World Health Organization-advocated stepladder approach to management of cancer pain.

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B.2. Which class of drugs does morphine sulfate belong to?

Morphine is an opiate (naturally occurring in opium) by definition and is a μ-receptor opioid agonist. An ideal opioid agonist would have a high specificity for receptors producing desirable effects (analgesia and minimal or no affinity for other receptors that cause side effects). Opioids are unique in producing analgesia without loss of consciousness.

Brunton LB, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566-578.

B.3. What is the difference between morphine and synthetic opioids?

Morphine is the principal phenanthrene alkaloid present in opium and hence is termed an opiate. It is highly ionized and water-soluble. The most active molecule of morphine is the levorotatory isomer of stereochemical structure. The synthetic or semisynthetic compounds are called opioids and contain the phenanthrene nucleus of morphine. The terms opiates and opioids are often used interchangeably in clinical practice. Clinically, histamine release by morphine differentiates it from the synthetic opioids. This may cause urticaria, allergic reactions, and hemodynamic instability, particularly in volume-depleted patients.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders/Elsevier; 2015:864-914.

B.4. How does mixed opioid agonist/antagonist differ from opioid agonist?

The mixed-action opioids bind to μ-receptors, where they are partial agonists or competitive antagonists. Antagonistic properties of these drugs can attenuate the efficacy of subsequently administered opioid agonists and cause withdrawal symptoms in patients already receiving opioid agonists. The advantages of these drugs include low potential for respiratory depression and physical dependence. A dysphoric reaction is very common with mixed-action opioids. Their use is limited because of a ceiling effect whereby progressive escalation in doses does not increase analgesia as with opioid agonists.

Brunton LB, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566-578.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders/Elsevier; 2015:864-914.

B.5. Describe the role of methadone in the management of cancer pain.

The efficient oral and rectal absorption with prolonged duration of analgesic action of methadone makes it a highly effective and attractive oral drug for cancer pain management.

Methadone is a synthetic opioid with a unique agonist-antagonist action. Methadone is a μ-receptor agonist and an *N*-methyl-D-aspartate (NMDA) receptor antagonist. Activation of NMDA receptors is involved in the development of hypersensitivity and central sensitization in neuropathic pain and tolerance to opioids. Because of the antagonistic effect at the NMDA receptor site, methadone is very effective in neuropathic pain secondary to cancer-related pathology and therapeutic interventions. The same antagonistic action of methadone minimizes the development of tolerance to opioids.

Brunton LB, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566-578.

Manfredi PL, Gonzalez GR, Cheville AL, et al. Methadone analgesia in cancer patients on chronic methadone maintenance therapy. *J Pain Symptom Manage*. 2001;21:169-174.

McLean S, Twomey F. Methods of rotation from another strong opioid to methadone for the management of cancer

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pain: a systematic review of the available evidence. *J Pain Symptom Manage*. 2015;50(2):248-259.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders/Elsevier; 2015:864-914.

B.6. What are the advantages and disadvantages of methadone?

Methadone has several advantages, including oral and rectal absorption with bioavailability to 95%, high potency, high lipid solubility, low cost, and no active metabolites. Methadone has a long half-life, and its analgesic effect lasts 6 to 8 hours. However, methadone has been used for a long time for heroin abusers as detoxification and maintenance; it carries a social stigma, which can interfere with adequate pain management. Methadone has a variable elimination half-life between 20 and 60 hours. Because of that, the cumulative effect of methadone causes sedation, makes titration difficult, and has led to the concept of individualization of methadone dosing.

Brunton LB, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566-578.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:594-595.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders/Elsevier; 2015:864-914.

B.7. What is the mechanism of action of opioids?

Opioids act as agonists at stereospecific opioid receptors that are normally activated by endogenous ligands known as endorphins in brainstem and spinal cord. Binding of opioid to the receptor inhibits adenylate cyclase activity and causes hyperpolarization of neurons, which results in suppression of spontaneous discharge and evoked potential. Opioids also interfere with transmembrane transport of calcium ion and interfere with the release of neurotransmitters such as acetylcholine, dopamine, norepinephrine, and substance P. Inhibition of acetylcholine release from nerve endings is the basis of analgesic activity of opioids.

Brunton LB, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566-578.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:1682-1710.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders/Elsevier; 2015:864-914.

B.8. What are the side effects of opioid therapy?

The opioid-related side effects occur because of opioid receptor pharmacodynamics, metabolites, or both. Sedation and respiratory depression are due to μ-receptor activation. Tolerance to these side effects is developed within a very short period of treatment. The dysphoric reaction is due to activation of κ-receptors. Psychotomimetic and depersonalization reactions are due to activation of τ-receptors. Nausea and vomiting are caused by direct stimulation of the chemoreceptor trigger zone. Increased intrabiliary pressure is due to spasm of the sphincter

of Oddi. Other side effects commonly observed are constipation, pruritus, and myoclonus. Almost all side effects diminish with time, except constipation and myoclonus. Patients with cancer who develop constipation secondary to opioid therapy are required to be on a regular bowel regimen to avoid subsequent serious consequences. In patients with compromised renal function, metabolites of morphine (M3G, M6G) cause excessive sedation and metabolites of meperidine (normeperidine) lower the seizure threshold.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott

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Williams & Wilkins; 2010:1682-1710.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders/Elsevier; 2015:864-914.

B.9. Define tolerance and physical dependence.

Tolerance occurs with the development of the need to gradually escalate the dose to achieve the same pain control, and it can develop in 2 to 3 weeks. Tolerance does not indicate abuse or addiction; it is commonly associated with increasing pain or disease progression. Physical dependence develops after chronic use of opioids, and it is characterized by development of withdrawal syndrome after administration of an opioid antagonist or abrupt discontinuation of the medication. The potential for tolerance is an agonistic effect of opioids.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:418-423.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders/Elsevier; 2015:864-914.

Streltzer J, Johansen L. Prescription drug dependence and evolving beliefs about chronic pain management. *Am J Psychiatry*. 2006;163(4):594-598.

B.10. How would you treat the side effects of opioid therapy?

Oversedation and respiratory depression are treated with a specific μ-receptor antagonist, naloxone, as well as supplemental oxygen. Naloxone, in a 1- to 4-μg per kg intravenous bolus, promptly reverses sedation, respiratory depression, and analgesia. Continuous intravenous infusion at the rate of 2 to 4 μg/kg/hr will reverse only side effects without reversing analgesia. Nausea and vomiting should be managed by antiemetics. Constipation should be treated with a regular bowel regimen of laxatives and stool softener. Peripheral μ-opioid receptor antagonists (e.g., alvimopan, which inhibits the μ-opioid receptors in the gut but not in the central nervous system) have been shown in preliminary studies to improve opiate-induced bowel dysfunction without reversing analgesia. Generalized pruritus may respond to one more doses of antihistamine; however, pruritus may not be related to histamine release.

Cherny N, Ripamonti C, Pereira J, et al. Strategies to manage the adverse effects of oral morphine: an evidence based report. *J Clin Oncol*. 2001;19:2542-2554.

Slatkin N, Thomas J, Lipman AG, et al. Methylnaltrexone for treatment of opioid-induced constipation in advanced illness patients. *J Support Oncol*. 2009;7:39-46.

B.11. What is tramadol?

Tramadol (Ultram) is a nonopioid synthetic analgesic with weak μ-receptor agonistic activity and is thought to exert its analgesic effects by inhibition of reuptake of norepinephrine and serotonin. It should be started at 50 to 100 mg every 6 to 8 hours. It may exhibit μ-receptor-related clinical side effects such as respiratory depression and constipation. Prolonged use may lead to physical and psychological dependence. Tramadol was placed into Schedule IV of controlled substances effective August 18, 2014.

Tapentadol is a centrally acting pain reliever, with agonist activity at the μ-receptor, and inhibition of norepinephrine reuptake. Compared to oxycodone IR, tapentadol showed a reduction in gastrointestinal side effects, specifically nausea, constipation, and vomiting. Tapentadol should be administered first in the 50-mg strength and can be increased to 100 mg every 4 to 6 hours as needed. Of note, it too can also cause respiratory depression because it shows μ-opioid agonist activity and is a controlled substance.

Both tramadol and tapentadol can cause life-threatening serotonin syndrome with the use of other serotonin-norepinephrine uptake inhibitors, selective serotonin reuptake inhibitors, tricyclic antidepressants, or monoamine oxidase inhibitors and, therefore, should be used with caution in patients on these medications.

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Brunton LB, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566-578.

Drug Enforcement Administration, Department of Justice. Schedule of controlled substances: placement of tramadol into schedule IV. Final rule. *Fed Regist*. 2014;79(127):37623-37630.

Grond S, Sablotzki A. Clinical pharmacology of tramadol. *Clin Pharmacokinet*. 2004;43:879-923.

B.12. When would you consider adjuvant analgesics as part of the treatment plan?

In cancer pain management, adjuvant drugs are considered to enhance pain relief. The adjuvant analgesics are a heterogeneous group of medications originally developed for purposes other than pain relief. These drugs may become necessary in the multimodal approach to treat pain, the adverse effects of analgesic medications, or to treat concomitant psychological disturbances such as insomnia, anxiety, depression, and psychosis. The most useful adjuvants used clinically to manage cancer pain are as follows:

- Corticosteroids
- Tricyclic antidepressants (e.g., amitriptyline)
- Anticonvulsants (e.g., gabapentin, pregabalin)
- Amphetamines
- NMDA receptor antagonists (e.g., methadone, ketamine)
- α_2-Agonists (e.g., clonidine)
- Antihistaminics
- Phenothiazines

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:1682-1710.

Haywood A, Good P, Khan S, et al. Corticosteroids for the management of cancer-related pain in adults. *Cochrane Database Syst Rev*. 2015;(4):CD010756.

Oosterling A, Te Boveldt N, Verhagen C, et al. Neuropathic pain components in patients with cancer: prevalence, treatment, and interference with daily activities [published online ahead of print April 10, 2015]. *Pain Pract*. doi:10.1111/papr.12291.

B.13. The patient and his family are worried about addiction. How would you approach this problem?

Unfortunately at times, it becomes difficult to differentiate between drug abuse and the deterioration in physical or psychosocial functioning caused by the disease and its treatment. For example, questionable drug-related behaviors would be difficult to recognize in a patient who develops social withdrawal or cognitive changes following brain irradiation for metastases.

Addiction is defined as a persistent pattern of dysfunctional use of opioids that may involve adverse consequences associated with continued use, loss of control over use of opioids, compulsive use of drug, craving for the drug, and a typical drug-seeking behavior. Patients with chronic pain who are using opioids are not at higher risk of addiction than the general population. The goals of treatment including palliation of pain and improvement in the patient's quality of life must be clearly defined and explained to the patient and his relatives. At no time should patients with cancer pain be undertreated because of the fear of addiction. The patient and his family should be educated about the common misconception that addiction is a common outcome of opioid therapy.

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Berger A, Shuster JL, Von Roenn JH, eds. *Principles and Practice of Palliative Care and Supportive Oncology*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:593-603.

Heit HA. Addiction, physical dependence and tolerance: precise definitions to help clinicians evaluate and treat chronic pain patients. *J Pain Palliat Care Pharmacother*. 2003;17:15-29.

B.14. Describe different routes of opioid administration.

Oral medications should be used as the first-line approach in most patients with cancer pain who are receiving opioid analgesics. Table 49.1 outlines the routes of opioid administration and available opioid preparations.

The rectal or transdermal route should be chosen before considering invasive therapy for cancer pain. The sublingual route is limited by the inability to deliver large doses.

The intramuscular route is not preferred for long-term administration because it requires repeated painful injections and offers no pharmacodynamic advantages. Intravenous administration provides quick onset and is ideal for painful crises in patients with cancer as PCA.

The equianalgesic doses of opioids used orally and parenterally are listed in Table 49.2.

Brunton LB, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566-578.

Mercadante S. Recent progress in the pharmacotherapy of cancer pain. *Expert Rev Anticancer Ther*. 2001;1(3):487-494.

B.15. Describe advantages and complications of patient-controlled analgesia (PCA). What is minimum effective analgesic concentration (MEAC)?

Intravenous PCA is very advantageous for patients with chronic cancer pain because it allows patients to self-administer medication and find their own comfort zone between side effects and pain control within limits set by the physician. The PCA device is a computerized, programmable, lightweight, battery-operated portable pump with the capability of storage and retrieval of data by the microprocessor. The pump is programmed for three modes of drug delivery: (1) continuous per hour rate infusion only, which is preset by the physician and the patient has no control over it; (2) continuous with boluses for breakthrough pain, with boluses controlled by the patient; and (3) boluses with lockout time in minutes set by the physician and the patient can control his or her own requirement. If required, the physician or nurse can deliver extra boluses. Intermittent rescue doses for breakthrough pain, along with continuous infusion, decrease the total requirement of opioids. Only rescue-dose delivery mode is safer because patients will not take medication if there is no pain. However, continuous-delivery mode carries risks of over sedation and respiratory depression. The initial cost

of the drug-delivery device and training of the health care provider could be expensive. PCA can also be provided by subcutaneous, epidural, or intrathecal route.

TABLE 49.1 Routes of Opioid Administration

ROUTE OF ADMINISTRATION	AVAILABLE OPIOID PREPARATION
Oral	Morphine
	Hydromorphone (Dilaudid)

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	Methadone (Dolophine)
	Oxycodone, hydrocodone
	Codeine, meperidine
	Levorphanol
Rectal	Suppositories containing morphine
	Hydromorphone, oxycodone
Transdermal	Fentanyl patch
Sublingual	Fentanyl, methadone, buprenorphine
Intramuscular/subcutaneous	Morphine, hydromorphone, methadone
	Meperidine, levorphanol
Intravenous	Morphine, meperidine, methadone, fentanyl
	Hydromorphone, oxymorphone
Epidural/intrathecal	Morphine, methadone, hydromorphone
	Fentanyl, sufentanil, meperidine

TABLE 49.2 Opioids Used Orally or Parenterally to Treat Cancer Pain

	EQUIANALGESIC DOSE (mg)[a]	
DRUG	**ORAL**	**PARENTERAL**
Morphine	30	10
Hydromorphone	6	2
Oxycodone	20-30	NA
Methadone	10[b]	10[b]
Levorphanol	2-3[b]	2[b]
Codeine	130[c]	75

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NA, not available in the United States.

[a]Suggested doses are guidelines only. Doses are based on chronic opioid use.

[b]Particular care with titration is recommended because doses may need to be reduced significantly when steady-state levels are reached after 2 to 3 days.

[c]Codeine doses greater than 65 mg may be associated with significant constipation.

MEAC is the minimum effective analgesic concentration of the opioid that is the lower level of the therapeutic window (Fig. 49.2).

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA:

Lippincott Williams & Wilkins; 2010:537-679.

Mercadante S. Recent progress in the pharmacotherapy of cancer pain. *Expect Rev Anticancer Ther*. 2001;1:487-494.

B.16. What is meperidine? How is it different from other opioids?

Meperidine is a synthetic opioid that pharmacologically resembles morphine. Meperidine is not an ideal drug for chronic pain because of its short duration of action and its high

potential for abuse. The by-product normeperidine is exclusively excreted via the kidney, with an elimination half-life of 36 to 40 hours. In patients with compromised renal function, by-product accumulation has been associated with central nervous system toxicity, including myoclonus, tremulousness, hallucinations, and seizures. Meperidine possesses anticholinergic activity similar to atropine, causing mydriasis, orthostatic hypotension, and tachycardia. Compared with other opioids, meperidine very rarely causes pruritus when given neuraxially. It is extremely effective in the treatment of postoperative shivering. Meperidine also demonstrates local anesthetic actions. It is contraindicated in patients who are receiving monoamine oxidase inhibitors because of the risk of a potentially fatal syndrome characterized by hyperthermia, rigidity, and seizures.

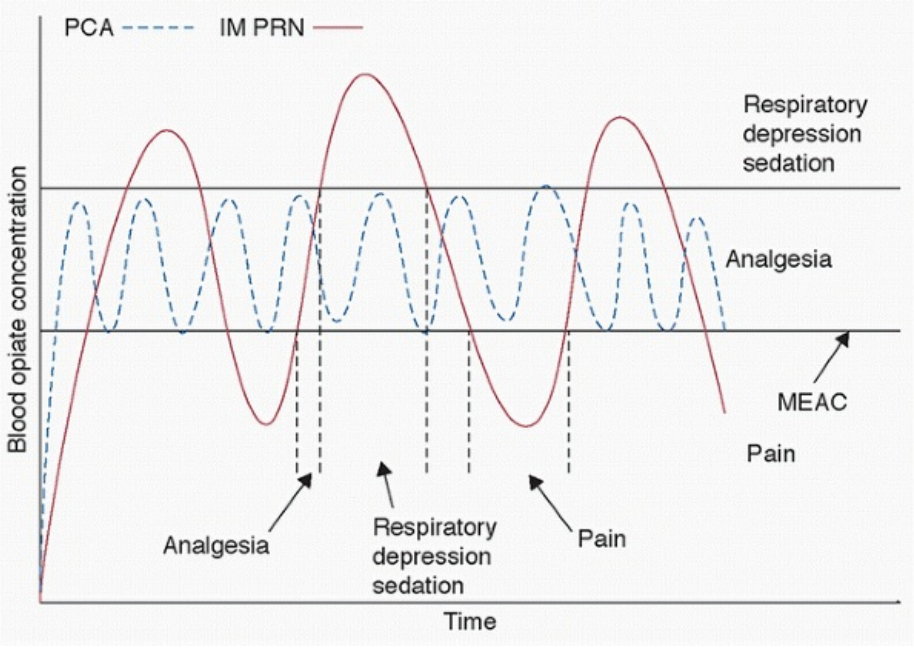


FIGURE 49.2 The MEAC is the minimum effective analgesic concentration of the opioid that is the lower level of the therapeutic window. IM, intramuscular; PCA, patient-controlled analgesia; PRN, as needed. (From Ashburn M, Smith K. The management of postoperative pain. *Surg Rounds*. 1991;14:129-134, with permission.)

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Brunton LB, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566-578.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders/Elsevier; 2015:864-914.

B.17. What is rotation of opioids? When would you consider rotation of opioids?

The sequential trial of changing one opioid to another when either treatment-limiting toxicity or poor responsiveness develops has become known as *opioid rotation*. The variable response from opioid to opioid in an individual has led to this approach; changing to an alternative opioid may yield a far better balance between side effects and analgesia.

For those patients in whom pain control is inadequate and who have intolerable side effects, different strategies are implemented to improve analgesia. Opioid rotation is a simple strategy that almost all physicians can implement. Depending on equianalgesic potency ratio guidelines, switch is made to other opioids such as methadone or transdermal fentanyl patch. This should be done under close supervision and preferably in an inpatient environment.

Afsharimani B, Kindl K, Good P, et al. Pharmacological options for the management of refractory cancer painwhat is the evidence? *Support Care Cancer*. 2015;23(5):1473-1481.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:537-679.

C. Interventional Pain Management

C.1. Describe the role of peripheral nerve blocks in cancer pain management.

The following nerve blocks can be considered depending on the location and distribution of the thoracic or abdominal pain and the involvement of viscera:

- Intercostal nerve blocks
- Interpleural blockade
- Splanchnic nerve blocks
- Celiac plexus block
- Hypogastric plexus block
- Thoracic and lumbar paravertebral somatic nerve blocks
- Rectus abdominis block
- Iliac crest block
- Ilioinguinal and iliohypogastric nerve block
- Cave of Retzius (space between urinary bladder and symphysis pubis) block

Various combinations of peripheral nerve blocks can be performed to aid in the global comfort of the patient by providing better pain control and reducing the total dose of medications and thereby the side effects. The most useful blocks for the upper abdomen and thorax are intercostal nerve blocks and celiac plexus blocks. The splanchnic nerve block and superior hypogastric blocks are the other two that can be considered depending on the location and involvement of the viscera. Thoracic and lumbar paravertebral blocks are performed to obtain spinal nerve segmental analgesia. The intercostal and thoracic paravertebral nerve blocks carry the risk of pneumothorax due to proximity of the pleura and lung. The peripheral

nerve blocks are performed at anatomic sites away from the central neuraxis. More distal blocks have greater chances of incomplete blocks due to spatial distribution, overlap of nerves, and difficulty in blocking multiple branches of arborizing

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nerve.

de Leon-Casasola OA. *Cancer Pain: Pharmacological, Interventional and Palliative Care Approaches*. Philadelphia, PA: Saunders; 2006:531-533.

Moeschler SM, Rosenberg C, Trainor D, et al. Interventional modalities to treat cancer-related pain. *Hosp Pract (1995)*. 2014;42(5):14-23.

Waldman SD, ed. *Interventional Pain Management*. 2nd ed. Philadelphia, PA: WB Saunders; 2001:541-553.

C.2. Describe the role of celiac plexus block in cancer pain management.

Diagnostic celiac plexus block with a local anesthetic is performed to precisely differentiate sympathetically maintained pain and localize retroperitoneal or upper abdominal pain. A positive result of the diagnostic block is an indication for more definitive neurolysis in chronic cancer and nonmalignant pain. Success rates of celiac plexus neurolysis are lower in patients suffering from chronic nonmalignant abdominal pain than in those suffering from abdominal pain of neoplastic origin. Neurolysis of celiac plexus with alcohol or phenol is performed under fluoroscopic guidance or computed tomography-guided technique and strict sterile condition by using a single-needle periaortic technique, single-needle transaortic technique, single-needle anterior technique, or endoscopic ultrasound (EUS)-guided technique. Individual skills of the treating physician, available facilities, patient's general condition, and extent of the spread of tumor should be considered in determining the type of technique to use.

Many pain physicians for celiac plexus neurolysis commonly use 40 to 50 mL of 50% to 70% alcohol or 6% to 10% phenol. Smaller volumes are recommended for absolute alcohol and higher concentration of phenol. Neurolysis with phenol is less painful because of its local anesthetic action, whereas alcohol neurolysis is very painful and should be blocked with pretreatment with local anesthetics.

Arcidiacono et al. did a Cochrane review from 1990 to 2010 to determine the efficacy and safety of celiac plexus neurolysis in reducing pancreatic cancer pain. It was found that there is minimal statistical evidence for the superiority of pain relief over analgesic therapy; however, because celiac plexus block causes fewer adverse effects than opioids, it is important to recognize for patients.

Arcidiacono PG, Calori G, Carrara S, et al. Celiac plexus block for pancreatic cancer pain in adults. *Cochrane Database Syst Rev*. 2011;(3):CD007519.

de Leon-Casasola OA. *Cancer Pain: Pharmacological, Interventional and Palliative Care Approaches*. Philadelphia, PA: Saunders; 2006:401-416.

Waldman SD, ed. *Interventional Pain Management*. 2nd ed. Philadelphia, PA: WB Saunders; 2001:541-553.

C.3. What are the complications of celiac plexus block?

Serious complications should rarely occur in the hands of a skilled clinician. Hypotension and increased gastrointestinal motility are the most common complications of this block. Neurologic complications include subarachnoid or epidural injection and lumbar nerve root injury, causing long-lasting paresthesia. A potentially severe complication can occur as a result of accidental injection into the nutrient artery of the spinal cord (artery of Adamkiewicz), causing paraplegia. Injury to the kidney may cause temporary hematuria that may not need any treatment. Other complications have been reported due to proximity of other vital structures include pneumothorax, chylothorax, intradisc injection, retroperitoneal hematoma, and failure to ejaculate.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:605-618.

C.4. Would you consider neuraxial opioid infusion in this patient?

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Discuss complications of this procedure.

In properly selected patients, epidural, intrathecal (subarachnoid), or intraventricular infusions of opioids have the advantage of producing profound analgesia without motor, sensory,

or autonomic blockade. These routes are considered to deliver preservative-free medications when pain is not well controlled by noninvasive (oral, subcutaneous, or intravenous) routes and escalation of doses is limited by intolerable side effects. The potency ratio of oral to epidural morphine is 1:30, and that from oral to intrathecal morphine is 1:300. The decrease in the size of dose from oral to intrathecal greatly reduces the side effects and improves pain control and quality of life. The PCA technique can also be employed for epidural routes. Programmable intrathecal pumps can deliver medications at the prescribed dose. Fixed or flexible doses of morphine can deliver via the intrathecal pumps. Recently approved patientcontrolled device allows patient-activated doses via the intrathecal pump (Personal Therapy Manager or PTM, Medtronic Neurological, Minneapolis, MN). Morphine is the most commonly used drug. Other opiates, local anesthetics, ziconotide, *α*-agonists, etc., can be used as recommended by the polyanalgesic consensus panel.

These routes require a skilled experienced clinician, meticulous technique, and family and facility support in which close monitoring and follow-up can be done. These procedures are reversible but involve expenses for specialized care and operating room costs. Intraspinal opioids may produce the same side effects of nausea, mental clouding, and sedation as in oral and parenteral dosing. Infection (e.g., meningitis and epidural abscess) and hematoma are potentially devastating complications that can cause permanent neurologic deficit if not dealt with in a timely basis. Pruritus and urinary retention are more common than with oral or parenteral administration.

Carrillo-Ruiz JD, Andrade P, Godinez-Cubillos N, et al. Polyanalgesic Consensus Conference 2012: Recommendations for the management of pain by intrathecal (intraspinal) drug delivery: report of an interdisciplinary expert panel by Timothy R. Deer, MD et al., that was published in your prestigious journal under the following reference: Neuromodulation 2012;15:436-466 [letter]. *Neuromodulation*. 2013;16(4):387.

Stearns L, Boortz-Marx R, Du Pen S, et al. Intrathecal drug delivery for the management of cancer pain. *J Support Oncol*. 2005;3:399-408.

C.5. Which medications can be used intrathecally? What is ziconotide?

Morphine is the most commonly used drug; other opiates such as hydromorphone, fentanyl, and sufentanil can be used intrathecally. In addition, local anesthetics, *α*-agonist such as clonidine, and baclofen can be used as recommended by the polyanalgesic consensus panel.

Recently, ziconotide (Prialt), a synthetic equivalent of a naturally occurring peptide found in marine snails, has been shown to be effective in pain relief when used intrathecally. It is a selective voltage-gated calcium channel blocker that inhibits release of proglutamate, calcitonin, and substance P in the brain and spinal cord. Side effects include dizziness, nausea, confusion, and psychosis, and therefore, patients trialed on ziconotide should be mentored for cognitive impairment, hallucinations, or changes in mood and consciousness.

Only morphine, baclofen, and ziconotide have been approved by the U.S. Food and Drug Administration (FDA).

Carrillo-Ruiz JD, Andrade P, Godinez-Cubillos N, et al. Polyanalgesic Consensus Conference 2012: Recommendations for the management of pain by intrathecal (intraspinal) drug delivery: report of an interdisciplinary expert panel by Timothy R. Deer, MD et al., that was published in your prestigious journal under the following reference: Neuromodulation 2012;15:436-466 [letter]. *Neuromodulation*. 2013;16(4):387.

Stearns L, Boortz-Marx R, Du Pen S, et al. Intrathecal drug delivery for the management of cancer pain. *J Support Oncol*. 2005;3:399-408.

Williams J, Day M, Heavner JE. Ziconotide: an update and review. *Exp Opin Pharmacother*. 2008;9:1575-1583.

C.6. What is a Personal Therapy Manager (PTM) and what role does it play in neuraxial pain relief?

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Increasingly being used is a patient-controlled device that allows patient-activated doses via the intrathecal pump (Personal Therapy Manager [PTM], Medtronic Neurological, Minneapolis, MN). The PTM enables the patient to activate delivery of physicianprogrammed supplemental doses of intrathecal medication. This is especially useful for patients experiencing intermittent pain of varying intensity that cannot be adequately

managed with a simple continuous infusion, have an unpredictable need for varying doses of drug, or experience inadequate pain relief or intolerable side effects from supplemental systemic breakthrough pain medications. Nevertheless, risk of sedation, respiratory depression, and other adverse effects are just as possible as when taking oral opiate supplementation, and therefore, caution and careful programming should be ensured. Also see section C.3.

de Leon-Casasola OA. *Cancer Pain: Pharmacological, Interventional and Palliative Care Approaches*. Philadelphia, PA: Saunders; 2006:417-429.

Ilias W, le Polain B, Buchser E, et al. Patient-controlled analgesia in chronic pain patients: experience with a new device designed to be used with implanted programmable pumps. *Pain Pract*. 2008;8(3):164-170.

Rauck RL, Cheery D, Boyer MF, et al. Long-term intrathecal opioid therapy with a patient-activated, implanted delivery systems for the treatment of refractory cancer pain. *J Pain*. 2003;4:441-447.

Stearns L, Boortz-Marx R, Du Pen S, et al. Intrathecal drug delivery for the management of cancer pain. *J Support Oncol*. 2005;3:399-408.

C.7. Would you consider neuraxial neurolysis in this patient to manage his pain? Discuss advantages and disadvantages of these blocks.

Due to physical separation of motor and sensory nerve roots in the spinal canal and intrathecal space, chemical neurolytic procedures allow sensory blockade without loss of motor functions. Inadequate pain control with intolerable side effects makes this patient an ideal candidate for neuraxial neurolysis; however, complications of the procedure should be weighed against benefits. Epidural or intrathecal (subarachnoid) neurolytic blocks are considered for severe intractable pain from advanced cancer as an adjuvant to relieve pain and suffering and improve quality of life. These blocks are primarily effective in relieving pain of somatic origin and less effective for visceral and neuropathic pain.

In selected patients in whom pain relief is not achieved by less invasive measures, these blocks can provide rapid analgesia and allow dosage (and side effects) reduction of systemic drugs. However, risks of postural hypotension, bowel and bladder incontinence, and motor and sensory deficit in the lower extremities cannot be overemphasized. These blocks are irreversible and require a skilled clinician to perform the procedure.

de Leon-Casasola OA. *Cancer Pain: Pharmacological, Interventional and Palliative Care Approaches*. Philadelphia, PA: Saunders; 2006:501-507.

McHugh ME, Miller-Saultz D, Wuhrman E, et al. Interventional pain management in the palliative care patient. *Int J Palliat Nurs*. 2012;18(9):426-428, 430-433.

C.8. Which neuroablative procedures can be considered in the terminal stage of pancreatic cancer?

Based on the location and type of pain (somatic, visceral, deafferentation), the general condition of the patient, the stage of tumor and metastasis, the life expectancy, and the expertise available, the following neurosurgical procedures could be considered:

- Peripheral neurectomy
- Dorsal rhizotomy
- Anterolateral cordotomy (spinal tractotomy)
- Commissural myelotomy

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- Hypophysectomy

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:537-679.

C.9. Describe the role of radiation therapy in cancer pain.

Radiation therapy can be curative or palliative to relieve pain from metastasis and symptoms from local extension of the disease. Radiation therapy is complementary to chemotherapy, surgery, and analgesic drug therapies to enhance the effectiveness of pain control. Radiating therapy can palliate when disease cannot be controlled. Along with therapeutic effectiveness of radiation treatment, the absence of complete specificity for disease may exacerbate or

even cause new pain. It is most commonly used for bone metastasis. The radiation dosage should be administered in the fewest fractions possible to promote pain control during and after treatment.

Benzon H, Rathmell J, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis, MO: Mosby; 2008:418-426.

Johnstone C, Lutz ST. The role of hypofractionated radiation in the management of non-osseous metastatic or uncontrolled local cancer. *Ann Palliat Med*. 2014;3(4):291-303.

McQuay HJ, Collins SL, Carroll D, et al. Radiotherapy for the palliation of painful bone metastases. *Cochrane Database Syst Rev*. 2000;(2):CD001793.

D. Nonpharmacologic Management

D.1. What are the various nonpharmacologic techniques of cancer pain management?

Eisenberg et al. demonstrated that cancer and other chronic pain syndromes such as AIDS and arthritis may get benefit from alternative modalities. Practicing physical activity and sport during cancer modifies fatigue and quality of life and reduces symptoms of depression.

The common therapies offered are as follows:

- Physical therapy and physical modalities
- Physical activity and sport
- Relaxation and massage
- Chiropractic manipulation
- Spiritual healing
- Biofeedback and hypnosis
- Magnetic and low-power laser therapy
- Transcutaneous electrical nerve stimulation
- Homeopathy
- Acupuncture
- Prayer

Benzon H, Rathmell J, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis, MO: Mosby; 2008:418-426.

Bouillet T, Bigard X, Brami C, et al. Role of physical activity and sport in oncology: scientific commission of the

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National Federation Sport and Cancer CAMI. *Crit Rev Oncol Hematol*. 2015;94:74-86.

Bradley LA, McKendree-Smith NL, Cianfrini LR. Cognitive-behavioral therapy interventions for pain associated with chronic illness: evidence for their effectiveness. *Semin Pain Med*. 2003;1:44-54.

Eisenberg DM, Kessler RC, Foster C, et al. Unconventional medicine in the United States. Prevalence, costs, and patterns of use. *N Engl J Med*. 1993;328:246-252.

Schneider J, Gilford S. The chiropractor's role in pain management for oncology patients. *J Manipulative Physiol Ther*. 2001;24(1):52-57.

D.2. What physical modalities have been successfully tried in cancer pain management?

Physical modalities may be useful in conjunction with conventional systemic and interventional treatments used to control cancer-related pain, especially in patients with movementassociated pain. Physical modalities may help decrease stiffness, increase blood flow to the part, help relax the patient, and reduce the dose of analgesics. They include cutaneous stimulation, superficial heat and cold therapy, massage, vibration, and pressure. Cold therapy (cryotherapy) causes vasoconstriction, reduces inflammation, and decreases muscle spasm. Superficial application of heat (thermotherapy) acts through conduction or convection to increase blood flow to the skin and superficial organs. Heat also decreases joint stiffness and increases muscle flexibility. Physical therapy and exercise help to strengthen weak muscles, mobilize stiff joints, and restore coordination. Exercise may reduce pain by 25%. Weightbearing exercises are avoided if an impending fracture is suspected.

Benzon H, Rathmell J, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis, MO: Mosby; 2008:418-426.

Bouillet T, Bigard X, Brami C, et al. Role of physical activity and sport in oncology: scientific commission of the National Federation Sport and Cancer CAMI. *Crit Rev Oncol Hematol*. 2015;94:74-86.

Cheville AL, Basford JR. Role of rehabilitation medicine and physical agents in the treatment of cancerassociated pain. *J Clin Oncol*. 2014;32(16):1691-1702.

D.3. Describe the role of neuromodulation in cancer pain management.

Neuromodulation techniques such as spinal cord stimulation and deep brain stimulation have not been popular in cancer pain management. Neuromodulation techniques have variable outcome results with success rates between 18% and 80% depending on the study cited. Much of the literature is about chronic nonmalignant pain syndromes. The consensus among most pain physicians is that neuropathic pain syndromes are more effectively treated as spinal cord syndromes than as nociceptive pain syndromes. Acupuncture is a neuromodulatory technique that treats pain with insertion of needles in skin and underlying muscles. Based on various Chinese scientific principles, acupuncture is becoming very popular in Western medical systems. Many intrinsic factors contribute to the success of acupuncture, and in selected patients, it does control pain. Transcutaneous electrical nerve stimulation and acupuncture are believed to activate endogenous pain-relieving pathways. Low-voltage stimulation to large myelinated peripheral nerves via cutaneous electrodes may significantly reduce pain. Spinal cord stimulation appears to be a promising therapy for intractable cancer pain can offer relief of neuropathic pain, which is present in 15% to 40% of cancer pain patients. Recently, high-frequency stimulation and magnetic resonance imaging (MRI)-compatible spinal cord stimulation systems may increase the role of this therapy in cancer patient. Studies have shown significant pain relief in postthoracotomy pain, back pain, leg pain, groin pain, and testicular pain related to carcinoma.

Tsubota S, Higaki N, Nagaro T. A case of neuropathic cancer pain in the lower extremities successfully treated with spinal cord stimulation [in Japanese]. *Masui*. 2009;58:1460-1461.

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Yakovlev AE, Resch BE. Spinal cord stimulation for cancer-related low back pain. *Am J Hosp Palliat Care*. 2012;29:93-97.

Yakovlev AE, Resch BE, Karasev SA. Treatment of cancer-related chest wall pain using spinal cord stimulation. *Am J Hosp Palliat Care*. 2010;27:552-556.

D.4. What psychological techniques have been promoted for comfort care and pain relief?

Psychological distress impacts pain. Depression, anxiety, anger, and mood disturbances have been correlated with higher levels of perceived cancer pain. Patients with higher levels of social support have reported lower intensity of cancer pain. Psychological interventions are an important part of a multimodal approach to pain management in patients with cancer. Some techniques that are used are relaxation, biofeedback, hypnosis, imagery, and cognitive behavioral therapy. They help patients gain a sense of control over pain. Cognitive and behavioral techniques are designed to influence the interpretation of events and bodily sensations. Cognitive techniques help patients think differently about their pain and its management. Behavioral techniques help patients develop skills to cope with pain and help modify their reactions to pain. Patients who undergo psychotherapy report less pain. Relaxation therapy is a well-established modality in managing cancer pain. Several variations of relaxation strategies and techniques have been widely practiced in patients suffering from advanced cancer and have proven effective. Relaxation strategies such as deep breathing, muscle relaxation, and imagery are recommended for the promotion of comfort and relief of pain in hospitalized patients.

Relaxation and imagery are used to achieve a state of mental and physical relaxation, thereby relieving anxiety and muscle tension.

Bruera ED, Portenoy RK, eds. *Cancer Pain: Assessment and Management*. 2nd ed. New York: Cambridge University Press; 2010:89-105.

Byker GL, Leskuski D. Nonpharmacological management of pain. In: Berger A, Shuster J, Von Roenn JH, eds. *Principles and Practice of Palliative Care and Supportive Oncology*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:42-54.

NIH State-of-the-Science Statement on Symptom Management in Cancer: Pain, Depression, and Fatigue. Bethesda, MD: National Institute of Health; 2002.

D.5. What are distraction and reframing techniques? What is the role of hypnosis in cancer pain management?

Distraction and reframing techniques encourage focused attention on stimuli other than pain. This involves singing, talking, praying, and watching television. Reframing helps monitor and evaluate negative thoughts and images while encouraging positive thoughts and behavior.

Hypnosis by a skilled person decreases pain and anxiety in patients who have difficulty managing their pain. It also increases coping skills. This technique allows heightened awareness and focused concentration to manipulate perception of pain and has been effective in the management of cancer-related pain syndromes.

Benzon H, Rathmell J, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis, MO: Mosby; 2008:418-426.

Devine EC. Meta-analysis of the effect of psychoeducational interventions on pain in adults with cancer. *Oncol Nurs Forum*. 2003;30:75-89.

Ong AD, Zautra AJ, Reid MC. Chronic pain and the adaptive significance of positive emotions. *Am Psychol*. 2015;70(3):283-284.

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Chapter 50
Low Back Pain and Sciatica

David Y. Wang

Jeffrey Y. F. Ngeow

A 57-year-old former factory worker was injured on the job 8 years ago. He experienced severe low back and right leg pain after lifting a heavy piece of equipment and was found to have a herniated L4-L5 intervertebral disc with compression of the right L5 nerve root. He underwent a laminectomy and decompression; nevertheless, he has continued to complain of back pain.

A. Medical Disease and Differential Diagnosis

1. How great an issue is low back pain in the general population?
2. What is the prevalence of low back pain?
3. What is the societal cost of low back pain?
4. What causes low back pain?
5. What are the risk factors for low back pain?
6. What are the potential sources of pain in the spine?
7. What is the anatomy of the intervertebral discs? What is the mechanism of pain from herniated discs?
8. What is the anatomy of the spinal facets? How do the facet joints cause pain?
9. What are the important findings in the history and physical examination?
10. Which are the appropriate diagnostic studies for low back pain?
11. What is the differential diagnosis of low back pain?
12. What are the causes of multiple spine surgeries and persistent back pain?

B. Management of Low Back Pain and Sciatica

1. What are the noninterventional treatments available?
2. What are the traditional interventional treatments available and how should they be used?
3. What are recent considerations of improving safety for lumbar epidural steroid injection?
4. What are some of other approaches in minimally invasive interventions?
5. What are the concerns of magnetic resonance imaging (MRI) safety in spinal cord stimulator (SCS)?
6. When should surgery be considered?
7. What surgical options are available for treatment of disc disease?

A. Medical Disease and Differential Diagnosis

A.1. How great an issue is low back pain in the general population?

Disorders of the lumbosacral spine cause pain, disability, suffering, public health issues, and socioeconomic issues with far greater impact than disorders of any other part of the body.

Most adults will experience several episodes of low back pain during their lifetime. It is estimated that 80% of workers will lose work time because of this complaint. On the basis of primary diagnosis only, a National Ambulatory Medical Care Survey in 1989 to 1990 ranked low back pain as the fifth most frequent reason for adults to visit an office-based medical practice. In surveys employing a wider definition of low back pain, it was found to be the second most frequent symptom

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prompting physician office visits in the United States. In 2010, low back pain was ranked third next only to ischemic heart disease and chronic obstructive pulmonary disease in poor health and mortality burden in United States.

Hart LG, Deyo RA, Cherkin DC. Physician office visits for low back pain. Frequency, clinical evaluation, and treatment patterns from a U.S. national survey. *Spine*. 1995;20:11-19.

Manchikanti L. Epidemiology of low back pain. *Pain Physician*. 2000;3:167-192.

National Institute of Neurological Disorders and Stroke. *LowBack Pain Fact Sheet*. Bethesda, MD: National Institute of Neurological Disorders and Stroke; 2014:1-50. NIH publication 15-5161.

A.2. What is the prevalence of low back pain?

A global review of the prevalence of low back pain in the adult general population has shown its point prevalence to be approximately 12%, with a 1-month prevalence of 23%, a 1-year prevalence of 38%, and a lifetime prevalence of approximately 40%. Furthermore, as the population ages over the coming decades, the number of individuals with low back pain is likely to increase substantially. Low back pain usually begins in early life, with the highest frequency of symptoms occurring between ages 35 and 55 years. Of all adults in industrialized societies, 60% to 80% are affected at some point in their lives. Work absence and symptom duration increase with aging. An acute episode of low back pain usually resolves within 6 weeks. More persistent pain lasting beyond 3 to 6 months occurred in only 5% to 10% of patients with back pain. The U.S. Agency for Health Care Policy and Research reported that 90% of patients with acute low back pain recover their usual activity tolerance within 4 weeks of injury. The remaining 10% of patients who do not recover with time or routine therapy go on to develop chronic symptoms and secondary problems. At 1 year, the incidence of acute back pain conversion to chronic back pain is 20%. Recurrences of low back pain are also common, with the percentage of subsequent low back pain episodes ranging from 20% to 44% within 1 year for working populations to lifetime recurrences of up to 85%.

Freburger JK, Holmes GM, Agans RP, et al. The rising prevalence of chronic low back pain. *Arch Intern Med*. 2009;169:251-258.

Hoy D, Bain C, Williams G, et al. A systematic review of the global prevalence of low back pain. *Arthritis Rheum*. 2012;64(6):2028-2037.

Jackson T, Thomas S, Stabile V, et al. Prevalence of chronic pain in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet*. 2015;(385)(suppl 2):S10.

National Institute of Neurological Disorders and Stroke. *LowBack Pain Fact Sheet*. Bethesda, MD: National Institute of Neurological Disorders and Stroke; 2014:1-50. NIH publication 15-5161. Rubin DI. Epidemiology and risk factors for spine pain. *Neurol Clin*. 2007;25:353-371.

A.3. What is the societal cost of low back pain?

The costs of low back pain include functional impairment, activity limitations, reduced quality of life, disability, underemployment, reduced work productivity, and direct medical cost. It appears that the societal perception of disability has changed dramatically over period of time. This has resulted in an increased rate and cost of disability and overutilization of medical care, including surgical treatments. Back pain in workers 40 to 65 years of age costs employers an estimated $7.4 billion per year. Duke University Medical Center researchers found that patients suffering from back pain consume more than $90 billion annually in health care expenses, with approximately $26 billion of that amount directly attributable to treating the back pain. Their results demonstrate the enormous economic impact of back pain. The total $90 billion spent in 1998 represented 1% of the U.S. gross domestic product (GDP), and the $26 billion in direct back pain costs accounted for 2.5% of all health care expenditures for that year. These data came from the Medical Expenditure Panel Survey (MEPS) in 1998. The MEPS is a national survey conducted by the Agency of Healthcare

Research and Quality (AHRQ) and the National Center for Health Statistics. The team found that 25.9 million adults

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reported back pain in 1998, with 172.7 million reporting no back pain. The figures do not include information about back pain in nursing home patients, who in the 1977 research accounted for about 20% of medical costs. As a result, the costs of care for back pain almost certainly top $100 billion. In addition, the Duke study did not include nonmedical cost of back pain, such as lost productivity. A study in the *Journal of the American Medical Association* found chronic pain conditions, including arthritis, back problems, and other ailments, drain $61.2 billion a year from the U.S. economy. Back pain accounted for about a quarter of the lost or unproductive work, second only to headaches as the most frequent pain complaint of workers.

Dagenais S, Caro J, Haldeman S. A systemic review of low back pain cost of illness studies in the United States and internationally. *Spine J*. 2008;8:8-20.

Luo X, Pietrobon R, Sun SX, et al. Estimates and patterns of direct health care expenditures among individuals with back pain in the United States. *Spine*. 2004;29(1):79-86.

Ricci JA, Stewart WF, Chee E, et al. Back pain exacerbations and lost productive time cost in United States workers. *Spine*. 2006;31:3052-3060.

Stewart WF, Ricci JA, Chee E, et al. Lost productive time and cost due to common pain conditions in the US workforce. *JAMA*. 2003;290(18):2443-2454.

A.4. What causes low back pain?

Majority of low back pain is mechanical in nature caused by injury, compression, tears, and bone and disc degeneration. Common causes include the following:

- Sprains and strains
- Intervertebral disc degeneration
- Herniated or ruptured disc
- Radiculopathy
- Sciatica
- Spondylolisthesis
- Traumatic injury
- Spinal stenosis
- Skeletal irregularity (scoliosis, kyphosis)
- Other underlying conditions
  - Infections
  - Tumors
  - Abdominal aortic aneurysms
  - Kidney stones
  - Endometriosis
  - Fibromyalgia

National Institute of Neurological Disorders and Stroke. *LowBack Pain Fact Sheet*. Bethesda, MD: National Institute of Neurological Disorders and Stroke; 2014:1-50. NIH publication 15-5161.

A.5. What are the risk factors for low back pain?

Traditional beliefs suggested that heavy physical jobs required high energy demand and significant stress and strain on

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the spine, whereas light jobs required low energy demand. Many lowenergy jobs, nevertheless, are static, which is an inherent risk factor for low back pain. Low back pain, degenerative disc disease, and disc herniation are associated with the following:

- Repetitive heavy lifting
- Static work posture (sitting or standing)
- Frequent twisting and bending
- Vibration (operation of motor vehicle or industrial device)
- The common vibration of construction vehicles and industrial devices ranges in frequency from 3.5 to 8.9 Hz.
- Low-frequency vibration, especially around 5 Hz, in conjunction with a prolonged seated position is associated with spine problems.

- The potential for damage to the disc through mechanical resonance is analogous to the high notes of an operatic soprano shattering wine glasses.
- Fatigue of the abdominal and paraspinal muscles has been demonstrated when subjected to 30 minutes of vibration. In the absence of this support, the spine is further susceptible to injury.
- A meta-analysis of 17 studies revealed that whole-body vibration is associated with an increased risk of low back pain, sciatica, and lumbar intervertebral disc disorders.
- Cigarette smoking. Smoking is linked to low back pain, sciatica, and lumbar disc herniation.
- In an animal model, cigarette smoking significantly affects the vasculature outside the intervertebral disc, where the most pronounced effect is the reduction of solute-exchange capacity, cellular uptake, and metabolism within the disc.
- Cross-country skiing. In a study of skiing and spinal trauma, the diagonal body position required for cross-country skiing was the most common back pain-inducing stance, whereas no skier experienced back pain when only downhill skiing.

The “oxidative stress hypothesis of aging” theory proposed that enhancement of oxygen consumption resulting from increased physical activity may accelerate disc degeneration. On the other hand, strenuous exercises may contribute to positive nutritional effect by facilitating the transport of small solutes into and out of the disc. Generally, it is believed that persons who are physically fit or who maintain a balanced exercise program appear to have a lower risk for chronic low back pain and a more rapid recovery after an episode of acute back pain.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:1106-1108.

Frymoyer JW, Pope MH, Clements JH, et al. Risk factors in low back pain. An epidemiological survey. *J Bone Joint Surg Am*. 1983;65:213-218.

Wilder DG, Woodworth BB, Frymoyer JW, et al. Vibration and the human spine. *Spine*. 1982;7:243-254.

A.6. What are the potential sources of pain in the spine?

In order to more easily identify the various sources of pain, the spine may be divided into three compartments: anterior, middle, and posterior.

The anterior compartment consists of the vertebral body and intervertebral disc. The anterior unit is bound together by cephalocaudal ligaments: anterior longitudinal ligament and posterior longitudinal ligament (PLL). The anterior longitudinal ligament is anatomically much broader and stronger than the PLL. The PLL is intact throughout the length of the vertebral column until it reaches the lumbar vertebrae. From L1, it becomes progressively narrower until at L5-S1 it is only half of its original width. This anatomic feature contributes to an inherent structural weakness in the lumbar spine. Hence, the lower lumbar spine is the region subjected to the greatest static stress and most spinal movement resulting in the greatest kinetic strain.

The middle (neuraxial) compartment contains all of the structures within the bony and ligamentous boundaries of the spinal canal. This includes the PLL, epidural space, meninges, spinal cord, dorsal and ventral nerve roots, root sleeves, dorsal

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root ganglia, and ligamentum flavum.

The posterior compartment contains the facet joints, laminae, vertebral arches, and structures posterior to the plane of the transverse processes and innervated by the dorsal rami of the spinal nerves. The ligaments are extremely important in stabilizing the vertebral column. The ligamentum flavum (yellow ligament), which connects the laminae of adjacent vertebrae, is the thickest and strongest ligament in the lumbar region. It can contribute to spinal stenosis by folding inward during upright posture, extension of the back, and hypertrophy.

The sinovertebral nerve originates lateral to the neural foramina and enters the spinal canal anterior to the dorsal root ganglion. It is a branch of the somatic ventral nerve root and the sympathetic grey ramus communicans. This specific nerve, also known as the nerve of Luschka, innervates the outer annulus of the disc, PLL, epidural membranes, and dura at the segmental level of origin and adjacent levels. It is important to note that central low back pain, with or without referred pain to the buttocks, may derive from irritation of the outer part of the annulus fibrosis or the PLL.

In summary, the potential sources of low back and radicular pain include the bony structure of vertebrae, muscles attached to the spine and hips, fasciae, ligaments, discs, facet joints, meninges, vessels, nerve roots, dorsal root ganglia, and nerves in the surrounding areas.

The natural wear and tear on the discs and facet joints results in microtrauma and degeneration. This can induce the release of neurohumoral mediators such as phospholipase A_2, serotonin, H^+, substance P, prostaglandin E_2, and so on, to produce inflammation of the nerve roots or meninges and sensitize local nociceptors. Furthermore, it has been theorized that material from the nucleus pulposus, sheltered from the immune system by the presence of the annulus fibrosis, might act as a foreign protein and trigger an autoimmune reaction. The recent demonstration of an activated immunocompetent cellular response at the epidural interface of the herniation of the nucleus pulposus supports the concept of the immunogenic capacity of the nucleus pulposus. Tissue injury or inflammation can cause a barrage of nociceptive input into the spinal cord. This may lead to a phenomenon called *central sensitization* or *windup* of neurons in the dorsal horn of the spinal cord. The release of excitatory amino acids and neuropeptides in the dorsal horn is thought to be the mechanism underlying the phenomenon of central sensitization. At the cellular level, there is an increase in spontaneous discharge and an expansion of neural receptive fields of wide-dynamic-range neurons located in Rexed lamina V of the spinal cord. Clinically, this is characterized by sensation of pain when exposed to nonnoxious stimuli (allodynia), significantly increased response to painful input (hyperalgesia), and increased response to repetitive stimulation (hyperpathia).

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A.7. What is the anatomy of the intervertebral discs? What is the mechanism of pain from herniated discs?

The intervertebral disc is a ring-like structure composed of a centrally located well-hydrated pliable proteoglycan matrix, the nucleus pulposus, which comprises two-thirds of the surface area of the disc. Surrounding the nucleus is a fibrocartilaginous ring composed predominantly of type I collagen, the annulus fibrosus, which makes up the remaining one-third of the surface area of the disc. The annulus fibrosus is stronger anteriorly but often defective posteriorly. As a self-contained fluid system, the disc absorbs shock, permits transient compression, and allows movement. It provides a

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cushion between the vertebral bodies and allows for greater flexibility.

As the disc ages, the number of viable cells in the nucleus pulposus decreases, and the proportion of cells that exhibit necrosis changes from 2% in infancy to 50% in young adults and 80% in the elderly. The water content in the young disc is 80% to 90% in the nucleus pulposus. With aging, the discs tend to dehydrate, losing up to 70% of their water content. As the nucleus pulposus further dehydrates, it becomes more fibrous and less compliant. A disc will usually herniate under strain and pressure. When overstressed, it will protrude along in the path of least resistance, usually posterolaterally. This can cause direct mechanical pressure on the nerve roots resulting in radiculopathy.

In the healthy back, only the outer third of the annulus fibrosus is innervated. In the degenerative or disrupted disc, small unmyelinated nerve fibers grow into the inner third of the annulus fibrosus and even into the nucleus pulposus. Internal disc disruption is a condition characterized by a degenerated nucleus pulposus with radial fissures extending into the peripheral annulus fibrosus. Upon rupture of the disc, the release of irritative material near the meninges can induce radiculitis and symptoms of radiculopathy without actual herniated disc material compressing the nerve roots. Under such circumstances, significant disc herniation might not be visualized on MRI or computed tomography (CT) scan. In brief,

the proposed mechanisms of radiculopathy include direct pressure on nerve fibers as a result of compression injury and indirect impact through impairment of microcirculation, chemical irritation and inflammation, immune reaction, edema formation secondary to permeability changes of the intraneural capillaries, and impairment of the nutritional transport to the nerve root.

Compression of the nerve roots is dependent upon the effective space available within the neural foramina, the osseous structures surrounding the neural foramina, and the tethering effects of the intraspinal and extraspinal ligaments. Posterolateral disc herniations can impinge on the lumbar dorsal root, which then initiates electrical discharges for as long as 25 minutes after the mechanical stimulus has been removed. Radiculopathy can be produced by either biochemical or mechanic stimulation of a swollen, stretched, or compressed nerve root. Approximately 3% to 12% of all lumbar disc herniations occur laterally and extend into or beyond the foraminal zone; in this setting, the patients will complain of sudden and severe radicular pain, often with dysesthesia. On the other hand, discogenic pain resulting from a central disc bulge or herniation stimulates several lumbar tissues such as the outer layer of the annulus fibrosus or PLL. Clinically, this is manifested as central low back pain without any radicular symptoms.

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A.8. What is the anatomy of the spinal facets? How do the facet joints cause pain?

The facet, or zygapophysial, joints consist of two arthrodial joints superiorly and inferiorly, each lined with synovium, lubricated by synovial fluid, and contained within a joint capsule. These synovial joints enhance spinal stability and flexibility. In the upper part of the lumbar spine (L1-L3), the facet planes lie in a generally vertical sagittal plane and permit flexion and extension but prevent lateral flexion or bending in the lordotic curve. The lumbosacral facet joints at the level of L5-S1 depart the farthest from the sagittal plane, allowing some rotation of the lower part of the lumbar spine. With slight forward flexion, the facets of the other lumbar vertebrae separate and permit a modest degree of lateral movement and rotation. Facet loading, if of a repetitive nature, may play a role in the degeneration of the facet joint. After repeated wear and tear, these joints are susceptible to osteoarthritis and associated synovial cyst formation. Hypertrophic facet joints or cysts can encroach on the spinal canal or the intervertebral foramina and contribute to the development of central spinal or

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foraminal stenosis.

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A.9. What are the important findings in the history and physical examination?

A problem-focused pain history should include onset, location, intensity (e.g., pain scale 0 to 10), characteristics (achy, spasmodic, stabbing, burning, shooting, etc.), and duration plus aggravating and alleviating factors. The essential purpose in the initial evaluation is to differentiate patients with serious underlying pathology from those with mild problems.

Patients with a disc problem will usually experience an exacerbation of their symptoms with spinal flexion, which increases intradisc pressure. By contrast, in the setting of spinal stenosis, standing or walking exacerbates back and leg pain, whereas forward flexion may

alleviate these symptoms. In moderate-to-severe spinal stenosis, extension of the spine may cause radicular pain.

TABLE 50.1 Differentiating Spinal Shock, Upper Motor Neuron Lesions, and Lower Motor Neuron Lesions

DISEASE STATE	DEEP TENDON REFLEX	PATHOLOGIC REFLEX/PLANTAR RESPONSE	SUPERFICIAL REFLEX (NORMAL)
Spinal shock	Absent	Absent	Absent
Upper motor neuron disease	Increased; rarely may be decreased in the acute setting	Positive/extensor Babinski sign + Oppenheim sign +	Decreased or absent For example, cremasteric reflex -
Lower motor neuron disease	Decreased	Negative/flexor	Present (but L1-L2 lesion will have cremasteric reflex -)

Patients with compression fractures typically present with severe back pain, often intense with minimal lateral rotation or with flexion and relieved by rest. A history of bladder, bowel, or sexual dysfunction may indicate compression of the cauda equina or conus medullaris. Unlike sciatica, often with its unilateral nerve root involvement, patients with cauda equina syndrome usually have bilateral involvement. Although motor function may be normal and pain uncommon in those with conus lesions, patients often demonstrate abnormalities of sensation in a saddle distribution, feeling touch or dysesthesias, but neither pain nor temperature. Causes of these symptoms may be a fracture of L1 or L2, tumor, large central disc herniations, or intramedullary cysts affecting the conus. These disorders are considered surgical emergencies and require aggressive evaluation and prompt surgical consultation.

The physical examination should include Lasègue's sign (the straight leg raising test), Braggard's test (dorsiflexion of the ankle with elevation of the leg), and the crossover test. These clinical tests are considered positive when sciatica is reproduced with elevation of the leg between 30 and 60 degrees. If testing the uninvolved leg produces contralateral

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symptoms, disc disease should be considered. A positive crossover sign occurs when straight leg raising of the patient's contralateral leg elicits pain on the affected side. It is usually a strong indication of nerve root irritation or compression. Extension of the knee while in a seated position, also known as *distracted straight leg raise*, can test sciatic nerve tension too. The patient with significant nerve root irritation tends to complain of increased pain or lean backward to reduce tension on the nerve. The differential diagnosis of spinal shock, upper motor neuron lesions, and lower neuron lesions is shown in Table 50.1. The nerve root signs are shown in Table 50.2.

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TABLE 50.2 Nerve Root Signs

ROOT LEVEL	REFLEX DECREASE	SENSORY DEFECT	MOTOR WEAKNESS
L4	Knee jerk	Anterior thigh, knee, and shin	“Single squat and rise test”; quadriceps (mostly L4)
L5	No easily elicited reflex	Lateral leg and middle dorsal foot	“Heel walk test”; dorsiflexion of foot and toes (L5 and some L4); especially big toe, extensor hallucis longus (EHL)
S1	Ankle jerk	Posterior calf and sole	“Toe walk test”; gastrocnemius/soleus; “toe flexors”

A.10. Which are the appropriate diagnostic studies for low back pain?

In the absence of signs of serious medical disease, there is no need for special studies because 90% of patients will recover spontaneously within 4 weeks of the onset of pain. Waiting 4 weeks before considering special tests allows these patients to recover spontaneously and avoid unneeded procedures. When pain persists beyond 4 to 6 weeks, plain radiographs of the spine should be considered. Pertinent findings include the height of the intervertebral spaces and vertebral bodies, and bony changes in the end plates. With oblique views, the facet joint space and any spondylolysis can be revealed. The lateral view can help estimate the severity of spondylolisthesis. A CT scan can show a herniated disc or fragment in the spinal canal. It can help to identify early epidural hematoma. With contrast, it can help further differentiate tumors, abscesses, and granuloma in the central nervous system. MRI provides excellent anatomic definition of the disc and its hydration status; it can also show the anatomy of the surrounding soft tissues. MRI with intravenous gadolinium is indicated for distinguishing between a recurrent disc herniation and recent postoperative scar tissue. It is particularly useful when distinguishing intrinsic from extramedullary or epidural spinal cord lesions. When MRI is contraindicated, a myelogram may reveal a filling defect at the level of posterior bulging discs. The myelogram in conjunction with a CT scan enables axial imaging of the spinal cord and subarachnoid space. A bone scan is helpful in the diagnosis of bone or bony fractures that may not be visible by radiography or CT scan, or whenever metastatic disease is suspected.

Discography/discogram/discomanometry (discometry) is a specialized diagnostic test specifically indicated to help diagnose discogenic pain. The presence of pain fibers in the outer third of the annulus fibrosus may explain back pain in some individuals with an annulus tear or internal disc disruption. The test involves an intradiscal puncture and instillation of contrast into the disc nucleus. It provides direct confirmation of nuclear morphology and integrity of the vertebral end plate and annulus.

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A.11. What is the differential diagnosis of low back pain?

There are numerous diagnostic labels used to describe low back pain, for example, lumbosacral sprain, lumbar discogenic syndrome, mechanical low back pain, spinal stenosis, spondylosis, spondylolisthesis, osteoarthritis/facet joint syndrome, myofascial pain syndrome, unstable low back, discitis, and failed back surgery syndrome. Each of these labels suggests its own underlying pathology. Acute lumbosacral sprain, by far the most common cause of new-onset low back pain, is often only associated with the presence of postural back pain. It frequently results from reflex muscle spasm secondary to local irritation of structures in the back. When muscle spasm occurs, the normal anatomy may be disturbed and undue force applied to surrounding tissues and structures. In every case, a careful history, physical examination, and the appropriate diagnostic studies will help elucidate the “pain generator.”

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A.12. What are the causes of multiple spine surgeries and persistent back pain?

Persistent back or leg pain after one or more spinal surgeries is called *failed back surgery syndrome* or *postlaminectomy syndrome*. Usually, the cause is a combination of both nociceptive and neuropathic pain. Over time, a strong psychological component can develop with

progressive disability as treatments fail. Approximately 37,500 patients are diagnosed with this syndrome annually in the United States.

When pain persists or recurs in a patient after spinal surgery, the most common neuroradiologic finding is usually that of epidural fibrosis and scarring besides recurrent disc herniations and spinal stenosis. Patients with this condition often report constant dull, aching, poorly localized low back pain with intermittent sharp episodes. They may also report pain or abnormal sensations with neuropathic characteristics such as burning, shooting, throbbing, stabbing, or pulling. The exact source of these complaints is unclear although the scar tissue or arachnoiditis is frequently implicated. When reoperation is performed for the purpose of neurolysis only, a transient improvement of sciatica may be seen, but it usually recurs within the first postoperative year. Success rates for reoperating on patients with failed back surgery syndrome have been highly variable, ranging from 25% to 80%. These patients are perhaps the most challenging of all. They deserve a comprehensive multidisciplinary evaluation, including orthopedic and neurosurgical consultations. Further, surgical intervention should be avoided in the absence of a clear indication. Repeated imaging studies add to the health care expenses and interventions that may not have a great therapeutic yield.

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B. Management of Low Back Pain and Sciatica

B.1. What are the noninterventional treatments available?

The cornerstone of treatment for low back pain and mild sciatica caused by a herniated lumbar disc is conservative care, which includes bed rest, medications, and physical therapy. Patients whose symptoms fail to respond to conservative care may require more invasive treatment.

Both clinical and epidemiologic evidence suggest that the longer the back pain and work loss persist, the less likely there will be improvement of the pain. The chance for return to work is even lower. Improved early management and greater access to primary care services should greatly reduce the number of patients with simple backache who require referral to hospitals. Over the last decades, there has been a paradigm shift in the treatment of low back pain away from focusing care exclusively on the pain in favor of helping patients improve their activity tolerance and function. An early return to activity seems to be associated with a better outcome than does prolonged bed rest (greater than 4 days).

Treatment varies depending on the cause of pain. In December 1994, the Agency for Health Care Policy and Research announced the following guidelines for the care of acute low back problems:

- A brief period of rest
- Over-the-counter pain relievers
- Trunk-strengthening exercises
- A single spinal manipulation

In order to avoid reinjury, an incremental, gradually increasing regimen of aerobic exercise (up to 30 minutes daily) can usually be started within the first 2 weeks of symptom onset. Such activities have been found to stress the back no more than sitting for an equal period on the side of the bed. The combination of aerobics for general fitness with some specific training to improve the strength and endurance of the back muscles is often beneficial.

The role of medications in the treatment of low back pain is to control pain, facilitate rehabilitation, restore normal sleep patterns, and improve mood and motivation. Nonsteroidal anti-inflammatory drugs are an essential part of the treatment of patients with inflammatory back pain, such as that associated with spondylitis. Other medications that have been shown

to be useful include tricyclic antidepressants and anticonvulsants. Muscle relaxants are often used to decrease muscle spasm and assist in promoting rest for patients with severe pain. These are usually indicated for short-term treatment and acute relief. Short-term therapy with opioid analgesics may be needed to promote rest as well as maintain activity in the acute phase of low back pain. Long-term use of these medications is generally discouraged but may be appropriate for carefully selected patients.

When recovery does not occur within 6 weeks and no additional pathology is detected, physical therapy is indicated. Patients should be encouraged to increase activity. Activities and postures that increase stress on the back also tend to aggravate back symptoms. Patients limited by back symptoms can minimize the stress of lifting by keeping any lifted object close to the body at the level of the navel. Activities such as twisting, bending, and reaching while lifting, also increase stress on the back. Prolonged sitting may aggravate back symptoms in discogenic pain patients because of progressive increase in pressure at specific points in the abnormal disc. Body weight optimization and a program that teaches good posture and body mechanics are also important. Neuromuscular reconditioning must be included to ensure a function-specific, task-oriented program. Essential and most importantly, the program must be geared to enhance functional recovery in the affected patient. The exercise training is designed as a step-by-step program to improve patients' function and optimal neutral spine posture. These programs include stabilization training to attain adequate dynamic control of lumbar spine forces and eliminate repetitive injury. Soft tissue flexibility, joint mobility, abdominal muscle strengthening, and aerobic exercise are also important factors.

Spinal manipulation is controversial and is neither recommended in patients with radiculopathy pain nor is it wise in those

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for whom a diagnosis has not been established. For appropriately selected patients, if manipulation has not resulted in symptomatic and functional improvement after 4 weeks, it should be stopped and the patient reevaluated.

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B.2. What are the traditional interventional treatments available and how should they be used?

Common traditional interventional treatment includes the following:

- Trigger point injection
- Traditional epidural steroid injection (interlaminar approach)
- Transforaminal epidural steroid injection (transforaminal approach)
- Facet joint intra-articular block or medial branch block

Interventional techniques such as trigger point injections and local infiltration are used to provide pain relief of short duration, so other activities and physical therapy that might otherwise be severely limited by pain may be pursued.

Corticosteroids play an important role against inflammation and reduction of edema. Steroids injected into the epidural space have been used for treating low back pain and radiculopathy for many decades. Despite widespread use, the results of epidural steroid injection are still in question because studies evaluating the response to this therapy have been small, poorly controlled, and lacking good long-term follow-up. Published studies of the effectiveness of epidural steroid injections have varied from 18% to 90%. Epidural steroid injections can be performed through the interlaminar route, the caudal canal, or the intervertebral foramina. The spread of solution in both caudal and interlaminar injection is less controllable because of inconsistent lateral flow into the ventral compartment. This renders the medication less effective as it is diverted away from the compartment, depending on the tightness of the lateral recess and the size of the dural sac. In normal volunteers, the transforaminal method showed good ventral flow, whereas the interlaminar approach showed predominantly dorsal flow, which was far from the usual site of impingement.

Patients who suffer from lumbar facet arthropathy may have symptoms, including bandlike low back pain and associated hip, groin, or thigh pain. Pain rarely radiates below the

knee in this condition. Blockade of the medial branch of the dorsal ramus of the spinal nerve or intra-articular injections of the lumbar facets are effective in short-term alleviation of this type of pain.

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B.3. What are recent considerations of improving safety for lumbar epidural steroid injection?

The working group (expert working group with facilitation from the U.S. Food and Drug Administration's Safe Use Initiative [SUI]) and the advising national organizations (representatives from leading specialty societies) unanimously agreed that epidural injections of steroid were rarely associated with serious complications due to injuries of the central nervous system. They agreed that transforaminal injections are associated with a risk of catastrophic neurovascular complications and that particulate steroids appear to be inordinately represented in case reports of these complications. Clinical considerations involving technical aspects of the procedures included use of appropriate image-guided views, injection of contrast under the real-time fluoroscopy, review of prior imaging studies, use of face mask and sterile gloves, use of extension tubing, and avoidance of heavy sedation. Although digital substraction imaging (DSI) may help to detect vascular uptake, the sensitivity was demonstrated to be 60% in one study as compared to aspiration sensitivity of 20%.

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B.4. What are some of other approaches in minimally invasive interventions?

There are several recent interventional techniques for the management of low back pain and sciatica that can be applied to appropriately selected patients. These include the following:

- Epidural neuroplasty or epidural adhesiolysis
- Epiduroscopy (spinal canal endoscopy)
- Percutaneous radiofrequency denervation of medial branches for facet joint pain
- Automated percutaneous discectomy (APD) or percutaneous automated discectomy (PAD) or percutaneous automated nucleotomy (PAN)
- Percutaneous laser disc decompression (PLDD)
- Intradiscal electrothermal therapy (IDET)
- Percutaneous disc decompression using nucleoplasty
- Percutaneous lumbar discectomy using Dekompressor probe
- Minimally invasive lumbar decompression (MILD) procedure
- Spinal cord stimulation (SCS)
- Intrathecal drug delivery
- Percutaneous vertebroplasty (PV) and percutaneous kyphoplasty (PK)

Epidural neuroplasty or epidural adhesiolysis is done with hypertonic saline and hyaluronidase to lyse epidural adhesions. This technique involves placing a rigid catheter into the epidural space, with manipulation of the catheter to physically breakdown the adhesions

and applying local anesthetic, steroid, hypertonic saline (10%), and hyaluronidase over several days.

Epiduroscopy (or spinal canal endoscopy) allows directly visualization of the epidural space using a flexible fiberoptic catheter. Adhesions are lysed with the catheter under direct vision; thereafter, better delivery of medications to the target area can be achieved.

Percutaneous radiofrequency denervation of the medial branches of the dorsal (or posterior) rami of segmental spinal

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nerves is achieved by applying heat to denature the nerves that innervate the painful facet joints. The success rate has been reported variably in the range of 17% to 90% for facet joint pain of a few weeks' to several months' duration. With this technique, the pain may return several weeks to months after the axons regenerate; repeating the procedure is then indicated.

Percutaneous manual nucleotomy was first presented in 1975. It was proposed as a method of preventing perineural and epidural scar formation by avoidance of entry into the spinal canal. Thereafter, APD or PAD or PAN was designed as a procedure using “nucleotome” (reciprocating suction-cutting probe) for intradiscal decompression in 1985. The cannula requires a sizable annular incision to reach the nucleus. Its success rate is approximately 70% to 80%.

PLDD is a technique, introduced in 1987, that uses neodymium:yttrium-aluminum-garnet (Nd:YAGq) laser to “vaporize” a small portion of the nucleus pulposus in an attempt to decompress the involved disc. It has been demonstrated that the inner pressure of the nucleus pulposus drops significantly after the disc ablation. Its success rate is approximately 78%. After 4 to 6 months from this treatment, it was demonstrated that one-third of repeat MRI scans showed modest to moderate decrease in the size of disc herniation. There is concern, nevertheless, that the technique is potentially hazardous to bone and nerve tissue because of the significant rise in temperature resulting from thermal energy transfer.

IDET or annuloplasty, first reported by Saal and Saal in 2000, has been shown to be effective in managing discogenic pain. It is a minimally invasive procedure in which a catheter is inserted into the nucleus pulposus through which an electrode is passed so that a controlled level of heat at a temperature of 90°C (194°F) can be applied to a broad section of the affected disc inner wall. This thermal therapy is postulated to alleviate discogenic pain by shrinking collagen at a target temperature of 65°C (149°F) to 75°C (167°F). Another proposed mechanism is denervation of exposed nociceptor endings in the outer disc annulus starting at 45°C (113°F).

Percutaneous disc decompression with nucleoplasty is used for those patients whose symptoms are attributed to radiographically contained discs, that is, disc with intact outer annulus.

Since 2000, by combining tissue removal with thermal treatment, disc decompression has been achieved. It applies a focused “coblation” technique, ablating while coagulating (by using bipolar radiofrequency) to reach the level of 40°C (104°F) to 70°C (15°F). At this temperature, molecular dissociation is achieved and thought to minimize the potential for surrounding tissue damage.

Percutaneous disc decompression using a Dekompressor probe is another option for those patients whose symptoms are attributed to radiographically contained discs. It provides objective evidence that disc was removed, the cellular character of that material, and provides a qualitative and quantitative measure.

MILD is a procedure involves limited percutaneous laminotomy and thinning of the ligamentum flavum in order to increase the critical diameter of the stenosed spinal canal.

SCS is a technique in which electrodes are passed into the posterior epidural space. Electrical stimulation of the spinal cord has been shown to be effective in the management of certain neuropathic pain syndromes and postlaminectomy syndromes. The exact mechanism by which pain relief is achieved remains controversial. The Axium system is a form of SCS that targets a neural structure within the spine called the dorsal root ganglion (DRG). The DRG contains the primary sensory neurons that transmit pain signals from the peripheral nerves to the brain. The system uses an implantable medical device to deliver mild electrical pulses to the DRG. These pulses mask or interrupt pain signals as they travel to the brain. Although this therapy is approved throughout Europe and Australia, the device is for investigation use only in the United States so far. The current “accurate study” is a prospective, randomized, multicenter, controlled clinical trial to assess the safety and efficacy of the Axium system in the treatment of chronic lower limb pain in the United States (ACCURATE Trial from ClinicalTrials.gov).

Intrathecal drug delivery directly into the cerebrospinal fluid through an implanted catheter and pump can be used to treat intractable pain from a variety of causes, both nociceptive and neuropathic. A variety of medications and combinations thereof can be used depending upon the type and location of symptoms. Among the experts, this is known as *intrathecal polyanalgesia*. This modality is indicated when increasing doses of opioid are required to achieve pain relief but at the expense of disabling side effects. The dose is effectively reduced to approximately 1/300, for example, when converting an oral dose of morphine to its equipotent equivalent delivered intrathecally.

PV and PK are both advanced techniques used in the treatment of painful compression fracture. In the United States, compression fractures occur in approximately 700,000 patients per year, and 80% of these fractures occur in women. The conventional management includes bed rest, analgesics, and bracing. PV was a technique developed in 1984 for the treatment of painful vertebral hemangiomas. It has since become popular for the treatment of osteoporotic vertebral body

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compression fracture. It involves the application of liquid cement (polymethylmethacrylate), tobramycin, and barium powder (as nonionic contrast) through a special metal needle inserted under fluoroscopy. The cement provides vertebral solidification and buttresses the compressed bone within the vertebral body. The procedure usually takes 45 to 60 minutes, and the patient may be discharged several hours later. Some risks are involved with this procedure, such as leakage of cement into surrounding areas (disc, spinal cord, and nerve roots), infection, bleeding, worsened pain, embolism, and paralysis. Overall, more than 80% of treated patients had moderate to marked pain relief.

PK is a recently developed technique similar to PV, which involves the additional application of an inflatable balloon inside the collapsed vertebral body. The compressed fracture is thus expanded, the lost height of the vertebral body is restored, and an inner space or cavity is created for the cement. This procedure was approved by the U.S. Food and Drug Administration (FDA) in 1998. A significant reconstitution of the curvature of the spine can be seen following kyphoplasty. According to Lieberman et al., in 70% of the collapsed vertebral bodies, the kyphoplasty restored 47% of the lost height. This newer technique offers the additional advantage of realigning the spinal column and restoring height to the fractured vertebrae.

PV and PK are associated with pain relief in 67% to 100% of cases. Most patients experience significant pain relief within the first 1 to 2 days. There is also a report of 95% improvement in pain and significant improvement in function following treatment by either of the two techniques.

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B.5. What are the concerns of magnetic resonance imaging (MRI) safety in spinal cord stimulator (SCS)?

MRI safety recommendations vary between the models of SCS. Certain SCS systems allow for MRI of the brain to be performed, and only one system (Medtronic, approved by FDA in 2013) allows for MRI of the entire body to be performed, both under strict labeling conditions. Before an MRI is performed, it is imperative to ascertain that the system is intact, without any lead breaks or low impedances, because these can result in heating of the SCS and injury to the patient. With SCS, there is a risk of thermal injury to the patient at any point along the course of the device because of induction of current by the magnetic fields during the MRI.

In some systems, an MRI of the brain has been possible under strict labeling conditions including that the stimulator has been interrogated and has appropriate impedance levels; that the stimulator has been turned off (or into “MRI Mode”); that the MRI is performed with a “transmit/receive” head coil; only a 1.5-T closed magnetic field with a maximum gradient slew rate of ≤200 T/m/sec per axis, maximum static field spatial gradient ≤40 T per m (4,000 G per cm, Boston Scientific) or 30 T per m (3,000 G per cm, St. Jude Medical), a radiofrequency (RF) of 64 MHz, and a specific absorption rate (SAR) ≤3.2 W per kg is allowed. These MRI scans are limited to less than or equal to 30 minutes. During these scans, there is potential for heating or discomfort, and the patient must be advised to communicate with the technicians should this occur. The devices are also at risk for permanent malfunction after MRI, which would require surgical replacement. After the scan, the device must be interrogated and turned back on. Open-MRI devices have not been tested with these implants and are not considered safe. Ultimately, these devices have specific conditions under which MRI may be performed, and physicians must consult the manual for the device, which is implanted before ordering MRI scans.

Of the three companies (Boston Scientific, Medtronic, and St. Jude Medical) that market SCS systems in the United States, only one (SureScan system of Medtronic) allows for an MRI of entire body to be performed while implanted. Protégé MRI SCS system (St. Jude Medical) is also FDA-approved for head and extremity (upper extremities: wrist only; lower extremities: all except hip) scan with transmit-receive RF coils on a 1.5-T system in normal operating mode.

In addition, when cautery is necessary, bipolar electrocautery is recommended and it should be used on the lowest possible power setting. The grounding pad is kept as far from the neurostimulator system as possible (keeping the path of current away from the SCS system by placing the grounding electrode on the contralateral side from the wires and pulse generator). As with MRI, electrocautery usage in patients with SCS systems with suspected breaks or abnormal impedances is unsafe and may cause injury to the patient.

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B.6. When should surgery be considered?

Several surgeries are indicated for low back pain and sciatica. These include laminectomy, macrodiscectomy or microdiscectomy, foraminotomy, intervertebral body insertion, and spinal fusion.

According to Weber's study, the long-term results appear to be no different in the surgery versus nonsurgery group in the case of low back pain. If the following situations occur, surgery should be considered:

- Failure to respond to conservative management for at least 3 months
- A profound or progressing neurologic defect such as a complete foot drop
- Recurring episodes of intractable sciatica involving the same segment—mainly to avoid the cumulative disability of repeated events

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Muscle weakness is a dubious indication for surgery if the paresis is of unknown duration. If the pressure on the nerve root can be relieved immediately after the appearance of the paresis, surgery has been regarded as the therapy of choice. Unfortunately, most patients are unaware of the subtle loss of motor function. The greatest concern and complaints are largely centered on pain, paresthesia, and immobility.

Within the first 3 months of acute low back symptoms, surgery is considered only when serious spinal pathology or nerve root dysfunction, obviously resulting from a herniated lumbar disc, is detected. Nerve root decompression can be considered for a patient if all of the following criteria exist:

- Sciatica is both severe and disabling.
- Symptoms of sciatica persist without improvement for longer than 4 weeks or with extreme progression.
- There is strong physiologic evidence of dysfunction of a specific nerve root with intervertebral disc herniation confirmed ipsilaterally at the corresponding level by imaging.

Patients with acute low back pain alone, without findings of serious conditions or significant nerve root compression, rarely benefit from a surgical consultation. With or without surgery, more than 80% of patients with obvious surgical indications eventually recover.

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B.7. What surgical options are available for treatment of disc disease?

- Artificial disc replacement (ADR)
- Interspinous process decompression system (X STOP)
- Decompression (laminotomy, laminectomy) or decompression with fusion

In the mid-1980s, German orthopedic surgeons developed a metal and plastic prosthesis that has been in clinical use since then. The prosthesis is known as the *SB CHARITÉ*. The prosthesis design is currently in its third generation. Other prosthetic discs are available, including ProDisc, Maverick, FlexiCore, and Kineflex. In October 2004, the CHARITÉ artificial disc became the first to be approved for disc replacement in the United States. It is composed of two metallic end plates and a polyethylene core that moves between them (Figs. 50.1, 50.2, 50.3 and 50.4). Traditional spinal fusion does change the mechanics of the segment that is fused. Adjacent segment degeneration can develop at approximately 3% per year (or 16.5% at 5 years, 36.1% at 10 years). One major theoretic advantage of ADR over spine fusion is that it results in no change in the biomechanics of the lower spine, thereby allowing the spine to maintain its normal range of motion and reducing or eliminating the risk for degeneration in the adjacent segments of the spine. The indications for ADR are similar to those for an anterior lumbar interbody fusion using interbody cages. The contraindications for ADR include infection, spinal stenosis, spondylolisthesis (or other types of instability in the spine, such as fracture or tumor), scoliosis, facet joint osteoarthritis, significant radiculopathy, osteoporosis, and pregnancy. Artificial discs are not perfect. The potential disadvantage of ADR is a limited durability. Because disc injury is a common cause of back pain in younger adults, an artificial disc in such patients needs to last for decades. The demands on that disc will be very great, and it may not outlast the lifetime of the patient, who may need revision surgery later. Revision ADR can be very dangerous because

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of scar tissue from the original surgery in nearby vascular structures. In addition, there is a 1% to 3% of complication of retrograde ejaculation in men. The recent study regarding Canadian

cohort of patients demonstrated satisfactory clinical and radiographic results in a carefully selected patient population. The radiographic assessment confirmed preservation and maintenance of motion of the replaced disc (L4-L5 or L5-S1) with a follow-up (2 to 7 years) averaging 55 months. In another meta-analysis, total disc replacement (TDR) showed significant safety and efficacy comparable to lumbar fusion at 2-year follow-up.

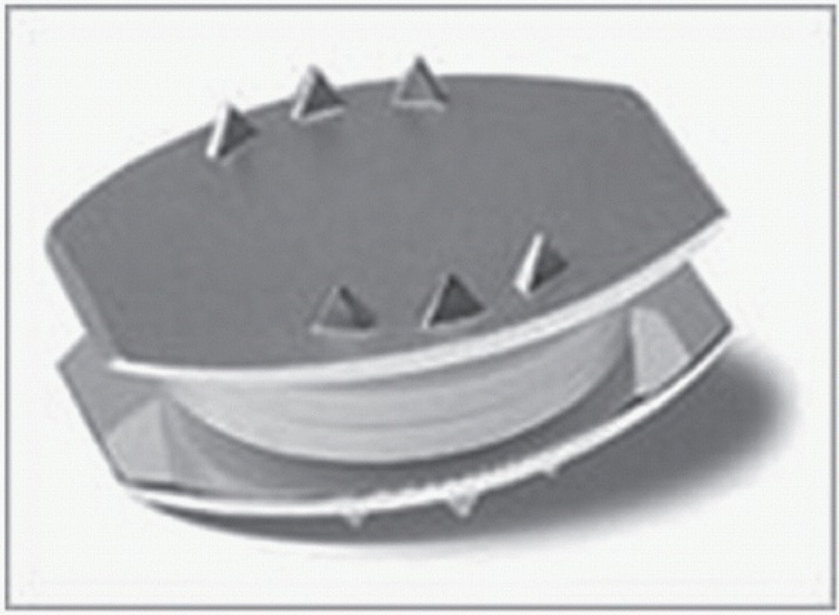


FIGURE 50.1 CHARITÉ disc.

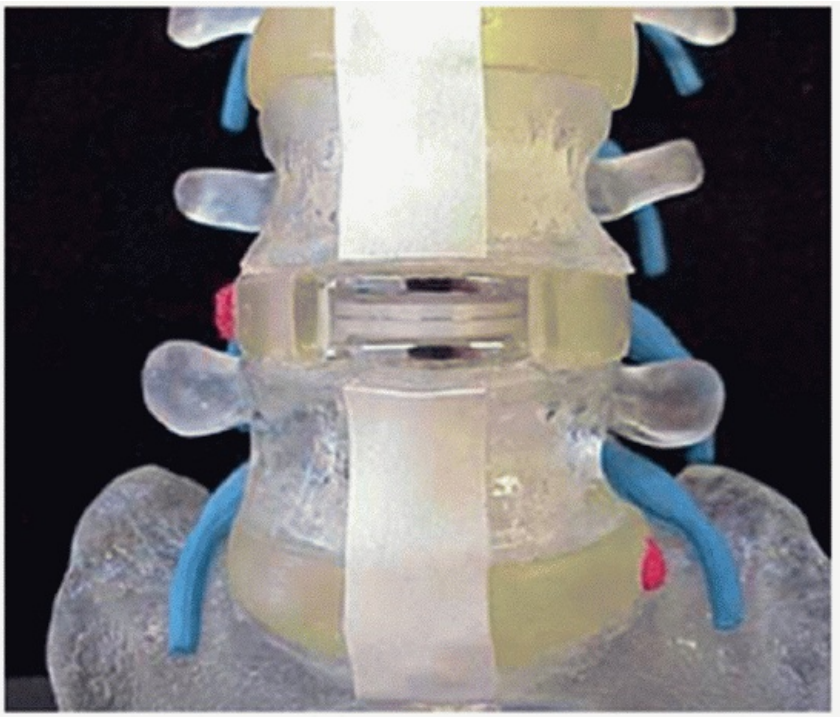


FIGURE 50.2 CHARITÉ disc replacement at L4-L5.

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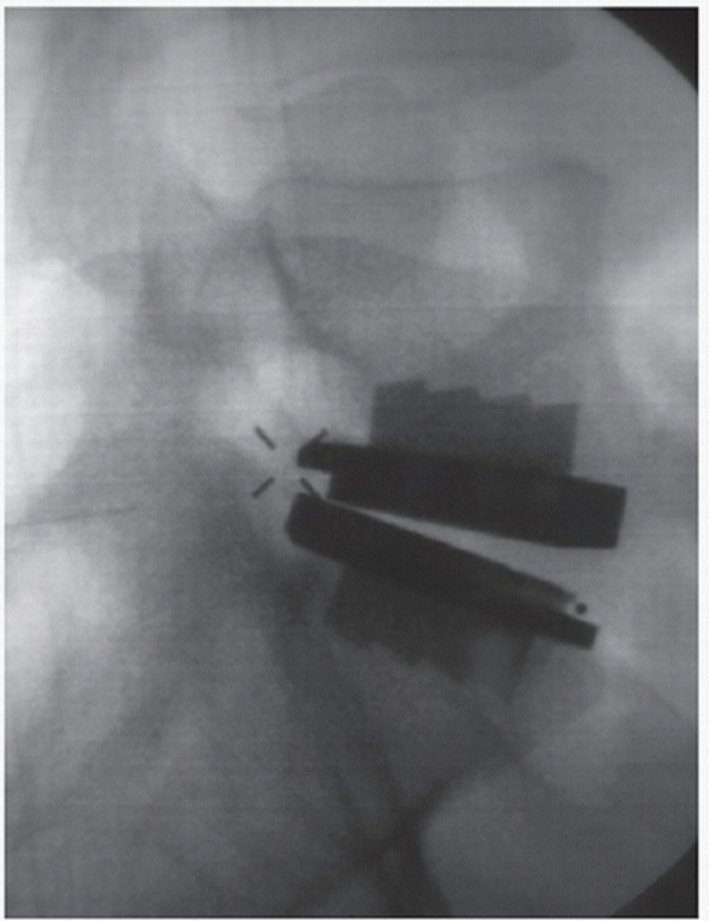


FIGURE 50.3 L5-S1 artificial disc replacement, lateral fluoroscopic view.

The interspinous process decompression system (X STOP) is a titanium metal implant made to fit between the lumbar spinous processes of the vertebrae (Figs. 50.5 and 50.6). It is designed to relieve narrowing of the spinal canal and neural foramen during extension, thereby reducing the symptoms of neurogenic intermittent claudication. The indications include spinal stenosis and degenerative lumbar spondylolisthesis. However, in a recent Norwegian study revealed the significant higher cost of X STOP is mainly due to implant cost and the significantly higher reoperation rate.

Degenerative spondylolisthesis in the lumbar spine occurs when the cephalad vertebral body slips relative to the caudal body. Symptoms may result from spinal stenosis and nerve root compression. Surgical management of this condition may entail decompression of the

spinal canal followed by posterolateral fusion with or without interbody. The idea of additional anterior stabilization of the vertebral column with an interbody reduces the incidence of nonunion, degree of slippage, and recurrence of deformity in patients with degenerative spondylolisthesis. The stated idea of additional anterior stabilization concept can be done by different approaches such as anterior lumbar interbody fusion (ALIF), posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF), and eXtreme lateral interbody fusion (XLIF).

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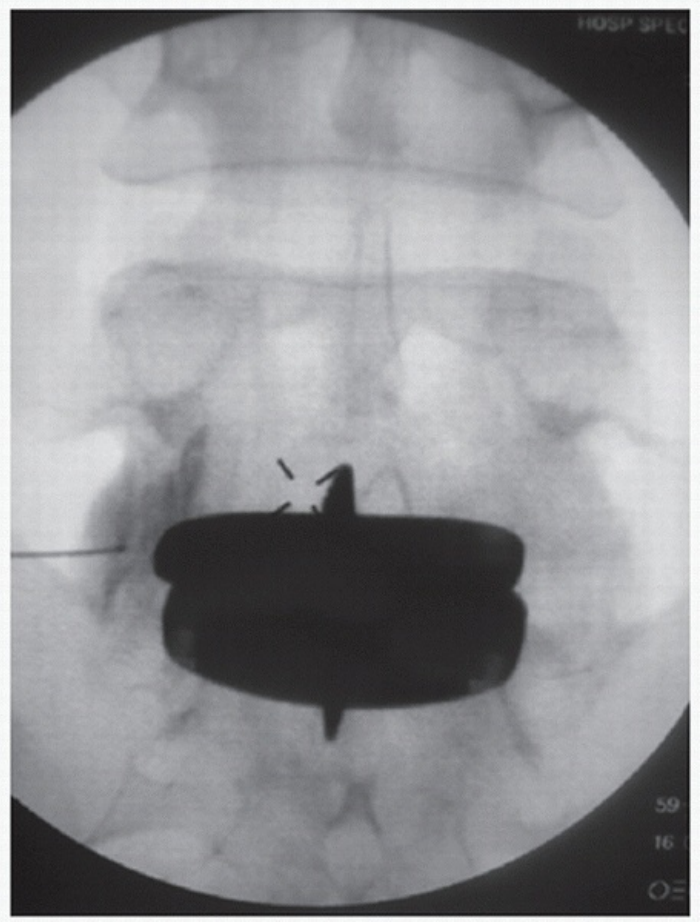


FIGURE 50.4 Anteroposterior fluoroscopic view of artificial disc replacement.

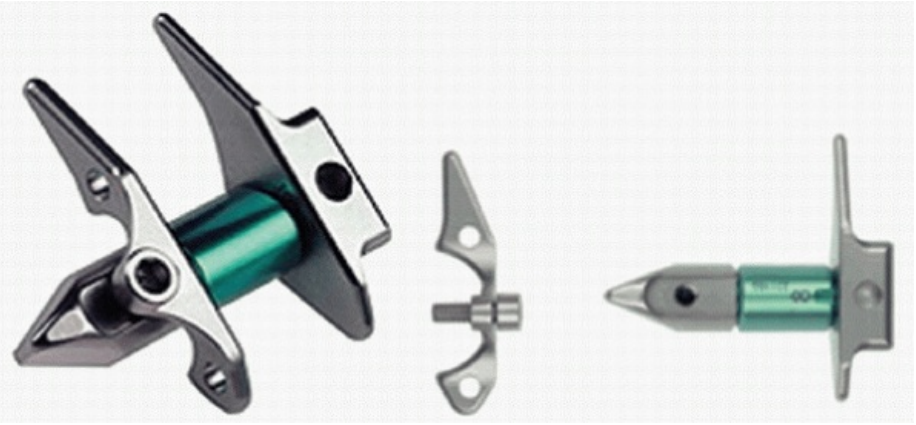


FIGURE 50.5 Interspinous process decompression system (X STOP).

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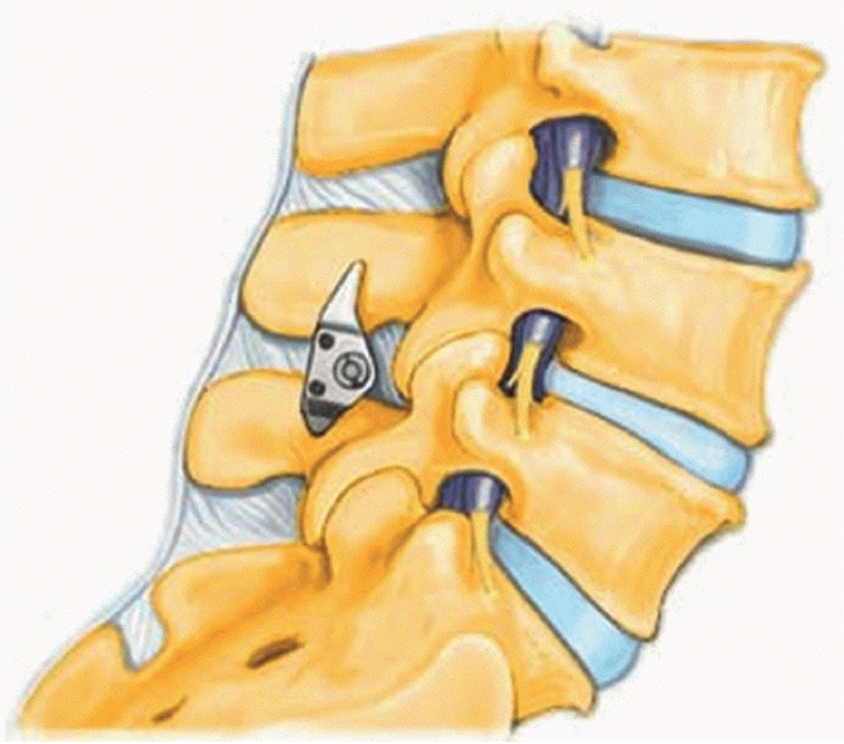


FIGURE 50.6 Interspinous process decompression system (X STOP).

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Chapter 51
Perioperative Pain Management

Anuj Malhotra

Vinod Malhotra

A 60-year-old-man with a smoking history of a pack of cigarettes a day for approximately 40 years and chronic obstructive pulmonary disease is scheduled for thoracotomy for removal of carcinoma in his right middle lobe.

A. Perioperative Pain Management for Thoracotomy

1. What would be your advice to the patient about the planned thoracotomy and postoperative pain relief?
2. How will you decide about the choice of anesthetic technique?
3. What is chronic postthoracotomy pain syndrome (PTPS)? Does video-assisted thoracic surgery reduce the risk of chronic pain after thoracotomy?
4. What would be your perioperative analgesic strategy?
5. Does the choice of analgesic technique influence postoperative outcome?
6. Does it matter if the epidural catheter is at the thoracic or lumbar level?
7. Does the choice of drugs influence the efficacy or safety of thoracic epidural analgesia (TEA)?
8. What are the usual doses and concentrations of the anesthetic combinations commonly employed in epidural analgesia?
9. If accidental dural puncture occurs during placement of the epidural needle, what steps should be taken?
10. What are the alternatives to TEA?
11. What is the usual clinical regimen for intravenous patient-controlled analgesia (IV-PCA) and is special patient monitoring required during its use?
12. What are the side effects and complications of epidural technique?
13. What recommendations for placement and removal of epidural catheter will you make if this patient is on antiplatelet or anticoagulant therapy or thromboprophylaxis is planned?

A 70-year-old woman with metastatic breast cancer has been treated for the last 6 months with transdermal fentanyl (Duragesic patch) for her cancer pain. She is currently on a 100-μg per hour patch every 72 hours. She is now scheduled for surgery for hip fracture after a fall. The patient was very dissatisfied with postoperative pain management after her breast surgery 3 months earlier.

B. Chronic Opioid Therapy and Perioperative Pain Management

1. How does chronic opioid therapy influence postoperative pain management?
2. What are the causes for increased postoperative pain and opioid consumption in patients chronically using opioids?

3. What are the main differences between a chronic opioid-consuming patient and a patient who abuses or is addicted to opioids?
4. What issues need to be considered in the opioid-tolerant patient who is scheduled for surgery?
5. What would be your strategy regarding preoperative information and choice of anesthesia technique?
6. What are the choices for perioperative pain management in opioid-tolerant patients?
7. What issues need to be considered before discharging an opioid-tolerant patient?

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A 38-year-old woman scheduled for ambulatory laparoscopic cholecystectomy requests to see the anesthesiologist preoperatively to discuss her postoperative analgesia strategy. She experienced severe pain at home for several days after a previous ambulatory laparoscopic gynecologic procedure.

C. Perioperative Pain Management for Ambulatory Surgery

1. What would be your preoperative considerations and advice to the patient?
2. What are the consequences of inadequate pain management after ambulatory surgery?
3. What is the role of premedication or preoperative analgesic?
4. Does the choice of anesthetic technique influence postoperative pain?
5. Are nonsteroidal anti-inflammatory drugs (NSAIDs) effective? If so, does the choice of drug matter?
6. What is the role of surgical technique in influencing postoperative pain after a laparoscopic cholecystectomy?
7. What would be your strategy for pain control after discharge home?

D. The Role of an Acute Pain Service

1. What is the extent of the problem, and which patients are at greatest risk of undertreatment?
2. What are the consequences of inadequate postoperative pain relief?
3. What is the role of an acute pain service (APS) in improving postoperative pain management?
4. Does an APS improve postoperative outcome?

A. Perioperative Pain Management for Thoracotomy

A.1. What would be your advice to the patient about the planned thoracotomy and postoperative pain relief?

It is essential that patients undergoing thoracotomy be informed about what to expect after surgery because an understanding of the procedure as well as realistic expectations of pain and rehabilitation can promote recovery and return to normal activity. Patients undergoing thoracotomy may suffer from severe acute postoperative pain if analgesia is not managed appropriately. Pulmonary function is impaired as a result of thoracic surgery and may be worsened by the effects of pain. Therefore, during the early postoperative period, pain control and maintenance of pulmonary function are the major goals. For preoperative improvement of pulmonary function, patients should be advised to stop smoking and be instructed in deep breathing exercises such as incentive spirometry.

Different techniques may be used to manage different levels of pain intraoperatively, immediately following surgery, within the first few postoperative days, and for discharge home. Pain management for these cases often involves a step-down approach from neuraxial

anesthesia and/or intravenous opioids to oral medication. The following issues should be addressed:

- Information must be given on how pain will be assessed, for example, the use of visual analog scores.
- Patients require a realistic expectation of the intensity and duration of postoperative pain.
- Pain management techniques that require patient involvement (IV-PCA, patient-controlled epidural analgesia [PCEA]) need to be properly explained.

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A.2. How will you decide about the choice of anesthetic technique?

The decision about which anesthetic technique to use for an individual patient is based on a review of their overall medical condition and any medications that they are taking. General anesthesia combined with epidural anesthesia or analgesia may be selected based on the patient's comorbidities and the planned procedure. Because lung volumes after thoracic surgery may be reduced by up to 50% through a combination of resection and splinting atelectasis, epidural analgesia can

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have benefit not only for pain relief but also for improving pulmonary function. Other factors such as surgeon preference, anesthesiologist experience and practice, and institutional protocols for postoperative pain relief may also influence the choice of anesthetic technique. If placement of an epidural catheter is included in the anesthetic plan, it may remain inactive throughout the case, used as an adjunct to general anesthesia, or bolused at the end of the case prior to a postoperative infusion. Again, this decision is often based on patient and surgical considerations, such as potential blood loss, hypotension, need for fluid restriction, and invasiveness of surgery. Intraoperative epidural use prior to wake up has the benefit of ensuring epidural catheter function and can facilitate a more comfortable transition to the immediate postoperative period.

The use of TEA has become widely used for management of pain associated with thoracic and major abdominal surgery. Clinical studies have shown that TEA can have effects far beyond pain relief, including decreased opioid consumption, reduced risk of nausea and vomiting, increased lung volumes, reduced risk of pulmonary complications, improved bowel recovery, and a significant reduction in the incidence of myocardial infarction. There is also evidence that neuraxial block decreases the risk of recurrence after certain cancer resections, likely through an opioid-sparing effect.

Biki B, Mascha E, Moriarty DC, et al. Anesthetic technique for radical prostatectomy surgery affects cancer recurrence: a retrospective analysis. *Anesthesiology*. 2008;109:180-187.

Christopherson R, James KE, Tableman M, et al. Long-term survival after colon cancer surgery: a variation associated with choice of anesthesia. *Anesth Analg*. 2008;107:325-332.

Exadaktylos AK, Buggy DJ, Moriarty DC, et al. Can anesthetic technique for primary breast cancer surgery affect recurrence or metastasis? *Anesthesiology*. 2006;105:660-664.

Freise H, Van Aken HK. Risks and benefits of thoracic epidural anaesthesia. *Br J Anaesth*. 2011;107(6):859-868.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1942-2005.

Pöpping DM, Zahn PK, Van Aken HK, et al. Effectiveness and safety of postoperative pain management: a survey of 18 925 consecutive patients between 1998 and 2006 (2nd revision): a database analysis of prospectively raised data. *Br J Anaesth*. 2008;101:832-840.

A.3. What is chronic postthoracotomy pain syndrome (PTPS)? Does video-assisted thoracic surgery reduce the risk of chronic pain after thoracotomy?

Chronic PTPS is defined as pain that recurs or persists along a thoracotomy scar at least 2 months after surgery and is not related to the recurrence of a tumor or an infection. PTPS is generally neuropathic in nature and varies in severity, with a reported incidence of 44% to 80%. Several studies suggest that severe perioperative pain is a predictor for development of chronic postoperative pain and thus aggressive management of early postoperative pain may be important to prevent this transition.

Although used with increasing frequency, thoracoscopic approaches have not had the favorable impact on pain that many had anticipated. Surprisingly, video-assisted thoracic

surgery is associated with a prevalence of chronic pain comparable to that of open procedures, with rates of PTPS ranging from 22% to 63%, likely due to intercostal nerve and muscle damage from trocar insertion and chest tube placement.

Gerner P. Postthoracotomy pain management problems. *Anesthesiol Clin*. 2008;26(2):355-367.

Gottchalk A, Cohen SP, Yang S, et al. Preventing and treating pain after thoracic surgery. *Anesthesiology*. 2006;104:594-600.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2000-2005.

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A.4. What would be your perioperative analgesic strategy?

The analgesic plan should consider the entire perioperative period. A multimodal approach would be preferable to account for the multiple pathways by which nociceptive input is conveyed to the central nervous system, the number of pharmacologically distinct mechanisms of modulating this input, the need for effective analgesia throughout the perioperative period and after discharge, and the importance of minimizing side effects, particularly respiratory depression.

TEA is the mainstay of recommended therapy for the reasons previously discussed. Contraindications to a thoracic epidural include patient refusal, coagulopathy, thrombocytopenia, therapeutic anticoagulation, previous thoracic spine surgery, and local infection over the entry site. When epidural catheters fail intraoperatively or have patchy coverage, intercostal nerve blocks (ICNBs) or paravertebral blocks may supplement epidural analgesia or serve as a bridge to the immediate postoperative period when an epidural catheter can be safely replaced.

NSAIDs are useful for treating shoulder pain secondary to referred diaphragmatic pain. This nociceptive input is carried by vagal and phrenic nerves and is often refractory to epidural analgesia. A concern with NSAIDs is platelet dysfunction; however, their efficacy and lack of respiratory side effects makes them an optimal choice for adjunct analgesia when possible. Cyclooxygenase 2 (COX-2) inhibitors have more limited effects on platelets aggregation and comparable efficacy to traditional NSAIDs and thus may be of use in this setting. Adverse cardiac side effects are unlikely with short-term perioperative dosing. Regular administration of paracetamol or acetaminophen (APAP) may also be useful for treating shoulder pain and can be used in addition to NSAIDs. Topical lidocaine patch or use of gabapentinoids may also have a role is select patients.

Gottchalk A, Cohen SP, Yang S, et al. Preventing and treating pain after thoracic surgery. *Anesthesiology*. 2006;104:594-600.

Mac TB, Girard F, Chouinard P, et al. Acetaminophen decreases early post-thoracotomy ipsilateral shoulder pain in patients with thoracic epidural analgesia: a double-blinded placebo-controlled study. *J Cardiothorac Vasc Anesth*. 2005;19(4):475-478.

Manion SC, Brennan TJ. Thoracic epidural analgesia and acute pain management. *Anesthesiology*. 2011;115:181-188.

Senard M, Deflandre EP, Ledoux D, et al. Effect of celecoxib combined with thoracic epidural analgesia on pain after thoracotomy. *Br J Anaesth*. 2010;105:196-200.

A.5. Does the choice of analgesic technique influence postoperative outcome?

Evidence from multiple studies strongly suggests that epidural analgesia is associated with lower rates of perioperative morbidity and, in particular, fewer pulmonary and cardiac complications. More recently, a meta-analysis of patients receiving TEA versus PCA after surgery requiring general anesthesia demonstrated decreased mortality in the thoracic epidural group. Compared with systemic opioids, epidural opioids decrease the incidence of postoperative atelectasis, hypoxemia, and pulmonary complications overall. Effective pain control with an epidural technique leads to improved pulmonary function, more effective coughing, earlier mobilization, and improved cooperation with respiratory physiotherapy.

Postoperative myocardial infarction rates are reduced when TEA is incorporated into anesthesia and extended at least 24 hours into the postoperative period. Supraventricular tachyarrhythmias, which are the most common form of cardiac morbidity after pulmonary resection and occur in up to 50% of cases, are reduced by TEA, even when compared with alternative analgesic regimens that confer equivalent pain control. The cardioprotective mechanism of TEA is believed to relate to its sympatholytic effects.

Epidural analgesia also provides superior postoperative analgesia compared with IV-PCA. As discussed earlier, better postoperative pain relief may decrease the likelihood of developing chronic postsurgical pain, although it should be noted

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that this has not yet been demonstrated in longitudinal studies.

Dworkin RH, McDermott MP, Raja SN. Preventing chronic postsurgical pain: how much of a difference makes a difference? *Anesthesiology*. 2010;112(3):516-518.

Pöpping DM, Elia N, Van Aken HK, et al. Impact of epidural analgesia on mortality and morbidity after surgery: systematic review and meta-analysis of randomized controlled trials. *Ann Surg*. 2014;259(6):1056-1067.

Wu CL, Cohen SR, Richman JM, et al. Efficacy of postoperative patient-controlled and continuous infusion epidural analgesia versus intravenous patient-controlled analgesia with opioids: a meta-analysis. *Anesthesiology*. 2005;103(5):1079-1088.

A.6. Does it matter if the epidural catheter is at the thoracic or lumbar level?

TEA is currently the standard for analgesia for thoracic surgery, and in the absence of contraindications, all patients undergoing major open thoracic surgical procedures should have a thoracic epidural catheter placed preoperatively. The tip of the catheter should ideally reside at the dermatome along which the incision will be made.

Thoracic (versus lumbar) placement of the epidural catheter is dose saving and decreases side effects such as hypotension and bladder dysfunction at equianalgesic doses. Thoracic placement also reduces motor block of the lower extremities, which allows for improved postoperative ambulation. However, if thoracic epidural placement is contraindicated or cannot be achieved, lumbar epidural anesthesia can be utilized. Lumbar placement can be efficacious, particularly when used with hydrophilic opioids such as morphine; however, local anesthetic volume dosing is significantly higher and may be limited by toxicity.

Grant GJ, Zakowski M, Ramanathan S, et al. Thoracic versus lumbar administration of epidural morphine for postoperative analgesia after thoracotomy. *Reg Anesth*. 1993;18:351-355.

Manion SC, Brennan TJ. Thoracic epidural analgesia and acute pain management. *Anesthesiology*. 2011;115:181-188.

A.7. Does the choice of drugs influence the efficacy or safety of thoracic epidural analgesia (TEA)?

Effective postoperative pain control may be achieved by delivering an opioid, local anesthetic, or a combination of both into the thoracic epidural space. Combinations are the standard because synergy between opioids and local anesthetic agents can enable an optimum balance between analgesia and minimizing blockade of motor function of the thorax and dynamic consequences of sympatholysis. Common components include opioids, such as morphine, fentanyl, or hydromorphone, and local anesthetic agents, such as bupivacaine, levobupivacaine, or ropivacaine. Systemic absorption effects (e.g., sedation) tend to be more common with the lipophilic opioids, such as fentanyl, presumably because of increased absorption into the epidural fat. Hydrophilic opioids, such as morphine, produce a wider dermatomal band of analgesia with less systemic absorption. Of the three commonly used local anesthetic agents, bupivacaine possesses the least favorable cardiac safety profile. In theory, ropivacaine offers the advantage of differential dose-dependent sensory and motor blockade; however, when used in dilute concentrations in combination with opioids, it is unlikely that any advantage of one agent over the other will be apparent. Addition of low-dose ketamine to epidural infusion has not demonstrated beneficial effects in preventing postthoracotomy pain.

Freise H, Van Aken HK. Risks and benefits of thoracic epidural anaesthesia. *Br J Anaesth*. 2011;107(6):859-868.

Ryu HG, Lee CJ, Kim YT, et al. Preemptive low-dose epidural ketamine for preventing chronic postthoracotomy pain: a prospective, double-blinded, randomized, clinical trial. *Clin J Pain*. 2011;27:304-308.

A.8. What are the usual doses and concentrations of the anesthetic

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combinations commonly employed in epidural analgesia?

Before the initiation of PCEA, a test dose of 3 mL of 1.5% lidocaine with epinephrine 1:200,000 is usually employed to rule out intrathecal or intravascular placement of catheter.

Once malposition is ruled out, the catheter is usually bolused (as allowed by hemodynamic status) prior to beginning continuous infusion.

Commonly employed combinations of epidural drugs vary. However, in the interest of patient safety, compliance, auditing, and quality assurance, standardization within the institution is recommended. Solutions and volumes can later be titrated to effect or to avoid side effects, for example, increasing or decreasing local anesthetic concentration to change block density, increasing or decreasing volume infused to increase spread, and adding or subtracting opioids to increase analgesia or decrease side effects such as itching, nausea, or sedation.

The following drugs and drug combinations are often used at a starting infusion rate of 4 to 6 mL per hour with each demand bolus of 2 to 3 mL as needed.

- Bupivacaine 0.0625% to 0.1% with fentanyl 5 μg per mL with a lockout period of 10 to 20 minutes between boluses
- Bupivacaine 0.0625% to 0.1% plain with a lockout of 20 minutes
- Fentanyl 5 to 10 μg per mL with a lockout period of 10 to 20 minutes
- Bupivacaine 0.0625% to 0.1% with Dilaudid 100 μg per mL with a lockout period of 20 minutes

(See sample order form, Fig. 51.1.)

A.9. If accidental dural puncture occurs during placement of the epidural needle, what steps should be taken?

If accidental dural puncture occurs during placement of epidural needle, the general practice is to remove the needle and place the epidural catheter at adjacent intervertebral spaces. The likelihood of intrathecal spread should be carefully assessed with the test dose. Epidural infusion may be started at the usual rate. Frequent monitoring for sensory and sympathetic block should continue in a controlled setting until the efficacy and safety of the epidural analgesia is established. In addition, the patient should be assessed for any symptoms of neuropathy relevant to the level attempted. The patient should be informed of the dural puncture and the potential for postdural puncture headache, although this is less frequent than with lumbar dural puncture.

Freise H, Van Aken HK. Risks and benefits of thoracic epidural anaesthesia. *Br J Anaesth*. 2011;107(6):859-868.

Manion SC, Brennan TJ. Thoracic epidural analgesia and acute pain management. *Anesthesiology*. 2011;115:181-188.

A.10. What are the alternatives to TEA?

There are times when for technical, medical, or other reasons thoracic epidural catheter placement is unsuccessful, undesirable, or not possible. Alternatives to mid-TEA include lower thoracic and lumbar epidural catheter placement, ICNBs, paravertebral blocks, intrathecal opioids, intrapleural catheters, local anesthetic infiltration, and systemic analgesia with one or more agents.

Lumbar epidural placement can be efficacious, particularly when used with hydrophilic opioids such as morphine to increase dermatomal spread. Lumbar epidurals are most limited by the need for increased local anesthetic dosing and the higher incidence of side effects such as hypotension and urinary retention versus thoracic epidurals.

If epidural placement is ruled out altogether for the reasons previously discussed, ICNBs can be performed percutaneously using anatomic or ultrasound-guided techniques or under direct vision intraoperatively, using single injections or placement of an intercostal catheter. While often initially effective, unpredictable spread of local anesthetic and rapid local anesthetic absorption by surrounding vessels make this technique less effective than epidural analgesia. Furthermore, indwelling intercostal catheters cannot adequately control pain after posterolateral thoracotomy because posterior primary rami and sympathetic fibers are not blocked. Additionally, percutaneous positioning and securing of intercostal catheters may be technically problematic.

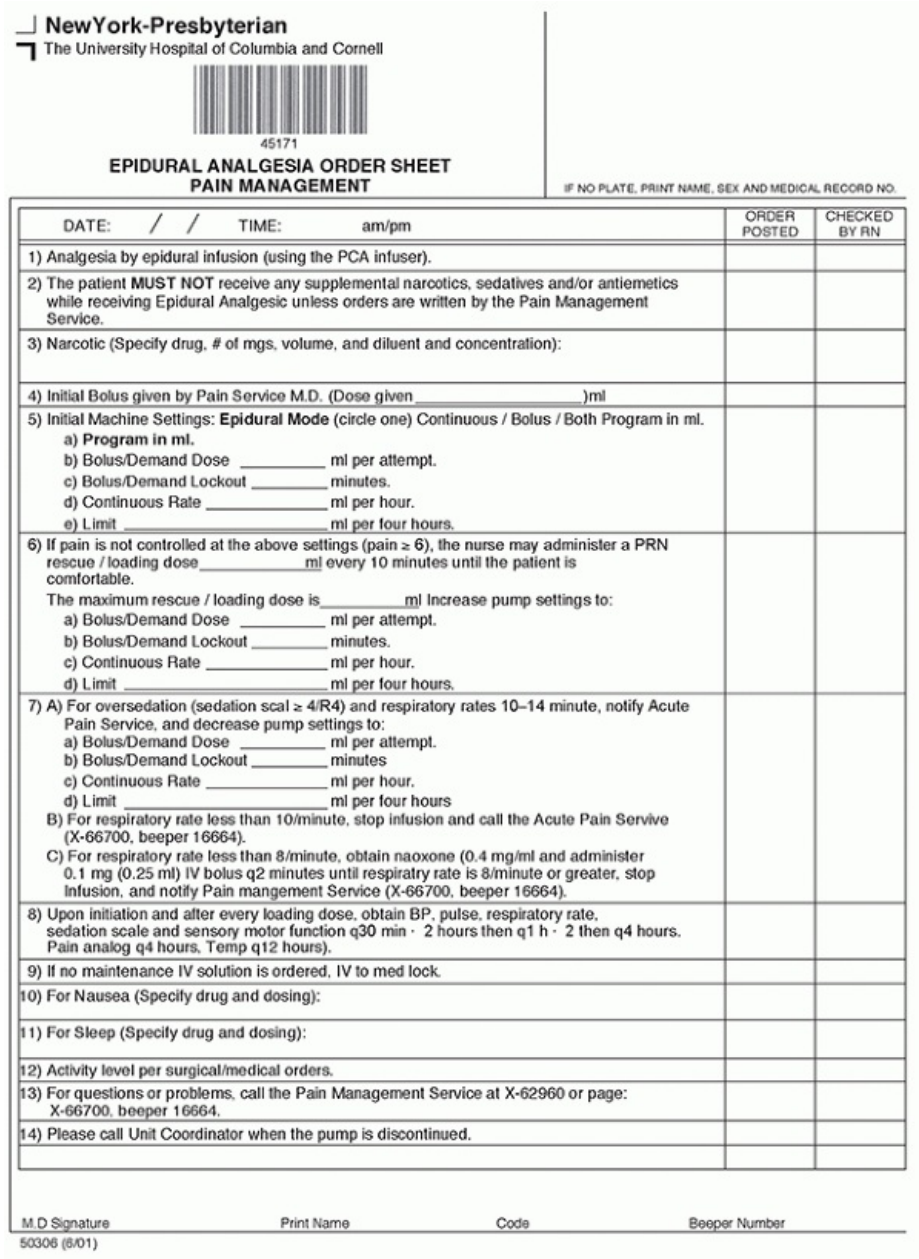
Paravertebral block results in ipsilateral somatic and sympathetic nerve blockade in multiple contiguous thoracic

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dermatomes above and below the site injection. Paravertebral analgesia has been found to produce good pain relief and preservation of pulmonary function after

thoracotomy and is probably the best available alternative to epidural analgesia. Because the concomitant sympathetic blockade is unilateral, the incidence of adverse effects, such as hypotension and urinary retention, is lower. Paravertebral blocks can be performed as single injections or through a paravertebral catheter. Paravertebral catheters can be placed percutaneously via anatomic or ultrasound-guided approaches or intraoperatively under direct vision and may be more suitable than epidural catheters when coagulopathy is of concern. In some studies, paravertebral blocks have been shown to be as effective as TEA with respect to pain control and preservation of pulmonary function after thoracotomy.



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EPIDURAL ANALGESIA ORDER SHEET
PAIN MANAGEMENT

IF NO PLATE, PRINT NAME, SEX AND MEDICAL RECORD NO.

DATE: / / TIME: am/pm	ORDER POSTED	CHECKED BY RN
1) Analgesia by epidural infusion (using the PCA infuser).		
2) The patient **MUST NOT** receive any supplemental narcotics, sedatives and/or antiemetics while receiving Epidural Analgesic unless orders are written by the Pain Management Service.		
3) Narcotic (Specify drug, # of mgs, volume, and diluent and concentration):		
4) Initial Bolus given by Pain Service M.D. (Dose given _____)ml		
5) Initial Machine Settings: **Epidural Mode** (circle one) Continuous / Bolus / Both Program in ml. a) **Program in ml.** b) Bolus/Demand Dose _____ ml per attempt. c) Bolus/Demand Lockout _____ minutes. d) Continuous Rate _____ ml per hour. e) Limit _____ ml per four hours.		
6) If pain is not controlled at the above settings (pain ≥ 6), the nurse may administer a PRN rescue / loading dose _____ ml every 10 minutes until the patient is comfortable. The maximum rescue / loading dose is _____ ml Increase pump settings to: a) Bolus/Demand Dose _____ ml per attempt. b) Bolus/Demand Lockout _____ minutes. c) Continuous Rate _____ ml per hour. d) Limit _____ ml per four hours.		
7) A) For oversedation (sedation scal ≥ 4/R4) and respiratory rates 10–14 minute, notify Acute Pain Service, and decrease pump settings to: a) Bolus/Demand Dose _____ ml per attempt. b) Bolus/Demand Lockout _____ minutes c) Continuous Rate _____ ml per hour. d) Limit _____ ml per four hours B) For respiratory rate less than 10/minute, stop infusion and call the Acute Pain Servive (X-66700, beeper 16664). C) For respiratory rate less than 8/minute, obtain naoxone (0.4 mg/ml and administer 0.1 mg (0.25 ml) IV bolus q2 minutes until respiratry rate is 8/minute or greater, stop Infusion, and notify Pain mangement Service (X-66700, beeper 16664).		
8) Upon initiation and after every loading dose, obtain BP, pulse, respiratory rate, sedation scale and sensory motor function q30 min · 2 hours then q1 h · 2 then q4 hours. Pain analog q4 hours, Temp q12 hours).		
9) If no maintenance IV solution is ordered, IV to med lock.		
10) For Nausea (Specify drug and dosing):		
11) For Sleep (Specify drug and dosing):		
12) Activity level per surgical/medical orders.		
13) For questions or problems, call the Pain Management Service at X-62960 or page: X-66700, beeper 16664.		
14) Please call Unit Coordinator when the pump is discontinued.		

M.D Signature Print Name Code Beeper Number

50306 (6/01)

FIGURE 51.1 Epidural analgesia order sheet.

A preoperative single bolus of spinal morphine as part of multianalgesic regimen can be considered in order to decrease the need for systemic opioids. Alternatively, pleural catheters may be placed intraoperatively to decrease pleural and visceral pain; however, they do not affect incisional pain and require high volumes of local anesthetic to be effective. Similarly, direct local anesthetic infiltration can be used but must be combined with longer acting strategies to provide adequate pain control throughout the perioperative period. Although systemic opioids have been well documented to reduce postthoracotomy pain, their adverse effects on the respiratory system after general anesthesia, even using patient-

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controlled delivery systems, and their inability to provide optimal dynamic pain relief favor regional anesthetic techniques, when possible, in thoracotomy patients. Systemic analgesics are best suited as adjuncts to these techniques and should become the mainstay of analgesic therapy only when invasive approaches are discontinued.

Debreceni G, Molnár Z, Szélig L, et al. Continuous epidural or intercostal analgesia following thoracotomy: a prospective randomized double-blind clinical trial. *Acta Anaesthesiol Scand*. 2003;47:1091-1095.

Liu N, Kuhlman G, Dalibon N, et al. A randomized, double-blinded comparison of intrathecal morphine, sufentanil and their combination versus IV morphine patient-controlled analgesia for thoracotomy pain. *Anesth Analg*. 2001;92(1):31-36.

Perttunen K, Nilsson E, Heinonen J, et al. Extradural, paravertebral and intercostal nerve blocks for postthoracotomy pain. *Br J Anaesth*. 1995;75:541-547.

Pöpping DM, Zahn PK, Van Aken HK, et al. Effectiveness and safety of postoperative pain management: a survey of 18 925 consecutive patients between 1998 and 2006 (2nd revision): a database analysis of prospectively raised data. *Br J Anaesth*. 2008;101:832-840.

A.11. What is the usual clinical regimen for intravenous patient-controlled analgesia (IV-PCA) and is special patient monitoring required during its use?

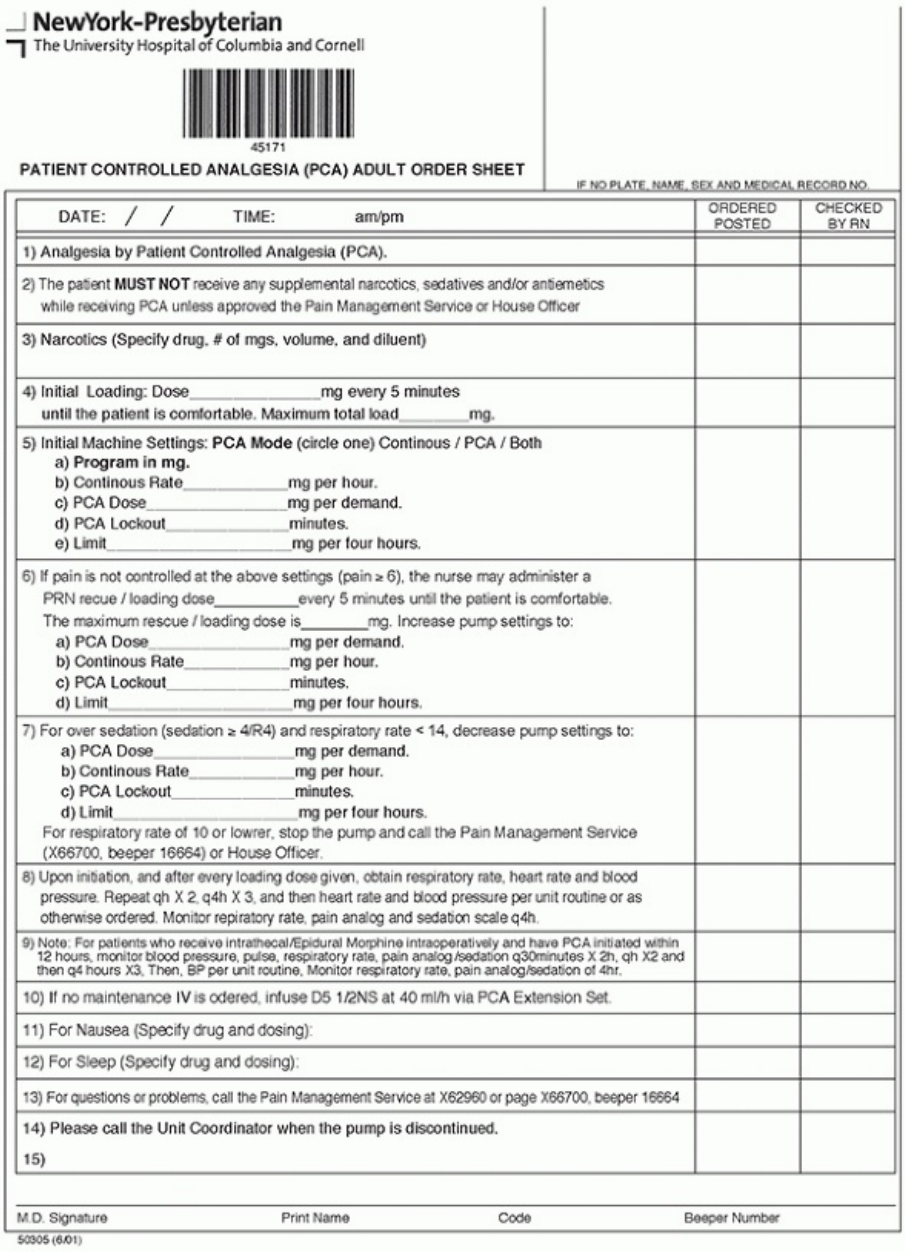
Clinical regimens for IV-PCA vary among institutions, but the most commonly used opioids are fentanyl, morphine, and hydromorphone. Continuous delivery, or basal rate, of the drug is commonly avoided to decrease the likelihood of respiratory depression. For opioid-naive patients, boluses of fentanyl 10 to 15 μg, morphine sulfate 1 to 2 mg, or Dilaudid 0.2 to 0.3 mg are given per demand with a lockout period of 8 to 10 minutes. Incremental boluses may be given by the nurse if pain is not controlled. The dose may be decreased or the opioid may be discontinued if respiratory depression occurs. Close monitoring and rescue strategies must be in place to ensure patient safety, particularly for at-risk individuals, including central monitoring of oxygenation and ventilation (see sample order form, Fig. 51.2).

A workshop of the Anesthesia Patient Safety Foundation (APSF) looked at the issue of dangers of postoperative opioids. The observed incidence of respiratory depression in these cases is 0.1% to 1.0% and increases to 3.2% in those older than 80 years. Patients with obstructive sleep apnea and the elderly are understandably at a higher risk of opioid-induced respiratory depression, but there is also a low and unpredictable incidence of life-threatening respiratory depression in young, healthy patients. The workshop highlighted the argument that in the United States, The Joint Commission's emphasis on pain as the “fifth vital sign” has had the unintended consequence of creating an expectation among patients that they will have little to no pain after surgery. As a result, more patients may be receiving inappropriate amounts of analgesics to meet this expectation. The conclusions of the APSF committee were that continuous monitoring of oxygenation and ventilation can prevent patient harm; any monitoring system should be centrally linked so that a health care professional can be summoned in a timely manner; programs should be instituted to educate providers and patients about the risks of opioid-associated life-threatening respiratory depression; governmental

agencies and nongovernmental entities should provide increased support for scientific research in this area; and while treatment of postoperative, opioid-induced depression is an important consideration, prevention may be the more effective strategy.

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PATIENT CONTROLLED ANALGESIA (PCA) ADULT ORDER SHEET

IF NO PLATE, NAME, SEX AND MEDICAL RECORD NO.

DATE: / / TIME: am/pm	ORDERED POSTED	CHECKED BY RN
1) Analgesia by Patient Controlled Analgesia (PCA).		
2) The patient **MUST NOT** receive any supplemental narcotics, sedatives and/or antiemetics while receiving PCA unless approved the Pain Management Service or House Officer		
3) Narcotics (Specify drug, # of mgs, volume, and diluent)		
4) Initial Loading: Dose_____mg every 5 minutes until the patient is comfortable. Maximum total load_____mg.		
5) Initial Machine Settings: **PCA Mode** (circle one) Continous / PCA / Both a) **Program in mg.** b) Continous Rate_____mg per hour. c) PCA Dose_____mg per demand. d) PCA Lockout_____minutes. e) Limit_____mg per four hours.		
6) If pain is not controlled at the above settings (pain ≥ 6), the nurse may administer a PRN recue / loading dose_____every 5 minutes until the patient is comfortable. The maximum rescue / loading dose is_____mg. Increase pump settings to: a) PCA Dose_____mg per demand. b) Continous Rate_____mg per hour. c) PCA Lockout_____minutes. d) Limit_____mg per four hours.		
7) For over sedation (sedation ≥ 4/R4) and respiratory rate < 14, decrease pump settings to: a) PCA Dose_____mg per demand. b) Continous Rate_____mg per hour. c) PCA Lockout_____minutes. d) Limit_____mg per four hours. For respiratory rate of 10 or lowrer, stop the pump and call the Pain Management Service (X66700, beeper 16664) or House Officer.		
8) Upon initiation, and after every loading dose given, obtain respiratory rate, heart rate and blood pressure. Repeat qh X 2, q4h X 3, and then heart rate and blood pressure per unit routine or as otherwise ordered. Monitor repiratory rate, pain analog and sedation scale q4h.		
9) Note: For patients who receive intrathecal/Epidural Morphine intraoperatively and have PCA initiated within 12 hours, monitor blood pressure, pulse, respiratory rate, pain analog /sedation q30minutes X 2h, qh X2 and then q4 hours X3, Then, BP per unit routine, Monitor respiratory rate, pain analog/sedation of 4hr.		
10) If no maintenance IV is odered, infuse D5 1/2NS at 40 ml/h via PCA Extension Set.		
11) For Nausea (Specify drug and dosing):		
12) For Sleep (Specify drug and dosing):		
13) For questions or problems, call the Pain Management Service at X62960 or page X66700, beeper 16664		
14) Please call the Unit Coordinator when the pump is discontinued. 15)		

M.D. Signature Print Name Code Beeper Number

50305 (6/01)

FIGURE 51.2 Patient-controlled analgesia (PCA) adult order sheet.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2000-2005.

Weinger MB. Dangers of postoperative opioids. APSF workshop and white paper address prevention of postoperative respiratory complications. *APSF Newsl Winter*. 2006-2007;21(4):61-67.

A.12. What are the side effects and complications of epidural technique?

TEA interferes with sympathetic outflow and can produce hypotension through cardiodepressant action (blockade of cardiac accelerator fibers) and a reduction in systemic vascular resistance (blockade of sympathetic chain). The use of dilute local anesthetic solutions has led to clinically insignificant motor blockade while maintaining adequate sensory block, although some small-muscle weakness may be observed. Opioid-related side effects include sedation, nausea and vomiting, pruritus, delayed gastrointestinal motility, urinary retention, and respiratory depression. The incidence of delayed respiratory depression after administration of epidural opioids is very low, and epidural opioid analgesia can be used safely on most hospital units. All patients who receive epidural analgesia should have standard orders for the treatment of breakthrough pain and side effects.

The overall catheter-related complication rate is low and includes such complications as dural puncture, paresthesia,

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pneumothorax, and neurologic injury. The most common documented complication is unsuccessful placement, reported at about 6%. Paraplegia associated with epidural analgesia may result from epidural hematoma, or less commonly epidural abscess. The potentially catastrophic complications of epidural or intrathecal hematoma are best prevented by realization that motor blockade should not occur with dilute local anesthetic solutions, and postoperative motor weakness should trigger immediate imaging evaluation (MRI) and neurosurgical consultation. Clearly, significant concerns about coagulopathy or local overlying infection should limit epidural catheter placement.

Block BM, Liu SS, Rowlingson AJ, et al. Efficacy of postoperative epidural analgesia: a meta-analysis. *JAMA*. 2003;290:2455-2463.

Pöpping DM, Elia N, Van Aken HK, et al. Impact of epidural analgesia on mortality and morbidity after surgery: systematic review and meta-analysis of randomized controlled trials. *Ann Surg*. 2014;259(6):1056-1067.

A.13. What recommendations for placement and removal of epidural catheter will you make if this patient is on antiplatelet or anticoagulant therapy or thromboprophylaxis is planned?

On the basis of current practice and the third consensus statement for Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy developed by the American Society of Regional Anesthesia (ASRA), the following guidelines may be helpful. Of note, a fourth edition update is in progress and the recommendations of the 2015 Interim Update (available at www.asra.com) have been included as follows.

Prophylactic Unfractionated Heparin

In the setting of twice-daily subcutaneous prophylaxis with 5,000 U heparin, there is no contraindication to the use of neuraxial techniques. For patients receiving greater than 10,000 U daily or thrice-daily dosing, data are insufficient to determine if there is increased risk of hematoma. These patients should have individual risk/benefit assessments, and techniques to facilitate detection of hematoma (increased monitoring, dilute local anesthetic solutions) should be implemented. The clinician should keep in mind that subcutaneous heparin reaches peak effect 1 to 2 hours after administration.

Recommendations

- First dose of subcutaneous heparin should ideally be administered *after* block placement. Heparin dosing should be delayed at least 1 hour after epidural catheter placement.
- If the patient is already receiving prophylactic heparin, there is no contraindication to block placement. Some clinicians advocate delaying puncture 2 hours after the last dose.

- Because heparin-induced thrombocytopenia may occur during heparin administration, patients receiving heparin for more than 4 days should have a platelet count checked before neuraxial block placement and prior to catheter removal.
- An epidural catheter may be removed at any time. Some clinicians advocate waiting 2 hours after the last dose.

Therapeutic Intravenous Unfractionated Heparin

Neuraxial techniques combined with intraoperative anticoagulation (excluding the full anticoagulation of cardiac surgery) are acceptable with certain precautions as described in the subsequent text.

Recommendations

- Neuraxial techniques should be avoided in patients with baseline coagulopathies in addition to heparinization.
- Risk/benefit determinations are needed in patients receiving anticoagulant medications such as antiplatelet agents, warfarin, and low molecular weight heparin (LMWH). These medications may increase the risk of bleeding complications.
- Heparin administration should be delayed for 1 hour after block placement.
- Epidural catheters may be removed 2 to 4 or more hours after the last heparin dose and once laboratory coagulation values have been evaluated and are normalized.
- Bloody or difficult block placement may increase the risk of epidural hematoma formation in the setting of

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intraoperative anticoagulation; however, there is insufficient data to warrant canceling a case. Discussion of risks and benefits with the surgeon regarding proceeding is warranted.

- Postoperative care should monitor for signs of hematoma such as motor blockade. Use of weak local anesthetic solutions may facilitate detection.

Preoperative Low Molecular Weight Heparin

Neuraxial blockade should not be performed if the patient is on other antiplatelet or oral anticoagulant medications in combination with LMWH. This combination increases the risk of spinal and epidural hematoma formation in the setting of neuraxial blockade. In the case of traumatic placement, first dose of LMWH should be at 24 hours postoperatively. LMWH has its peak effect 2 to 4 hours after administration.

- *Prophylactic LMWH*. An example of a prophylactic dose is enoxaparin 40 mg every day or 30 mg every 12 hours. Block placement should occur no sooner than 10 to 12 hours after the last dose of LMWH and should be maintained only if single-daily dosing is planned. If LMWH is administered within 2 hours of surgery (prophylactic dose), neuraxial blockade should be avoided.
- *Treatment dose LMWH*. An example of a treatment dose is enoxaparin 1.5 mg per kg every day or 1 mg per kg every 12 hours. Block placement should occur no sooner than 24 hours after the last dose of LMWH and only if treatment dosing is being discontinued.

Postoperative Low Molecular Weight Heparin

- *Prophylactic LMWH, twice-daily dosing*. This dosing regimen may be associated with an increased risk of hematoma. The first dose of LMWH should be administered no sooner than 24 hours postoperatively. Epidural catheters should not be maintained in this situation but may be left in overnight and should be removed at least 2 hours before the first LMWH dose.
- *Prophylactic LMWH, single-daily dosing*. Epidural catheters may be maintained in this situation but only after a thorough risk/benefit analysis. The first dose of LMWH should be given 6 to 8 hours postoperatively. The second dose should be given no sooner than 24 hours after the first dose. The epidural catheter should be removed 10 to 12 hours after the last dose of LMWH, and the subsequent dose should be given no sooner than 2 hours after catheter removal.
- *Treatment dose LMWH*. Epidural catheters should not be maintained in this situation. The first dose of LMWH should be given 24 hours after catheter removal.

Oral Anticoagulants

- *Aspirin*. There is no contraindication to neuraxial anesthesia in patients taking aspirin alone (81 mg or 325 mg).
- *NSAIDs*. There is no contraindication to neuraxial anesthesia in patients taking NSAIDs alone.
- *Preoperative Coumadin*

  a. Coumadin should be stopped 4 to 5 days before a neuraxial block, and the patient should not be on any additional antiplatelet or anticoagulant medications.

  b. The prothrombin time/international normalized ratio (PT/INR) should be measured before the block and should be normalized. Of note, if warfarin is stopped for less than 4 days, INR (determined mainly by factors II and X) may not be reflective of coagulation status (determined mainly by factor VII).

  c. Clinicians' threshold for neuraxial blockade vary. The recommendation is that the block may be placed once the INR is normalized. Many suggest an epidural may be placed if the INR is less than or equal to 1.2 and that a spinal may be placed if the INR is less than or equal to 1.3. This differs from INR threshold for patients not taking warfarin chronically, as in this case, the INR is more reflective of overall coagulation factor status and an INR less than or equal to 1.4 is adequate.

  d. For patients receiving an initial preoperative Coumadin dose, the PT/INR should be checked before neuraxial block if the first dose was given more than 24 hours earlier or if a second dose has been given.

- *Postoperative Coumadin*

  a. Epidural catheters may be maintained in patients on Coumadin up until the INR is less than 1.5. The PT/INR should

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be monitored daily and assessed before catheter removal.

b. Epidural catheters should be removed while the INR is less than 1.5.

c. If the INR is greater than 1.5, consider discontinuing other medications that may affect coagulation or administration of fresh frozen plasma followed by a repeat coagulation profile prior to epidural catheter removal. These patients should be monitored closely after removal of the catheter for signs of neurologic dysfunction.

- *Preoperative clopidogrel (Plavix) and ticlopidine (Ticlid)*

a. Plavix must be held for a minimum of 7 days before neuraxial block placement.

b. Ticlid must be held for a minimum of 14 days before neuraxial block placement.

- *Preoperative abciximab, eptifibatide, and tirofiban*

a. GPIIb/IIIa inhibitors are profound inhibitors of platelet aggregation. Consider confirming platelet function prior to neuraxial block.

b. Abciximab must be held for a minimum of 24 to 48 hours prior to neuraxial blockade.

c. Eptifibatide and tirofiban must be held 4 to 8 hours prior to block placement.

Interim Update

In advance of the fourth edition guidelines, ASRA has provided recommendations for newer anticoagulant and antiplatelet agents that are commonly being used. Because many of these medications have not been available long, little post-market surveillance data is available to determine complication rates. Accordingly, many of the following recommendations are based on pharmacokinetics and the goal of allowing five half-lives to elapse to allow drug clearance prior to neuraxial blockade. All medications are recommended to be restarted greater than 6 hours after manipulation/catheter removal.

a. Apixaban should be held 3 days prior to neuraxial blockade.

b. Rivaroxaban should be held 3 days prior to neuraxial blockade.

c. Dabigatran should be held 5 days prior to block placement.

d. Ticagrelor should be held 5 to 7 days prior to neuraxial block placement.

e. Prasugrel should be held 7 to 10 days prior to block placement.

Gupta R. New anticoagulants present new challenges. *APSF Newsletter*. 2012;27(1):9-17.

Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (third edition). *Reg Anesth Pain Med*. 2010;35(1):64-101. http://www.asra.com. Accessed November 9, 2015.

B. Chronic Opioid Therapy and Perioperative Pain Management

B.1. How does chronic opioid therapy influence postoperative pain management?

In recent years, a greater emphasis has been placed on pain as an important health problem, with The Joint Commission even labeling pain as the “fifth vital sign.” Consequently, opioids now play a greater role in the treatment of chronic pain of various causes. This has resulted in a rapid increase in the consumption of opioid analgesics. For example, between 1999 and 2003, the annual sales of outpatient opioid analgesics in the United States increased by approximately 130%. Because more patients are treated chronically with opioids, every anesthesiologist is likely to be confronted with acute pain management issues in these patients. Chronic opioid-consuming patients can experience significant postoperative pain given that health care professionals are not accustomed to their markedly increased opioid requirements.

Patients on long-term opioid therapy are more likely to require higher doses of opioids postoperatively. Although the prevalence of chronic opioid-consuming patients who present for surgery is not described, the growing use of opioids is

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likely to increase the number of such patients. Patients with chronic pain are more likely to have high levels of postoperative pain, and increased postoperative pain has been associated with an increased risk of chronic postsurgical pain. Therefore, the aggressive treatment of postoperative pain is important for patients with chronic pain because they may represent a population that is particularly vulnerable to develop chronic postsurgical pain.

Although available data are limited, the management of postoperative pain seems to be more difficult in chronic opioid-consuming patients even when they consume only a modest daily opioid dose. Tolerance to any one opioid preparation results in a clinically measurable increased tolerance to most others.

Carroll IR, Angst MS, Clark JD. Management of perioperative pain in patients chronically consuming opioids. *Reg Anesth Pain Med*. 2004;29:576-591.

Mehta V, Langford RM. Acute pain management for opioid dependent patients. *Anaesthesia*. 2006;61:269-276.

Swenson JD, Davis JJ, Johnson KB. Postoperative care of the chronic opioid-consuming patient. *Anesthesiol Clin North America*. 2005;23:37-48.

B.2. What are the causes for increased postoperative pain and opioid consumption in patients chronically using opioids?

Chronic exposure to opioids may result in a need to increase the dose over time to maintain the desired analgesic effect. The need for escalating the dose is often attributed to the development of tolerance. However, dose escalation can be the result of other factors, such as the progression of the underlying disease.

Recent evidence points to opioid-induced hyperalgesia as an alternative neuropharmacologic phenomenon to explain the need to escalate the opioid dose over time. Paradoxically, administration of opioids may induce an increased sensitivity to pain (hyperalgesia). Further complicating matters, the phenomena of tolerance and hyperalgesia can coexist.

Clinical surveys of long-term opioid use in patients with both cancer and non-malignancyassociated pain have not shown escalating drug dosage to be inevitable; however, some degree of dose increase over time is often observed, particularly in younger patients and with use of short-acting opioids.

Carroll IR, Angst MS, Clark JD. Management of perioperative pain in patients chronically consuming opioids. *Reg Anesth Pain Med*. 2004;29:576-591.

Malhotra V, Bal R, Diwan S. Perioperative pain management. In: *AUA Update Series*. Linthicum, MD: American Urological Association, Education and Research; 2007;26:338-343.

Mitra S, Sinatra RS. Perioperative management of acute pain in the opioid-dependent patient. *Anesthesiology*. 2004;101:212-227.

B.3. What are the main differences between a chronic opioid-consuming patient and a patient who abuses or is addicted to opioids?

Patients undergoing surgery may not admit that they are actively abusing or addicted to pain medications; however, several differences may clue the practitioner to possible aberrant use.

First, the daily dose of opioid consumed by opioid-abusing patients before surgery is typically larger and may differ from that reported, which can often be confirmed by checking a prescription monitoring program, available in many states. Second, opioid-abusing or opioid-addicted patients often suffer from coexisting psychiatric diseases. For example, heroin addicts have an elevated prevalence of depression, anxiety, psychosis, and personality disorders. Depression and anxiety are independent predictors of severe pain after surgery and may complicate the management of postoperative pain. Although it is useful to identify abuse or addiction, many of the perioperative management issues with respect to chronic pain opioid-consuming patients also apply to patients who abuse or are addicted to opioids. The attitude of health care providers toward the use of opioids for controlling pain may be influenced by the abuse history, which makes these patients particularly vulnerable to inadequate postoperative pain control.

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Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148.

Hudson S, Wimsatt LA. How to monitor opioid use for your patients with chronic pain. *Fam Pract Manag*. 2014;21(6):6-11.

Lewis NL, Williams JE. Acute pain management in patients receiving opioids for chronic and cancer pain. *Contin Educ Anaesth Crit Care Pain.* 2005;5(4):127-129.

B.4. What issues need to be considered in the opioid-tolerant patient who is scheduled for surgery?

Tolerance develops at different rates to desired (analgesia) and undesired effects (sedation, nausea, euphoria, respiratory depression, constipation). Long-term use of opioids results in tolerance to some opioid effects such as analgesia, nausea, sedation, and respiratory depression but not to miosis or constipation. Cross-tolerance with other opioids also occurs. Opioid-tolerant patients report higher pain scores at rest and on movement and also remain longer under the care of APSs than do other patients. The incidence of opioid-induced nausea and vomiting, however, may be lower in opioid-tolerant patients.

Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148.

Jage J, Bey T. Postoperative analgesia in patients with substance use disorders: part I. *Acute Pain*. 2000;3:141-156.

Lewis NL, Williams JE. Acute pain management in patients receiving opioids for chronic and cancer pain. *Contin Educ Anaesth Crit Care Pain.* 2005;5(4):127-129.

Rapp SE, Ready LB, Nessly ML. Acute pain management in patients with prior opioid consumption: a casecontrolled retrospective review. *Pain*. 1995;61:195-201.

B.5. What would be your strategy regarding preoperative information and choice of anesthesia technique?

Acute pain management in opioid-dependent patients is a complex issue. There is a tendency among providers to use opioids sparingly, resulting in both poor pain management and withdrawal phenomena. As a result, patients may react with a degree of suspicion, mistrust, or even hostility. Patients need to be reassured that their drug history and dependence will not be an obstacle to the relief of pain. During assessment, care should be exercised to maintain privacy and confidentiality.

Despite the increasing prevalence of opioid dependency, there are few controlled studies available to guide the anesthesiologist in optimizing anesthetic and analgesic care. Because the minimum daily opioid dose that significantly increases postoperative opioid requirements and pain is not known, all patients on chronic opioids should be informed about the potential for severe pain and increased opioid requirements during the postoperative period. Patients should be informed about alternative analgesic techniques that complement opioids.

The selection of anesthesia technique has to be done on an individual basis because there are no data available favoring general, regional, or combined anesthesia for this specific patient population. Although there is no evidence indicating superiority of regional anesthesia for chronic pain patients, individual consideration is likely to favor regional anesthesia. Expert opinion suggests that opioid-tolerant patients should be offered regional or neuraxial anesthesia

or analgesia. Advantages of a regional anesthetic and analgesic approach include reduction in opioid requirements and improvement in distal perfusion as a result of sympathetic blockade.

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Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148.

Kopf A, Banzhaf A, Stein C. Perioperative management of the chronic pain patient. *Best Pract Res Clin Anaesthesiol*. 2005;19:59-76.

Lewis NL, Williams JE. Acute pain management in patients receiving opioids for chronic and cancer pain. *Contin Educ Anaesth Crit Care Pain.* 2005;5(4):127-129.

B.6. What are the choices for perioperative pain management in opioid-tolerant patients?

Management of these patients should focus on two main goals: (1) effective analgesia and (2) prevention of withdrawal. Preexisting opioid medications must be continued throughout the perioperative period to provide baseline analgesia and to avoid withdrawal. This applies for general anesthesia as well as regional anesthesia. During surgery, the required opioid dose consists of the daily opioid dose taken before surgery and the opioid dose necessary for the surgical intervention. The use of a continuous infusion of opioid may be the best way to provide a steady serum concentration if the oral route is unavailable, as is the case intraoperatively.

Catching up on the opioid dose in the postoperative period can be difficult because of inevitable delays in obtaining and administering opioids at the bedside, the high levels of pain that patients may experience, and a possible reluctance of recovery room staff to administer a sufficiently large opioid dose. Requirements for individual patients are difficult to predict; however, patients who use even modest opioid doses (<50 mg per day oral morphine equivalent) before surgery may often require their baseline opioid dose plus two or more times the amount of opioids typically used for adequate pain control in opioid-naive patients.

Regional anesthesia techniques have many benefits and may be particularly useful in chronic opioid-consuming patients because they provide excellent analgesia to patients prone to severe postoperative pain experiences and avoid the need for high-dose opioids. Neuraxial opioids have also been used effectively in opioid-tolerant patients, and although higher doses are often required, these generally do not result in an increase in adverse effects.

Nevertheless, chronic opioid-consuming patients treated with regional and neuraxial techniques for postoperative pain control should also have access to systemic opioids by the intravenous or oral route for prevention of opioid withdrawal. IV-PCA is a useful modality for pain relief in opioid-tolerant patients, provided that pain intensity and opioid consumption are monitored and background requirements are provided if the patient cannot take their usual opioid. Larger bolus doses will often be needed. Opioid rotation (i.e., using an opioid that is different from their preadmission opioid) may also be of use. If preoperative opioid use is substantial, a long-acting intravenous agent such as methadone or a basal rate PCA may be required, although in general the amount of opioid to avoid withdrawal is much lower than the patient's usual dose.

Withdrawal from opioids should be prevented by maintenance of normal preadmission opioid regimens where possible, or appropriate substitutions with another opioid or the same opioid through another route. It may be of benefit to check preadmission opioid doses with the patient's doctor or pharmacist. The use of unauthorized additional opioids (licit or illicit) or diversion may affect both pain relief and the risk of adverse effects.

Ketamine can reduce opioid requirements in opioid-tolerant patients, both intraoperatively and postoperatively. It is an *N*-methyl-D-aspartic acid receptor antagonist and results in analgesia by inhibiting the processing of nociceptive information. Evidence shows that the addition of *N*-methyl-D-aspartic acid receptor antagonists with other analgesics or as a sole agent for chronic (e.g., complex regional pain syndrome), ischemic, or neuropathic pain states can reduce the requirement for other analgesic agents. When ketamine is used as a continuous infusion in the postoperative setting, it can have an opioid-sparing effect, although there is no reduction in opioid-related side effects. It can also serve as a bridge until the patient is able to tolerate home oral regimen. Perioperatively, ketamine is best used as an adjunct to opioid medications.

Multimodal analgesic regimens including combinations of NSAIDs, APAP, gabapentinoids, and topical local anesthetics are likely to provide benefit as well. Opioid antagonists (naloxone, naltrexone) or mixed agonist-antagonists (e.g., buprenorphine, pentazocine) should be avoided because their use precipitates acute withdrawal reactions.

Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148.

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Hocking G, Cousins MJ. Ketamine in chronic pain management: an evidence-based review. *Anesth Analg*. 2003;97:1730-1739.

Lewis NL, Williams JE. Acute pain management in patients receiving opioids for chronic and cancer pain. *Contin Educ Anaesth Crit Care Pain.* 2005;5(4):127-129.

Subramaniam K, Subramaniam B, Steinbrook RA. Ketamine as adjuvant analgesic to opioids: a quantitative and qualitative systematic review. *Anesth Analg*. 2004;99:482-495.

B.7. What issues need to be considered before discharging an opioid-tolerant patient?

Discharge planning must take into account the potential for prescribed opioids to be abused or misused. Appropriate use of nonopioid analgesics where possible, communication with the primary physician, and patient education and support must all be considered.

Chronic opioid-consuming patients typically require significantly higher postoperative opioid doses for adequate pain control than they received before surgery for their chronic pain symptoms. Attempting to discharge chronic opioid-consuming patients on the same opioid regimen they adhered to before surgery often results in inadequate pain control. Whatever the final oral dose chronic opioid-consuming patients are stabilized on at discharge, a slow tapering from this dose toward the preoperative opioid dose over 2 to 4 weeks is often a reasonable goal. In the case under consideration, the transdermal fentanyl patch should be left in place to provide the patient's preexisting opioid requirement, and additional shortacting analgesics should be prescribed for postoperative pain. It is also advisable to counsel the patient to discuss opioid prescribing with the existing outpatient providers because many physicians require an opioid contract with single-provider prescribing for controlled substances.

Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148.

Lewis NL, Williams JE. Acute pain management in patients receiving opioids for chronic and cancer pain. *Contin Educ Anaesth Crit Care Pain.* 2005;5(4):127-129.

C. Perioperative Pain Management for Ambulatory Surgery

C.1. What would be your preoperative considerations and advice to the patient?

Adequate postoperative pain management is often the limiting factor when determining whether a patient can have surgery performed as an ambulatory surgical procedure. Ensuring that the patient has appropriate expectations of the outcome of laparoscopic cholecystectomy is critical for a successful conclusion to the procedure, especially with regard to postoperative pain. Unrealistic expectations for no pain at all can be met with anger, disappointment, and the fear and anxiety that something has gone wrong. Failure to meet unrealistic expectations can even lead to litigation.

Planning for postoperative pain management should begin in the preoperative period. Patient education regarding the degree of pain that might be expected and discussion of the pain assessment tools and modalities of pain treatment that might be utilized should reduce the patient's anxiety and the fear of unrelieved pain. Reduced patient anxiety has been shown to reduce the incidence and severity of postoperative pain. In addition, patients have to be made aware of the importance of communicating their analgesic needs. Patients should receive instruction on the importance of coughing, deep breathing, ambulation, and postoperative rehabilitation. Patient information on acute postoperative pain management is available from public sources such as the American Society of Anesthesiologists website, and patients can be directed to these sources for self-study.

Details of the complications of laparoscopic cholecystectomy given to patients vary between countries and cultures. The most relevant for postoperative pain is to mention the risk of conversion to open laparotomy in a small percentage of

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cases, which will be associated with a significantly larger incision, more pain, and longer period of hospitalization. Patients need to be informed that there are three types of pain often associated with laparoscopic cholecystectomy: (1) incisional, (2) visceral, and (3) shoulder pain. It is helpful to describe, in particular, the high incidence of referred pain in the shoulders and to reassure the patient that this is related to the laparoscopy and not necessarily his or her heart or chest. The patient should be informed that there is a relatively high risk of postoperative nausea and vomiting after laparoscopic cholecystectomy (˜30% to 50%) and that appropriate prophylaxis will be administered (antiemetic strategies can be tailored based on clinical risk assessments such as the Apfel risk score for nausea and vomiting).

Predischarge patient information should also include the following: (1) that patients will receive analgesic and/or antiemetic medications for management of pain and postoperative nausea and vomiting at home, (2) that the care team will make a follow-up call and schedule a follow-up appointment, and (3) that they will get contact telephone numbers in case there are problems or questions.

Apfel CC, Heidrich FM, Jukar-Rao S, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. *Br J Anaesth*. 2012;109(5):742-753.

Crews JC. Multimodal pain management strategies for office-based and ambulatory procedures. *JAMA*. 2002;288:629-632.

Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148.

Rawal N. Analgesia for day-case surgery. *Br J Anaesth*. 2001;87:73-87.

C.2. What are the consequences of inadequate pain management after ambulatory surgery?

In the ambulatory setting, the type of surgery is a significant predictor of severity of postoperative pain. Even when postoperative pain is effectively treated in the postanesthesia care unit, it often recurs once the patient has returned home. A common example is a peripheral nerve block for orthopedic surgery, which provides excellent analgesia until the block has worn off several hours later.

Uncontrolled pain is associated with an increased incidence of postoperative nausea, agitation, prolonged postanesthesia care unit stay, delayed discharge from an ambulatory facility, and unanticipated hospital admission. Inadequate postoperative pain control is also the most frequent reason for patients to contact their family practitioner after discharge from the hospital. Importantly, the presence of postoperative symptoms including pain contributes to patient dissatisfaction with their surgical experience (see Table 51.1).

Chung F, Ritchie E, Su J. Postoperative pain in ambulatory surgery. *Anesth Analg*. 1997;85:808-816.

Rawal N, Hylander J, Nydahl PA, et al. Survey of postoperative analgesia following ambulatory surgery. *Acta Anaesthesiol Scand*. 1997;41:1017-1022.

TABLE 51.1 Consequences of Inadequate Pain Management after Ambulatory Surgery

Increased postanesthesia care unit stay

Increased phase II unit stay

Delayed discharge at home

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Unanticipated hospital admission

Increased contact with family practitioner

Delayed return to daily living function

Decreased patient satisfaction

C.3. What is the role of premedication or preoperative analgesic?

Preoperative administration of opioid or nonopioid analgesics reduces analgesic requirements and pain scores in the immediate postoperative period. However, opioid premedication is controversial in the ambulatory setting because it may increase the incidence of opioidrelated side effects and even delay recovery. Premedication with oral NSAIDs or gabapentinoids given before surgery can avoid these concerns and reduce the degree of postoperative pain, analgesic requirements, and time to discharge, although no effect on development of chronic pain has been demonstrated.

Preemptive analgesia refers to the concept that an analgesic medication or intervention administered before surgical tissue injury may produce a greater effect than the same medication or intervention administered following surgical tissue injury. This preemptive analgesic effect has been demonstrated for several different medications in animal models, but clinical studies do not support a significant role for preemptive analgesia in human patients. For multiple surgical procedures including thoracic and abdominal procedures, laparoscopic, and open, there is no strong evidence that preincisional timing of analgesic administration (preemptive analgesia) decreases the intensity or duration of postoperative pain, when compared with intraoperative or postoperative administration.

Elvir-Lazo OL, White PF. The role of multimodal analgesia in pain management after ambulatory surgery. *Current Opin Anesthesiol*. 2010;23:697-703.

Møiniche S, Kehlet H, Dahl JB. A qualitative and quantitative systematic review of preemptive analgesia for postoperative pain relief: the role of timing of analgesia. *Anesthesiology*. 2002;96:725-741.

C.4. Does the choice of anesthetic technique influence postoperative pain?

The choice of anesthetic technique has been shown to have a significant influence on postoperative analgesia in patients undergoing ambulatory surgery. Regional anesthesia techniques offer a number of advantages in outpatient surgery, including prolonged postoperative analgesia.

Opioids remain the primary drugs used to provide intraoperative analgesia. However, the role of opioids in ambulatory surgery remains controversial. The use of opioids may be associated with a dose-dependent increase in adverse effects, including nausea, vomiting, sedation, bladder dysfunction, and respiratory depression, all of which may contribute to a delayed recovery.

One peer-reviewed study prospectively examined the effect of a neuraxial technique on postoperative pain management in patients for laparoscopic cholecystectomy. This study examined combined epidural and general anesthesia (CEGA) versus total intravenous anesthesia (TIVA) and showed a reduction in postoperative pain scores for CEGA versus TIVA. However, an epidural technique is not recommended for routine anesthetic management in patients undergoing laparoscopic cholecystectomy because the majority of patients do not convert to open procedures and thus the incisions are small and minimally painful. Nevertheless, in certain high-risk patients (multiple prior abdominal surgeries, poor pulmonary reserve, etc.), CEGA can be justified.

TIVA offers an alternative to inhalational anesthesia, and although rapid recovery from anesthesia and reduction in nausea and vomiting are recognized benefits, the analgesic components of TIVA have a very short duration and do not contribute to improved postoperative analgesia.

There is enough evidence in the literature to support the use of incisional local anesthetic infiltration at end of surgery. Infiltration of the surgical wound with local anesthetic can provide excellent analgesia that outlasts the duration of action of

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the local anesthetics themselves. Another simple and effective method of reducing the intensity of postlaparoscopic pain is intraperitoneal instillation of local anesthetic. Evidence suggests significant pain relief after laparoscopic cholecystectomy when 15 to 20 mL of 0.5% bupivacaine is administered into the hepato-diaphragmatic space.

Gupta A, Thörn SE, Axelsson K, et al. Postoperative pain relief using intermittent injections of 0.5% ropivacaine via an intra-abdominal catheter following laparoscopic cholecystectomy. *Anesth Analg*. 2002;95:450-456.

Kehlet H, Gray AW, Bonnet F, et al. A procedure-specific systematic review and consensus recommendations for postoperative analgesia following laparoscopic cholecystectomy. *Surg Endosc*. 2005;19:1396-1415.

C.5. Are nonsteroidal anti-inflammatory drugs (NSAIDs) effective? If so, does the choice of drug matter?

The opioid-sparing effects of NSAIDs lower the risk of postoperative nausea and vomiting, pruritus, constipation, and respiratory depression, thereby improving patient comfort and allowing for an earlier discharge.

The introduction of a parenteral preparation of NSAID and the widespread acceptance of the concept of multimodal “balanced” analgesia has increased the popularity of NSAIDs in the management of perioperative pain. NSAIDs available for intravenous use include ketorolac, diclofenac, indomethacin, ketoprofen, tenoxicam, ibuprofen, and lornoxicam.

However, NSAIDs have weaker analgesic properties than opioids or local anesthetics and also exhibit a “ceiling effect” with respect to their maximum analgesic effect. Despite their limitations, NSAIDs may decrease the risk of breakthrough pain because of their more prolonged duration of action and are valuable adjuvants when used in combination with opioids and local anesthetics.

There is no documented evidence of superiority of any particular NSAID for perioperative use. Therefore, the choice of NSAID is dependent upon the route of administration, the duration of the analgesia, propensity for side effects, and the cost. The oral availability of most NSAIDs is high. Overall, NSAIDs appear to be safe and well tolerated in patients undergoing ambulatory surgery.

COX-2 inhibitors have been demonstrated in multiple clinical trials to produce analgesic efficacy equal to that of the traditional nonselective NSAIDs without the COX-1-mediated adverse effects of inhibition of platelet aggregation or gastroduodenal ulceration. COX-2 inhibitors used over a short period for postoperative analgesia have not been demonstrated to cause any major adverse events in healthy patients.

Kehlet H, Gray AW, Bonnet F, et al. A procedure-specific systematic review and consensus recommendations for postoperative analgesia following laparoscopic cholecystectomy. *Surg Endosc*. 2005;19:1396-1415.

Lemos P, Jarrett P, Phillips B, eds. *Day Surgery Development and Practice*. London: International Association for Ambulatory Surgery; 2006:209-227.

Malhotra V, Bal R, Diwan S. Perioperative pain management. In: *AUA Update Series*. Linthicum, MD: American Urological Association, Education and Research; 2007;26:338-343.

C.6. What is the role of surgical technique in influencing postoperative pain after a laparoscopic cholecystectomy?

There are three types of pain after laparoscopic cholecystectomy: incisional, subphrenic, and shoulder pain. Factors responsible for the pain may be related to surgical incisions, carbon dioxide insufflation, and the intra-abdominal pressures maintained during the laparoscopic procedure. Higher insufflation pressures should be avoided because they can significantly increase the severity of postoperative pain. Subphrenic and shoulder pain after laparoscopic procedures appear to arise from diaphragmatic and phrenic nerve irritation due to insufflated carbon dioxide. This pain tends to be aggravated by ambulation and may persist for several days after surgery. Residual insufflating gas can also increase the intensity of postlaparoscopic pain. Therefore, the abdomen should be actively deflated at the end of the laparoscopic procedure.

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Evidence from prospective studies to prevent postoperative pain after laparoscopy includes the following findings:

- Low-pressure CO_2 pneumoperitoneum is superior to conventional CO_2 pneumoperitoneum.
- There is insufficient data to recommend warmed CO_2 pneumoperitoneum for reducing postoperative pain.
- Peritoneal lavage after CO_2 pneumoperitoneum is effective in reducing postoperative pain.
- Helium pneumoperitoneum has no advantage versus CO_2 pneumoperitoneum.

Alexander JI. Pain after laparoscopy. *Br J Anaesth*. 1997;79:369-378.

Phelps P, Cakmakkaya OS, Apfel CC, et al. A simple clinical maneuver to reduce laparoscopy-induced shoulder pain: a randomized controlled trial. *Obstet Gynecol*. 2008;111(5):1155-1160.

C.7. What would be your strategy for pain control after discharge home?

After discharge, APAP, NSAIDs, or opioids, either alone or in combination, are frequently used to provide postoperative pain relief.

APAP and paracetamol are thought to work through central inhibition of prostaglandin synthesis. They are commonly used due to easy tolerability and good safety profile. Care should be taken when using opioid/APAP combination products as the APAP component of the combination should be considered the limiting factor for use, generally no more than 3 to 4 g daily.

NSAIDs inhibit cyclooxygenase, thereby decreasing inflammation and pain related to local tissue injury. They inhibit platelet function to variable degrees and for this reason are sometimes contraindicated in the immediate postoperative period. Nonetheless, because the majority of postoperative pain is nociceptive and inflammatory, NSAIDs can often be of great benefit.

Opioids are indicated in the acute postoperative period, exerting their effects centrally in the spinal cord and brain. Generally, because postsurgical pain is acute rather than chronic in nature, short-acting opioids such as oxycodone, hydromorphone, or hydrocodone for breakthrough pain every 3 to 4 hours as needed are sufficient. If necessary, a dose range may be provided to cover mild, moderate, and severe pain. In patients with frequent need for breakthrough dosing, however, a long-acting formulation (methadone, fentanyl patch, or extended-release formulation of a short-acting opioid) on a scheduled basis may also be required.

If pain does not improve or if escalating rather than tapering doses of opioids are observed, antineuropathic agents are often initiated. These include topical agents such as lidocaine 5% cream or patch, gabapentinoids, tricyclic antidepressants, and selective norepinephrine reuptake inhibitors. If a patient requires these additional interventions, they will often benefit from an APS consult and possible outpatient pain management follow-up.

Malhotra, A. Pain management: interventional and pharmacologic approaches. In Jacob B, Chen D, Towfigh S, eds. *SAGES Manual of Groin Pain*. Switzerland: Springer International. In press.

Rawal N. Analgesia for day-case surgery. *Br J Anaesth*. 2001;87:73-87.

D. The Role of an Acute Pain Service

D.1. What is the extent of the problem, and which patients are at greatest risk of undertreatment?

Pain relief after surgery continues to be a major medical challenge. Despite a significant improvement over the last decade in our understanding of acute and chronic pain mechanisms and the establishment of APSs, recent studies continue to report that postoperative pain management is not satisfactory for many patients. In addition, publications of guidelines for acute pain management, the introduction of pain as “the fifth vital sign,” and the incorporation of the standards advocated by The Joint Commission have not yet translated into improved postoperative analgesia.

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More than 30% of patients report moderate to severe pain after surgery. More recent surveys of postdischarge pain put that number even higher. Clinical risk scores to identify patients most at risk for postoperative pain are scarce and not commonly used in practice. Certain patient subpopulations are at greater risk of undertreatment, including infants and children, the elderly, ethnic minorities, and patients with psychiatric illness or those unable to communicate.

Apfelbaum JL, Chen C, Mehta SS, et al. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. *Anesth Analg*. 2003;97:534-540.

Ashburn MA, Caplan RA, Carr DB, et al. Practice guidelines for acute pain management in the perioperative setting. *Anesthesiology*. 2004;100:1573-1581.

D.2. What are the consequences of inadequate postoperative pain relief?

Evidence suggests that inadequate relief of postoperative pain results in harmful physiologic and psychological consequences that lead to significant morbidity, delaying recovery and the return to activities of daily living. Postoperative splinting can lead to atelectasis, and autonomic overactivity associated with pain can result in increased myocardial oxygen demand and increased incidence of perioperative myocardial infarction in at-risk adults. In children, postoperative pain has been found to be an important cause for long-lasting temper tantrums and behavioral changes. In addition, the presence of postoperative pain significantly contributes to patients' dissatisfaction with their anesthesia and surgical experience.

Chronic pain after surgery, also referred to as persistent postsurgical pain, has long been recognized as a major factor in delaying recovery and return to normal daily living. Long-lasting pain is often reported after several common surgical procedures including thoracotomy, mastectomy, hernia repair, and limb amputation. Predisposing risk factors include the severity of preoperative and postoperative pain, intraoperative nerve injury, and psychological vulnerability. Specific early analgesic interventions may reduce the incidence.

Dworkin RH, McDermott MP, Raja SN. Preventing chronic postsurgical pain: how much of a difference makes a difference? *Anesthesiology*. 2010;112(3):516-518.

Joshi GP, Ogunnaike BO. Consequences of inadequate postoperative pain relief and chronic persistent postoperative pain. *Anesthesiol Clin North America*. 2005;23:21-36.

D.3. What is the role of an acute pain service (APS) in improving postoperative pain management?

The immediate solution to the problem of inadequate pain relief lies not so much in the development of new analgesic drugs or technologies but in the development of an appropriate organization to utilize existing expertise effectively.

Moreover, effective acute pain management results from education and organizational structure for the delivery of pain relief rather than the specific analgesic techniques themselves. Even simple methods of pain relief can be more effective if proper attention is given to their appropriate, evidence-based use. In many institutions, APSs assume responsibility for managing more advanced methods of pain relief such as patient-controlled analgesia, epidural analgesia, and peripheral nerve catheters to ensure patients receive optimum care from providers well-versed with these analgesic modalities. Additionally, APSs often follow chronic pain patients who are difficult for primary teams to manage and whose complex pain issues are best treated using a multimodal approach.

American Society of Anesthesiologists. Practice guidelines for acute pain management in the perioperative setting: an updated report by American Society of Anesthesiologists, Task Force on Acute Pain Management. *Anesthesiology*. 2012;116:248-273.

Rawal N. Organization, function, and implementation of acute pain service. *Anesthesiol Clin North America*. 2005;23:211-225.

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Werner MU, Søholm L, Rotbøll-Nielsen P, et al. Does an acute pain service improve postoperative outcome? *Anesth Analg*. 2002;95:1361-1372.

D.4. Does an APS improve postoperative outcome?

The introduction of APSs has led to an increase in the appropriate use of specialized analgesic techniques, such as IV-PCA, neuraxial blockade, and peripheral nerve catheters. The implementation of these techniques is an advance in improving analgesia and patient wellbeing and in reducing postoperative morbidity. In addition, an APS may reduce "analgesic gaps" that can occur during the transition from IV-PCA or epidural analgesia to oral analgesic therapy. Although evaluating the safety of analgesic techniques is an important objective of an APS, its role in preventing and reducing adverse events has not been well-documented; however, consolidation of decisions regarding pain regimens under one service is likely to have several benefits. First, standardization of protocols decreases prescription or drug administration error. Second, having one service responsible for pain orders decreases

the incidence of redundancy and multiple opioid orders. Finally, the availability of a service primarily dedicated to pain is likely to increase the efficacy of interventions and decrease patient pain scores.

In a literature review, Werner et al. evaluated the effects of an APS on postoperative outcome in 44 retrospective and 4 prospective clinical trials including 84,097 postoperative patients. The authors found that the implementation of an APS was associated with a significant decrease in pain intensity. In addition, the introduction of an APS was associated with less postoperative nausea and vomiting and urinary retention. However, the authors could not draw clear conclusions about patient satisfaction or postoperative morbidity due to a large variability in the studies regarding composition of the APSs and services provided.

Pöpping DM, Zahn PK, Van Aken HK, et al. Effectiveness and safety of postoperative pain management: a survey of 18 925 consecutive patients between 1998 and 2006 (2nd revision): a database analysis of prospectively raised data. *Br J Anaesth*. 2008;101:832-840.

Rawal N. Organization, function, and implementation of acute pain service. *Anesthesiol Clin North America*. 2005;23:211-225.

Werner MU, Søholm L, Rotbøll-Nielsen P, et al. Does an acute pain service improve postoperative outcome? *Anesth Analg*. 2002;95:1361-1372.

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Chapter 52
Acupuncture

Yuan-Chi Lin

A 68-year-old woman was scheduled for arthroscopic surgery of her right knee. She experienced severe postoperative nausea and vomiting in the postanesthesia care unit. Despite the use of conventional therapies, her nausea and vomiting persisted. Her past medical history was significant for a mastectomy for breast cancer, an anxiety disorder, headaches, chronic neck and back pain, osteoarthritis in her knees, peptic ulcer disease, and an allergy to Novocain. What role can acupuncture therapy play in her care?

A. Acupuncture as a Complementary Medical Therapy

1. What is acupuncture?
2. How is acupuncture practiced? (Videos 52.1 and 52.2)
3. What are the mechanisms of acupuncture analgesia?
4. What were the conclusions of the National Institutes of Health Consensus Conference about acupuncture?

B. Acupuncture for the Treatment of Chronic Conditions

1. Can acupuncture be used for the treatment of postoperative nausea and vomiting?
2. Can acupuncture be used for the treatment of chemotherapy-induced nausea and vomiting?
3. How effective is acupuncture for the management of chronic headache?
4. Can acupuncture be used for the treatment of chronic neck and back pain?
5. Can acupuncture be used for the treatment of osteoarthritis?
6. What role can acupuncture play in the care of patients with cancer?
7. Can acupuncture/acupressure be used for decrease anxiety?
8. In the clinical setting, is ear acupressure useful for alleviating anxiety and pain?

C. Complications

1. What are the possible complications of acupuncture treatment?

A. Acupuncture as a Complementary Medical Therapy

A.1. What is acupuncture?

Acupuncture is one of the treatment modalities of comprehensive traditional Chinese medicine. The word *acupuncture* is derived from the Latin words *acus*, “needle,” and *punctura*, “a pricking.” The original Chinese term for acupuncture is *Jin Jiao*, which describes the practice of “acupuncture and moxibustion.” Moxibustion, which is the burning of moxa (*Artemisia vulgaris*) over the acupuncture points, can also be used.

The history of traditional Chinese medicine can be traced back 3,000 years. The *Yellow Emperor's Classic of Internal Medicine* from the fourth century BC described the practice of

puncturing the body for pain relief. Traditional Chinese medicine is a system of thoughts and practices that are based on the investigations of nature, causes, and effects. It takes the principles of realism and ethics and employs them for the prevention and healing of illnesses.

The *yin and yang* concept underlies the theoretical framework of acupuncture. Yin and yang are two opposite dynamics that cannot exist in isolation. Rather, they are in a constant state of dynamic balance. If yin and yang are not balanced,

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illnesses may occur in the body.

The human body is controlled by a vital force called *Qi* (pronunciation “chee”). Qi circulates throughout the body and defends its various parts. There are 365 identified acupuncture points in the body, which fall along 12 principal and eight extrameridian systems. Qi is postulated to flow through these meridians in the body.

A.2. How is acupuncture practiced? (Videos 52.1 and 52.2)

Acupuncture utilizes a technique of inserting very fine thread-thin needles into strategic points in the body called *acupuncture points*. Acupuncture needles vary from 0.5 to 5 in. in length and from 36 to 42 gauge. There are a wide variety of needles currently available. In *Huang Di Nei Jin* (*The YellowEmperor's Internal Classic*), Ling Shu described nine shapes of acupuncture needles. Sterile, disposable stainless steel acupuncture needles are the current standard for acupuncture treatment.

After sterilizing the site of the needle entrance on the skin, the acupuncture needle is inserted few millimeters into the epidermis. Following placement of the acupuncture needle, stimulation of the acupuncture point may be achieved manually or by the application of lowvoltage electrodes onto the needle in a method called *electroacupuncture*.

Each acupuncture point has a prescribed depth of insertion. Manual techniques may involve the lifting and thrusting of the needle or twisting and twirling. *De-Qi* is a typical sensation that is associated with proper acupuncture needle position. Patients describe the sensation as a feeling of soreness, numbness, warmth, heaviness, or pressure around the area where the needle is inserted. The De-Qi sensation is mediated through nonmyelinated C fibers. Many practitioners consider this sensation to be crucial in achieving the effects of acupuncture. Electroacupuncture achieves a similar effect through the use of high- or lowfrequency electricity.

Very little pain is associated with acupuncture. For various conditions, multiple acupuncture treatment sessions over an extended period may be required to achieve its greatest effectiveness.

Auricular, hand, and scalp acupuncture can be used as microsystems of acupuncture. For example, for the auricular acupuncture (Fig. 52.1), the upper region of the external ear is manipulated to alleviate conditions in the leg and feet. The middle region of the external ear represents chest and back pain. The lower regions are used to relieve headache and neurologic conditions. Auricular acupuncture can also be used for preoperative anxiety control.

The frequency, as well as the number of acupuncture treatments, varies among acupuncture providers. Most practitioners would agree that more than one treatment is necessary to experience the full effect of acupuncture.

Chernyak GV, Sessler DI. Perioperative acupuncture and related techniques. *Anesthesiology*. 2005;102:1031-1049.

A.3. What are the mechanisms of acupuncture analgesia?

Acupuncture inhibits the transmission of pain according to the gate control theory. It may act by stimulating sensory A-β fibers, thereby directly inhibiting the spinal transmission of pain by a smaller A-δ and C fibers.

Acupuncture stimulates the production of endogenous opioid peptides, such as endorphins and enkephalins, and stimulates the endogenous descending inhibitory pathways. In human studies, analysis of cerebrospinal fluid showed elevated levels of serotonin, endorphins, and enkephalins following acupuncture treatments. Acupuncture analgesia is mainly achieved by the activation of the endogenous anti-nociceptive system to modulate pain transmission and pain response. Low-frequency (2 Hz) and high-frequency (100 Hz) electrical acupuncture

selectively induces the release of enkephalins and dynorphins in both experimental animals and humans. Acupuncture analgesia may be reversed by naloxone.

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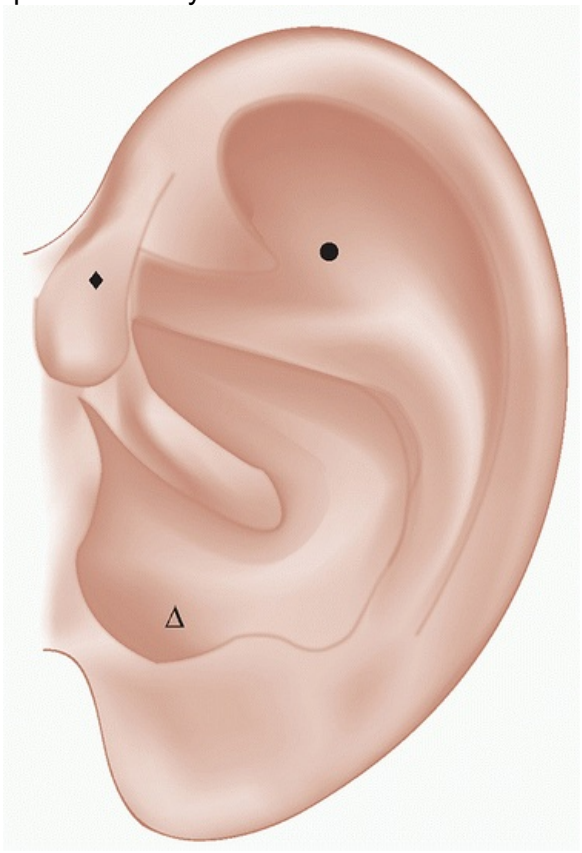


FIGURE 52.1 Auricular acupuncture. Δ, heart point; •, shen men; ♦, autonomic point.

Functional magnetic resonance imaging has been used to investigate the effect of acupuncture in normal volunteers. With functional magnetic resonance imaging, acupuncture needle manipulation on the LI 4 (Hegu) point (Fig. 52.2) is seen to modulate the activity of the limbic system and subcortical structure. Individual variation occurs in the cortical activation patterns elicited by electrical acupuncture stimulation. Real acupuncture elicited significantly higher activation than sham acupuncture over the hypothalamus and primary

somatosensorimotor cortex and deactivation over the rostral segment of anterior cingulated cortex.

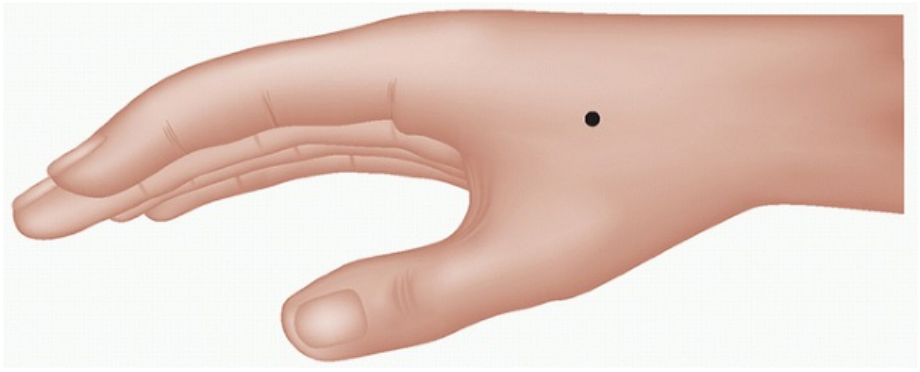


FIGURE 52.2 LI 4 (Hegu) acupuncture point is on the dorsum of the hand, between the first and second metacarpal bones, radial to the midpoint of the second metacarpal bone.

Han JS. Acupuncture and endorphins. *Neurosci Lett*. 2004;361(1-3):258-261.

Hui KK, Liu J, Makris N, et al. Acupuncture modulates the limbic system and subcortical gray structures of the human brain: evidence from fMRI studies in normal subjects. *Hum Brain Mapp*. 2000;9:13-25.

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Wu MT, Sheen JM, Chuang KH, et al. Neuronal specificity of acupuncture response: a fMRI study with electroacupuncture. *Neuroimage*. 2002;16:1028-1037.

Zhang R, Lao L, Ren K, et al. Mechanisms of acupuncture-electroacupuncture on persistent pain. *Anesthesiology*. 2014;120(2):482-503.

A.4. What were the conclusions of the National Institutes of Health Consensus Conference about acupuncture?

A National Institutes of Health Consensus Conference concluded that acupuncture is an effective therapeutic intervention that is widely practiced in the United States. Promising results have emerged supporting the efficacy of acupuncture in adult postoperative and chemotherapy-related nausea and vomiting and in postoperative dental pain. In other conditions, such as addiction, stroke rehabilitation, headache, menstrual cramps, tennis elbow, fibromyalgia, myofascial pain, osteoarthritis, low back pain, carpal tunnel syndrome, and asthma, acupuncture may also be useful as an adjunct treatment or as an acceptable alternative when included in a comprehensive management program. Further research is expected to uncover additional areas in which acupuncture interventions will be useful.

National Institutes of Health Consensus Conference. Acupuncture. *JAMA*. 1998;280:1518-1524.

B. Acupuncture for the Treatment of Chronic Conditions

B.1. Can acupuncture be used for the treatment of postoperative nausea and vomiting?

Postoperative nausea and vomiting occurs frequently following surgery and are best avoided whenever possible. Acupuncture is a commonly used therapy for the treatment of these symptoms. Stimulation of the acupuncture PC-6 (*Nei Guan acupuncture point*; in Chinese, this means *gate of the internal organ*) points by acupuncture needles, electrical apparatus, pressure, or magnets is used to achieve relief of nausea and vomiting. The PC-6 acupuncture point is located 2 cun (tsun), approximately 2.6 in., above the transverse crease of the wrist, between the tendons of the muscle palmaris longus and muscle flexor carpi radialis (Fig. 52.3).

Studies support the use of acupuncture for the treatment of postoperative nausea and vomiting. A systemic review was conducted of 33 randomized controlled trials of acupuncture

and acupressure. The results were positive in 27 of these trials. A randomized controlled trial of pediatric patients undergoing tonsillectomy using electroacupuncture in conscious patients showed significant reduction in the occurrence of nausea compared with those in the sham and control groups. The efficacy of acupuncture for postoperative nausea and vomiting prevention is similar to that of commonly used pharmacotherapies. A double-blind, randomized, placebo-controlled study revealed that hand acupressure is an effective method for reducing postoperative vomiting in children after strabismus repair.

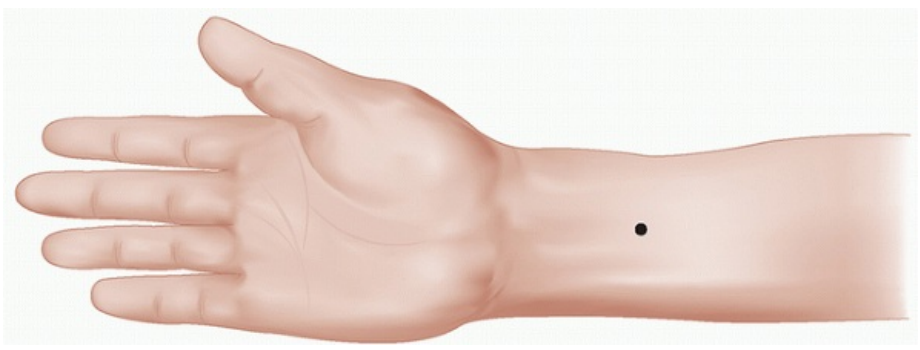


FIGURE 52.3 The PC-6 acupuncture point is located 2 cun (tsun), approximately 2.6 in., above the transverse

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crease of the wrist, between the tendons of the muscle palmaris longus and muscle flexor capri radialis.

PC-6 acupressure is a noninvasive method that may have a place as prophylactic antiemetic therapy during gynecologic surgery. Alkaissi et al. did a prospective randomized controlled trial of acupressure in the prevention of postoperative nausea and vomiting for women undergoing general anesthesia for elective gynecologic surgery with positive results.

Alkaissi A, Evertsson K, Johnsson VA, et al. P6 acupressure may relieve nausea and vomiting after gynecological surgery: an effectiveness study in 410 women. *Can J Anaesth*. 2002;49:1034-1039.

Frey UH, Scharmann P, Löhlein C, et al. P6 acustimulation effectively decreases postoperative nausea and vomiting in high-risk patients. *Br J Anaesth*. 2009;102:620-625.

Gan TJ, Diemunsch P, Habib AS, et al. Consensus guideline for the management of postoperative nausea and vomiting. *Anesth Analg*. 2014;118:85-113.

B.2. Can acupuncture be used for the treatment of chemotherapy-induced nausea and vomiting?

Acupuncture/acupressure at the PC-6 acupuncture point has been shown to have a protective effect on people experiencing chemotherapy-induced nausea and vomiting. A review of 11 randomized controlled trials studying the effectiveness of acupuncture point stimulation on chemotherapy-induced nausea and vomiting revealed that electroacupuncture reduced chemotherapy-induced acute vomiting.

Ezzo JM, Richardson MA, Vickers A, et al. Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. *Cochrane Database Syst Rev*. 2006;(2):CD002285.

B.3. How effective is acupuncture for the management of chronic headache?

Acupuncture therapy for migraine headaches has been reported to be effective in several adult studies. In a randomized controlled trial of 160 women with migraine, acupuncture was proven to be adequate for migraine prophylaxis. Relative to flunarizine, acupuncture treatment exhibited greater efficacy in the first months of therapy and better patient tolerance. A systemic review of 22 trials including a total of 1,042 patients suggests that acupuncture has a role in the treatment of recurrent headaches. In a randomized controlled trial of 401 patients with chronic migraine headache, it was also shown that through 12 months of follow-up acupuncture was relatively cost-effective. Compared with the patients in the control groups, patients receiving acupuncture used 15% less medication, made 25% fewer visits to general practitioners, and took 15% fewer sick days from work.

Cochrane database of systematic review of 11 trials with 2,317 patients with episodic or chronic tension-type headache revealed that acupuncture could be a valuable nonpharmacologic tool in patients with frequent episodic or chronic tension-type headaches. In regard to acupuncture for migraine prophylaxis, meta-analysis of 22 trials with 4,419 participants shows acupuncture to be at least as effective as, and possibly more effective than, prophylactic drug treatment with fewer adverse effects. Acupuncture should be considered a treatment option for patients willing to undergo this treatment.

Linde K, Allais G, Brinkhaus B, et al. Acupuncture for migraine prophylaxis. *Cochrane Database Syst Rev*. 2009;(1):CD001218.

Linde K, Allais G, Brinkhaus B, et al. Acupuncture for tension-type headache. *Cochrane Database Syst Rev*. 2009;(1):CD007587.

Melchart D, Linde K, Fischer P, et al. Acupuncture for recurrent headaches: a systematic review of randomized controlled trials. *Cephalalgia*. 1999;19:779-786.

Vickers AJ, Rees RW, Zollman CE, et al. Acupuncture for chronic headache in primary care: large, pragmatic,

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randomised trial. *BMJ*. 2004;328:744.

B.4. Can acupuncture be used for the treatment of chronic neck and back pain?

In a randomized controlled trial of 177 patients with chronic neck pain, the effectiveness of acupuncture, massage, and "sham" laser acupuncture were compared. A study followed 14,161 patients with chronic neck pain for a period of more than 6 months. The patients in the acupuncture group received up to 15 acupuncture sessions over 3 months. The reported neck pain levels and disability scores of the members of the acupuncture group were improved over those of the control group. Treatment success was followed and maintained for 6 months.

A large German clinical study involved 1,162 patients with chronic low back pain indicated that both "real" and "sham" acupuncture treatment were significantly better than conventional therapy for at least 6 months. Another large German study of 1,549 patients with chronic low back pain showed acupuncture plus routine care was associated with marked clinical improvements in patients with chronic low back pain and was relatively cost-effective. A systemic review that involved 23 trials of 6,359 patients with low back pain revealed that acupuncture can be a useful supplement to other forms of conventional therapy for nonspecific low back pain.

Haake M, Müller HH, Schade-Brittinger C, et al. German Acupuncture Trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with 3 groups. *Arch Intern Med*. 2007;167: 1892-1898.

Irnich D, Behrens N, Molzen H, et al. Randomised trial of acupuncture compared with conventional massage and "sham" laser acupuncture for treatment of chronic neck pain. *BMJ*. 2001;322:1574-1578.

Witt CM, Jena S, Brinkhaus B, et al. Acupuncture for patients with chronic neck pain. *Pain*. 2006;125:98-106.

Yuan J, Purepong N, Kerr DP, et al. Effectiveness of acupuncture for low back pain: a systematic review. *Spine*. 2008;33:887-900.

B.5. Can acupuncture be used for the treatment of osteoarthritis?

Evidence exists for the efficacy of acupuncture for reducing the pain and dysfunction of osteoarthritis. In a study of 300 patients with chronic osteoarthritis of the knee, participants were randomly assigned to acupuncture, minimal acupuncture, or wait-list control group. After 8 weeks of treatment, pain and joint function were improved more with acupuncture than with minimal or no acupuncture.

In another randomized controlled trial of 570 patients with osteoarthritis of the knee, the acupuncture group received 23 true acupuncture sessions over 26 weeks. Acupuncture was shown to provide improvement in function and pain relief as an adjunctive therapy for osteoarthritis of the knee when compared with credible sham acupuncture and education control groups.

In a trial of 30 patients with symptomatic osteoarthritis of the knee, participants were randomized into one of three treatment groups. One group of patients received acupuncture alone, another group of patients received acupuncture but continued on their symptomatic medication, and the third group of patients used their symptomatic medication for the first 5 weeks and then had a course of acupuncture added. The patients receiving acupuncture were treated twice weekly over 5 weeks. The results of this study concluded that manual and electroacupuncture causes a significant improvement in the symptoms of osteoarthritis of the knee, either alone or as an adjunct therapy, with no loss of benefit after 1 month.

Berman BM, Lao L, Langenberg P, et al. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med*. 2004;141:901-910.

Tukmachi E, Jubb R, Dempsey E, et al. The effect of acupuncture on the symptoms of knee osteoarthritis—an open randomised controlled study. *Acupunct Med*. 2004;22:14-22.

Witt C, Brinkhaus B, Jena S, et al. Acupuncture in patients with osteoarthritis of the knee: a randomised trial. *Lancet*.

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2005;366:136-143.

B.6. What role can acupuncture play in the care of patients with cancer?

A report of a randomized controlled trial of 90 patients with cancer pain revealed clear benefit from auricular acupuncture for cancer patients experiencing pain, despite stable analgesic treatment. It is reasonable to use acupuncture for the management of chronic cancer-related

pain management. Acupuncture can also be used in conjunction with standard antiemetics to control chemotherapy-related nausea and vomiting.

Alimi D, Rubino C, Pichard-Léandri E, et al. Analgesic effect of auricular acupuncture for cancer pain: a randomized, blinded, controlled trial. *J Clin Oncol*. 2003;21:4120-4126.

Ezzo JM, Richardson MA, Vickers A, et al. Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. *Cochrane Database Syst Rev*. 2006;(2):CD002285.

B.7. Can acupuncture/acupressure be used for decrease anxiety?

Acupuncture or acupressure on the extra 1, EX-HN3 (Yin-Tang) acupuncture point is effective in producing sedation. The extra 1, the location of EX-HN3 (Yin-Tang) acupuncture point is on the forehead, at the midpoint between the two eyebrows.

Acar et al. did a prospective, randomized, single-blind, controlled study of 52 patients receiving acupuncture on Yin-Tang or sham acupuncture. The bispectral index (BIS) values in the acupuncture group were significantly lower than in the sham group. Paraskeva et al. did a study of 50 patients randomly assigned to acupuncture of the Yin-Tang point or control point. Acupuncture application significantly decreased the BIS value compared to the control group.

Acar HV, Cuvaş O, Ceyhan A, et al. Acupuncture on Yintang point decreases preoperative anxiety. *J Altern Complement Med*. 2013;19(5):420-424.

Paraskeva A, Melemeni A, Petropoulos G, et al. Needling of the extra 1 point decreases BIS values and preoperative anxiety. *Am J Chin Med*. 2004;32(5):789-794.

B.8. In the clinical setting, is ear acupressure useful for alleviating anxiety and pain?

Auricular acupressure is an effective treatment for anxiety during ambulance transport. Kober et al. did a study of 36 patients who required ambulance transport to medical facilities; patients were randomized to receive auricular acupressure at the relaxation point or at a sham point. Patients in the auricular acupressure group reported significantly less anxiety than patients in the sham group on arrival to the hospital. Barker et al. reported a randomized controlled trial of 38 patients with acute hip fractures receiving either bilateral auricular acupressure or the sham control during ambulance transport; the patients in the acupressure group had less pain, less anxiety, and lower heart rates on arrival to the hospital.

Auricular acupuncture points may be stimulated for a longer period of time by using ear seeds or ear tacks. Ear seeds can be small seeds from the dry Vaccaria plant or can be made from stainless seed. These seeds are held in place on the ear with a small piece of adhesive tape (Video 52.3).

Barker R, Kober A, Hoerauf K, et al. Out-of-hospital auricular acupressure in elder patients with hip fracture: a randomized double-blinded trial. *Acad Emerg Med*. 2006;13(1):19-23.

Kober A, Scheck T, Schubert B, et al. Auricular acupressure as a treatment for anxiety in prehospital transport settings. *Anesthesiology*. 2003;98(6):1328-1332.

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C. Complications

C.1. What are the possible complications of acupuncture treatment?

When compared with other available medical treatments, acupuncture is extremely safe. Rarely, a patient may have some bruising at an acupuncture site that is swiftly resolved. The major risk is infection from the use of improperly sterilized needles. This can be avoided by using disposable sterile acupuncture needles and the proper insertion of the needles. Extremely rare reports have documented a pneumothorax caused by improperly inserted acupuncture needles.

A study of the adverse effects of 34,000 acupuncture consultations in the United Kingdom revealed that the most common adverse events were bleeding, needling pain, and aggravation of symptoms. None of these events were serious. Similarly, a review of nine surveys showed that the most common adverse events were needle pain, tiredness, and bleeding. Feelings of faintness and syncope were uncommon. Feelings of relaxation were reported by as many as

86% of patients. The report of pneumothorax was extremely rare, occurring only twice in nearly a quarter of a million treatments.

A study was conducted involving a prospective postal audit of treatments performed by 1,848 professional acupuncturists in the United Kingdom over a 4-week period. They reported 43 minor adverse events, a rate of 1.3 per 1,000 treatments. The events report included severe nausea, fainting, prolonged aggravation of the symptoms, pain, and bruising. The overall frequency of acupuncture-related adverse events is exceptionally low, and prospective studies have indicated that even minor adverse events are uncommon. Acupuncture is considered to be a very safe intervention when applied appropriately by a competent practitioner; adverse effects from acupuncture are particularly uncommon.

Ernst E, White A. Prospective studies of the safety of acupuncture: a systemic review. *Am J Med*. 2001;110:481-485.

MacPherson H, Thomas K, Walters S, et al. The York acupuncture safety study: prospective survey of 34,000 treatments by traditional acupuncturists. *BMJ*. 2001;323:486-487.

von Riedenauer WB, Baker MK, Brewer RJ. Video-assisted thoracoscopic removal of migratory acupuncture needle causing pneumothorax. *Chest*. 2007;131:899-901.

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Chapter 53
Myasthenia Gravis

James B. Eisenkraft

Stefan Samuelson

A 39-year-old woman with a history of fibroid uterus and menorrhagia presents for total abdominal hysterectomy. She was diagnosed 2 years ago with myasthenia gravis after developing progressive diplopia and dysphagia. Following inadequate response to medical therapy, she underwent a transcervical thymectomy 1 year ago, and her condition greatly improved. She has a history of generalized anxiety disorder; her medications at this time are pyridostigmine 60 mg per day, diazepam, and iron. Vital signs are: pulse rate, 70 beats per minute; blood pressure, 130/85 mm Hg; respiratory rate, 20 breaths per minute; and SpO_2, 97% breathing room air. She is 157 cm tall and weighs 93 kg, and her BMI is 38 kg per m^2.

A. Medical Disease and Differential Diagnosis

1. What is myasthenia gravis (MG)?
2. What is the etiology and pathophysiology of MG?
3. Describe the clinical classification of MG.
4. How is the diagnosis of MG made?
5. What should be considered in the differential diagnosis?
6. How does myasthenic syndrome (Lambert-Eaton syndrome) differ from MG?
7. What treatments are available for a patient with MG?

B. Preoperative Evaluation and Preparation

1. Describe the preoperative evaluation of this patient.
2. What preoperative laboratory data are required?
3. How should the patient's medications be managed preoperatively?

C. Intraoperative Management

1. What are your considerations in choice of anesthetic technique?
2. How should this patient be monitored intraoperatively?
3. What anesthetic regimen would you choose for this patient?
4. Can neuromuscular blocking drugs be used in a patient with MG?
5. Should the MG patient who is in remission be managed differently?

D. Postoperative Management

1. What factors will help you predict this patient's need for continued intubation or other postoperative ventilatory support?
2. How will you determine if this patient can be safely extubated?
3. How will you manage postoperative analgesia?
4. How will you define and manage postextubation ventilatory failure in this patient?

A. Medical Disease and Differential Diagnosis

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A.1. What is myasthenia gravis (MG)?

MG is a disorder of the neuromuscular junction and therefore of great significance to the anesthesiologist. It is a chronic disorder characterized by fluctuating painless weakness and fatigability of voluntary muscles made worse on exertion with improvement following rest. The onset is usually slow and insidious; any skeletal muscle or muscle group may be affected. The most common onset is ocular, presenting with ptosis and diplopia. If the symptoms remains localized to the eyes for 2 years, the likelihood of progression to generalized disease is low. In many cases, however, MG is generalized and may involve the bulbar musculature, causing problems with breathing, speaking, mastication, and swallowing. Proximal muscles are more commonly involved than distal. Peripheral muscle weakness may manifest as clumsiness, difficulty holding up the head, or in ambulating. Respiratory muscle weakness may cause dyspnea, a decrease in the ability to cough and therefore to remove secretions.

The incidence of MG appears to be increasing. The most accurate estimate of incidence of MG was around 30 per 1,000,000 per year. The incidence in children and adolescents aged 0 to 19 years was found to be between 1.0 and 5.0 per 1,000,000 per year. These rates may well be an underestimate of the true incidence rates because mild cases may have been missed and cases in the elderly may have been misdiagnosed. People of any age may be affected, but peaks of incidence occur in the third decade for women and the fifth decade for men.

Drachman DB. Myasthenia gravis. *N Engl J Med*. 1994;330:1797-1810.

McGrogan A, Sneddon S, de Vries CS. The incidence of myasthenia gravis: a systematic literature review. *Neuroepidemiology*. 2010;34:171-183.

Sathasivam S. Current and emerging treatments for the management of myasthenia gravis. *Ther Clin Risk Manag*. 2011;7:313-323.

A.2. What is the etiology and pathophysiology of MG?

In normal neuromuscular transmission, the acetylcholine released from the motor nerve terminal stimulates postsynaptic nicotinic receptors at the motor end plate to generate an action potential leading to depolarization of the membrane and contraction of the motor unit. The normal neuromuscular junction has a very large number of postsynaptic acetylcholine receptors (AChRs) such that muscle weakness only becomes apparent when 70% or more of the receptors have been blocked. This excess of receptors has been termed the “margin of safety of neuromuscular transmission.” MG patients have a significant decrease in the number of postsynaptic AChRs at the end plates of affected muscles resulting in a decreased margin of safety of neuromuscular transmission.

MG is an autoimmune disorder, and about 80% of affected patients have detectable circulating antibodies to the nicotinic AChR. These anti-AChR antibodies may cause complementmediated lysis of the postsynaptic membrane, directly block the receptors, or may modulate the receptor turnover such that the rate of degradation exceeds the rate of resynthesis. Studies of the motor end plate area show loss of synaptic folds and a widening of the synaptic cleft. Some MG patients who do not have anti-AChR antibodies, have antibodies to muscle-specific tyrosine kinase (MuSK). These MuSK-antibody-positive MG patients often develop prominent oculobulbar muscle weakness.

The cause of MG is unknown but appears to be related in some way to the thymus gland. It has been suggested that thymic T cells are stimulated to produce antibodies following

sensitization by a protein similar to the AChR. MG patients also have a higher incidence of other autoimmune diseases including thyroid, lupus, and rheumatoid.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56:17-22.

Paton WD, Waud DR. The margin of safety of neuromuscular transmission. *J Physiol*. 1967;191:59-90.

A.3. Describe the clinical classification of MG.

Since the original clinical classification by Osserman and Genkins who described four classes and two subclasses, several others have been published. The Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of

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America Clinical Classification describes five main classes and several subclasses as follows:

- Class I: any ocular muscle weakness; may have weakness of eye closure; all other muscle strength is normal.
- Class II: mild weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity
  - Class IIa: predominantly affecting limb, axial muscles, or both; may also have lesser involvement of oropharyngeal muscles
  - Class IIb: predominantly affecting oropharyngeal, respiratory muscles, or both; may also have lesser or equal involvement of limb, axial muscles, or both
- Class III: moderate weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity
  - Class IIIa: predominantly affecting limb, axial muscles, or both; may also have lesser involvement of oropharyngeal muscles
  - Class IIIb: predominantly affecting oropharyngeal, respiratory muscles, or both; may also have lesser or equal involvement of limb, axial muscles, or both
- Class IV: severe weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity
  - Class IVa: predominantly affecting limb, axial muscles, or both; may also have lesser involvement of oropharyngeal muscles
  - Class IVb: predominantly affecting oropharyngeal, respiratory muscles, or both; may also have lesser or equal involvement of limb, axial muscles, or both; use of a feeding tube without intubation
- Class V: defined by the need for intubation, with or without mechanical ventilation, except when used during routine postoperative management

Jaretzki A III, Barohn RJ, Ernstoff RM, et al. Myasthenia gravis: recommendations for clinical research standards. Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America. *Neurology*. 2000;55:16-23.

Osserman KE, Genkins G. Studies in myasthenia gravis: review of a twenty-year experience in over 1200 patients. *Mt Sinai J Med*. 1971;38:497-537.

A.4. How is the diagnosis of MG made?

The diagnosis of MG is suspected from the patient's history and confirmed by clinical, electrophysiologic, pharmacologic, or immunologic testing. Typically, the patient cannot sustain or repeat muscular contraction. Clinical tests of fatigability include maintaining an upward gaze, holding out an affected limb, and respiratory function testing (vital capacity, maximum breathing capacity).

The electrical counterpart of fatigability is a decrement in the compound muscle action potentials evoked by repetitive stimulation of a motor nerve. Supramaximal stimulation of a peripheral nerve at 2 Hz is applied; a decrement in the size of the fourth or fifth response compared to the first is diagnostic. This is the most specific of the nerve tests for MG, but it can be performed only on certain muscles, which may not be the ones affected in an individual patient. A more sensitive electrophysiologic test is single-fiber electromyography (EMG) where an increase in jitter is found.

Pharmacologic testing is based on administration of an anticholinesterase and observing a rapid improvement in function. Mechanical and electrical (e.g., EMG), decrements

improve with 2 to 10 mg of intravenous edrophonium (Tensilon test). MG patients characteristically are sensitive to nondepolarizing muscle relaxants. When the routine EMG results are equivocal, a regional nondepolarizing muscle relaxant test may be performed using a tourniquet to isolate the limb and limit the action of the drug. In the regional nondepolarizer muscle relaxant test, EMGs are performed before and after the administration of 0.2 mg of curare. In MG, there is an exaggerated response to this small dose of curare.

Antibodies to the AChR are detectable in 80% of patients with MG. In equivocal cases, a positive result of a test for anti-AChR antibodies is considered diagnostic. Interestingly, the anti-AChR antibody titer is unrelated to the severity of the

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disease or the patient's prognosis.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56:17-22.

A.5. What should be considered in the differential diagnosis?

A number of disorders can mimic MG and should be included in the initial differential diagnosis.

Thyrotoxicosis can present with generalized weakness and abnormal thyroid function. Patients with neurasthenia characteristically have weakness, which disappears when individual muscle groups are tested. Progressive external ophthalmoplegia; restrictive cardiomyopathies; muscular dystrophies; brain tumors; amyotrophic lateral sclerosis; myasthenic polymyopathy with hypersensitivity to neostigmine; and drugs such as D-penicillamine, aminoglycosides, quinine, procainamide, and calcium channel blockers can also cause myasthenia-like symptoms.

Gilhus NE, Nacu A, Andersen JB, et al. Myasthenia gravis and risks for comorbidity. *Eur J Neurol*. 2015; 22:17-23.

A.6. How does myasthenic syndrome (Lambert-Eaton syndrome) differ from MG?

Myasthenic syndrome is a very rare immune-mediated disorder of neuromuscular transmission, associated with antibodies to the presynaptic voltage-gated calcium channel. The prevalence is estimated to be about 1 per 100,000. It is associated with small cell carcinoma of the lung in 50% to 60% of cases. Complaints of weakness may be mistaken for MG, but in Lambert-Eaton syndrome, symptoms do not respond to administration of anticholinesterases or steroids, and activity improves strength. The defect in this condition is prejunctional, is associated with diminished release of acetylcholine from nerve terminals, and is improved by facilitating agents such as 4-aminopyridine that increase repetitive firing. Affected patients are particularly sensitive to the effects of all muscle relaxants, which should be used with great caution or avoided entirely. The possibility of Lambert-Eaton syndrome should be considered in all patients with known malignant disease and those patients undergoing diagnostic procedures for suspected carcinoma of the lung. Anesthesia considerations in these patients are essentially the same as in those with MG.

Keogh M, Sedehizadeh S, Maddison P. Treatment for Lambert-Eaton myasthenic syndrome. *Cochrane Database Syst Rev*. 2011;(2):CD003279.

Petty R. Lambert Eaton myasthenic syndrome. *Pract Neurol*. 2007;7:265-267.

Weingarten TN, Araka CN, Mogensen ME, et al. Lambert-Eaton myasthenic syndrome during anesthesia: a report of 37 patients. *J Clin Anesth*. 2014;26:648-653.

A.7. What treatments are available for a patient with MG? Medical Therapy

Mary Walker was the first physician to report the similarity between the symptoms and signs of MG and curare poisoning and to use an anticholinesterase to treat MG. Anticholinesterases are used to prolong the action of acetylcholine at the postsynaptic membrane and may also exert their own agonist effect at the postsynaptic AChRs. They are the most commonly used therapy in MG. Interestingly, no randomized controlled trial has been conducted on the use of acetylcholinesterase inhibitors in patients with MG because the response in observational studies is so obvious that a placebo group could not be justified. MG patients

learn to regulate their acetylcholinesterase medication and titrate dose to optimum effect (Table 53.1). If several muscle groups/functions are affected, the patient titrates therapy according to the most important group. Acetylcholinesterase overdosage causes the muscarinic effects of acetylcholine and may cause a cholinergic crisis. Excessive amounts of acetylcholine at the neuromuscular junction cause persistent depolarization of the muscle membrane. Underdosage causes weakness or a myasthenic crisis. In a patient with weakness, distinction between the two types of crisis may be made by performing a Tensilon test or by examining pupil size, which will be large (mydriatic) in a myasthenic crisis but small (miotic) in a cholinergic crisis. Muscarinic side effects (bradycardia, bronchospasm, oral and respiratory tract

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secretions, and gastrointestinal cramps) are treatable with atropine; however, many MG patients treated with anticholinesterases seem to develop a resistance to the muscarinic effects.

TABLE 53.1 Anticholinesterase Drugs Used to Treat Myasthenia Gravis (dose in mg)

DRUG	ORAL	IV	IM	EFFICACY
Pyridostigmine (Mestinon)	60	2	2-4	1
Neostigmine (Prostigmin)	1.5	0.5	0.7-1.0	1

IM, intramuscular; IV, intravenous.

Pyridostigmine (Mestinon) is the anticholinesterase drug most commonly used to treat MG and has fewer muscarinic side effects than neostigmine (Prostigmin). Its onset of action following oral administration is 15 to 30 minutes, effect peaks at 1 to 2 hours, and duration of action is 3 to 4 hours. Daily dosage is typically 30 to 120 mg orally given in divided doses. For patients who are weak on awakening in the morning, a long-acting formulation of 180 mg is available and can be taken at bedtime.

The immunologic basis of MG has led to the use of short- and long-term immunosuppressive drugs. Steroids are used to complement anticholinesterase therapy and for shortterm immunosuppression. Prolonged use of steroids may produce unwanted effects, such as peptic ulcer and osteoporosis. Steroids often produce initial deterioration before an improvement. The usual regimen is prednisone 1 mg per kg on alternate days. For longterm effect, azathioprine, cyclophosphamide, cyclosporine, methotrexate, mycophenolate mofetil, rituximab, and tacrolimus have been used. Rapid short-term immunomodulation has been achieved in acute exacerbations or to improve muscle strength prior to surgery. Plasma exchange or plasmapheresis may produce dramatic but transient improvements in muscle strength with decreases in anti-AChR and anti-MuSK titers as well as other inflammatory mediators. Plasma exchange is usually reserved for severe MG and has been shown to improve respiratory function in both operated and non-operated patients with MG. Plasmapheresis has been used to decrease circulating levels of antibodies in patients in severe crisis or prior to surgery. It usually produces a rapid but short-lived improvement. Plasmapheresis also causes a decrease in plasma cholinesterase levels, which may prolong the effect of drugs such as succinylcholine that are normally broken down by this enzyme system.

Surgical Therapy

Long-term immunomodulation is achieved by surgical thymectomy with the goal of achieving a remission or at least a reduction in dosage of medications. Abnormalities are found in 75% of thymus glands removed from patients with MG (85% show hyperplasia, 15% show thymoma). After thymectomy, approximately 75% of patients either go into remission or show some improvement. Thymectomy is always indicated in those patients with thymoma and is now considered the treatment of choice in most patients with MG, except for those with only ocular myasthenia. Response to thymectomy is best if it is performed within the first 3 years following diagnosis. Clinical outcome from thymectomy is equivalent whether performed via a transsternal (open) or video-assisted transcervical (minimally

invasive) approach. A report describing anesthesia concerns in 17 patients who underwent robotic-assisted thoracoscopic thymectomy suggested that refinement of the surgical technique and positioning are required.

Kumar V, Kaminski HJ. Treatment of myasthenia gravis. *Curr Neurol Neurosci Rep*. 2011;11:89-96.

Maurizi G, D'Andrilli A, Sommella L, et al. Transsternal thymectomy. *Thorac Cardiovasc Surg*. 2015;63(3):178-186.

Mehndiratta MM, Pandey S, Kuntzer T. Acetylcholinesterase inhibitor treatment for myasthenia gravis. *Cochrane*

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Database Syst Rev. 2011;(2):CD006986.

Sathasivam S. Current and emerging treatments for the management of myasthenia gravis. *Ther Clin Risk Manag*. 2011;7:313-323.

Walker MB. Case showing the effect of prostigmin on myasthenia gravis. *Proc R Soc Med*. 1935;28:759-761.

B. Preoperative Evaluation and Preparation

B.1. Describe the preoperative evaluation of this patient.

Several problems must be considered: history of MG, open abdominal procedure in Trendelenburg position, anemia, obesity, and anxiety state.

The preoperative interview should be used to identify factors that suggest the need for postoperative ventilation. This information can guide the anesthesiologist in formulating the anesthetic plan, selection of preoperative medications, and arranging for postoperative care. When possible, patients with MG should be scheduled for elective surgery while in remission. The patient's physical and emotional states should be optimized. Current drug therapy should be reviewed, and possible drug interactions considered. The patient should be informed of the possible need for postoperative intubation and ventilation. In relation to *transsternal thymectomy*, predictors of need for postoperative ventilation include duration and severity of the disease and the total daily requirement of pyridostigmine and/or other medications. Predictors for MG patients undergoing open abdominal procedures have not been reported.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56:17-22.

B.2. What preoperative laboratory data are required?

Laboratory studies should be individualized to the patient. In addition to routine preoperative laboratory data, electrolyte abnormalities, particularly hypokalemia, which can exacerbate weakness, should be ruled out. If the patient is or has recently been receiving corticosteroids, blood glucose levels should be determined. Most likely this patient will require a general anesthetic for the planned procedure, so that a preoperative arterial blood gas analysis and pulmonary function tests would serve as baseline for determining readiness for extubation. A respiratory therapist should educate the patient about breathing exercises and the use of an incentive spirometer.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56:17-22.

B.3. How should the patient's medications be managed preoperatively?

Ideally, patients with MG should be scheduled to be the first case of the day in the operating room.

The management of anticholinesterase medication preoperatively should be individualized to the patient. Anticholinesterase therapy should be continued if the patient is physically or psychologically dependent on it. Traditional practice is to withhold pyridostigmine therapy on the morning of surgery so that the patient is weak on arrival to the operating room. This avoids interactions with other drugs used in the operating room. For example, anticholinesterase inhibits both plasma cholinesterase and acetylcholinesterase; therefore, the metabolism of succinylcholine will be slowed. Others recommend continuing pyridostigmine, including an oral dose just before induction (Table 53.1). Preoperative plasmapheresis has been discussed previously but should not be necessary for this patient. Anxiolysis is satisfactorily achieved with a benzodiazepine. Opioids are usually avoided because of the potential for causing respiratory depression.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56:17-22.

C. Intraoperative Management

C.1. What are your considerations in choice of anesthetic technique?

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Although regional and neuraxial anesthetic techniques have been used successfully in MG patients, in this particular patient, general anesthesia would be the better choice for several reasons:

- Open abdominal procedure with an obese patient in Trendelenburg position would likely make spontaneous ventilation more difficult.
- Any weakness would exacerbate her ventilatory difficulty.
- Anxiety might require administration of sedatives that could depress respiration.
- In the event of an ascending block level causing respiratory muscle weakness, emergent intubation and ventilation could become necessary. Securing the airway at the outset would be preferable.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56:17-22.

C.2. How should this patient be monitored intraoperatively?

Standard American Society of Anesthesiologists (ASA) monitors must be used. In addition, an arterial line might be useful to draw arterial blood samples for gas analysis intra- and postoperatively. A peripheral nerve stimulator, and ideally a means to quantify responses to stimulation (e.g., EMG, accelerometer, kinemyography), should be used from the beginning even if neuromuscular blocking drugs will be avoided. This is because the potent inhaled anesthetics also depress neuromuscular transmission, and a monitor of recovery from this effect is similarly needed. Once the patient is asleep, baseline recordings should be made before any potent inhaled or neuromuscular blocking drug is administered. Subsequent responses may then be quantitatively compared to baseline. In MG patients, fade in response to train-of-four and tetanic stimulation occurs in the affected muscles at baseline (see section A.4.).

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56:17-22.

C.3. What anesthetic regimen would you choose for this patient?

For the reasons given earlier, the safest approach is general endotracheal anesthesia. Maintenance of anesthesia in the intubated, ventilated MG patient can be achieved with an inhalational anesthetic, a balanced technique, or total intravenous anesthesia (TIVA).

Assuming the preoperative evaluation does not predict a difficult airway, the patient may be tracheally intubated once asleep rather than awake. Prior to induction of anesthesia, the patient should be preoxygenated breathing 100% oxygen until the end-tidal oxygen is greater than 90%. Ideally, it should be 95%, the other 5% of the exhaled gas mixture being carbon dioxide. Induction of anesthesia is readily achieved with propofol or etomidate. In most cases, intubation of the trachea, maintenance, and relaxation are all readily achieved using a potent inhaled anesthetic agent. Anesthetic depth is increased using the potent inhaled agent and the trachea intubated under its effect. MG patients are more sensitive than normal patients to the neuromuscular depressant effects of the potent inhaled agents. In patients with MG, isoflurane at 1.9 minimum alveolar concentration (MAC) end-tidal concentration induced a neuromuscular block of 30% to 50%, whereas halothane at 1.8 MAC induced a block of 10% to 20%. Both agents produced fade in the train-of-four ratio of 41% and 28%, respectively. The less soluble inhaled agents, sevoflurane and desflurane, are even more rapidly taken up and withdrawn; they are now the most commonly used anesthetic drugs for patients with MG. Whichever agent is used, at the end of the procedure, the inhaled agent is discontinued and recovery of neuromuscular function begins.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56:17-22.

Nilsson E, Muller K. Neuromuscular effects of isoflurane in patients with myasthenia gravis. *Acta Anaesthesiol Scand*. 1990;34:126-131.

Nitahara K, Sugi Y, Higa K, et al. Neuromuscular effects of sevoflurane in myasthenia gravis patients. *Br J Anaesth*. 2007;98:337-341.

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C.4. Can neuromuscular blocking drugs be used in a patient with MG?

If the patient cannot tolerate the depth of anesthesia needed to produce relaxation with the potent inhaled agent, neuromuscular blocking drugs may be used, titrating dose against monitored effect. Patients with MG are sensitive (i.e., show a decrease in ED_{50} and ED_{95} when compared with non-MG patients) to the nondepolarizing neuromuscular blocking drugs because of the decreased number of postsynaptic receptors at the motor end plate. All nondepolarizing relaxants have been successfully and uneventfully used with careful monitoring in patients with MG. Because the sensitivity of any individual MG patient is unknown, these drugs should be titrated in 1/10 of the usual dose. Cisatracurium may be preferred because of its short elimination half-life, small volume of distribution, lack of cumulative effect, and high clearance. Sensitivity to nondepolarizing relaxants is increased during the coadministration of a potent inhaled anesthetic. Upon completion of the surgical procedure, the residual relaxation may be reversed using incremental doses of an anticholinesterase drug while neuromuscular transmission is carefully monitored to obtain maximum antagonism yet avoid a cholinergic crisis. All anticholinesterases have been safely used, but edrophonium may be the drug of choice because its onset of action is rapid and higher doses have a prolonged duration of action.

Sugammadex is a novel cyclodextrin drug that was designed to bind rocuronium with a great affinity. It also binds vecuronium. Before the introduction of sugammadex, anticholinesterase drugs were the only options for antagonism of residual nondepolarizing neuromuscular blockade, and in MG patients, anticholinesterases must be administered with caution so as to avoid myasthenic or cholinergic crises. Sugammadex has been reported to safely reverse deep rocuronium-induced neuromuscular blockade within 210 seconds in a patient with MG. Sugammadex offers significant advantages in the management of the MG patient because anticholinesterase drugs would not be required for reversal.

MG patients are resistant to the neuromuscular blocking effects of succinylcholine due to the decrease in number of postsynaptic receptors at the motor end plate. The ED_{95} is 2.6 times normal in these patients. Clinically, however, the use of succinylcholine has been without incident, with the usual clinical doses producing adequate relaxation for endotracheal intubation and a normal recovery time, despite the occasionally reported early onset of phase II block. Doses of 0.2 to 1.0 mg per kg have been used in a number of patients with MG, and most did not show fasciculation before becoming paralyzed. Fade in response to train-of-four stimulation was observed in some patients during recovery, but recovery was not delayed. Prior administration of an anticholinesterase may complicate the response to succinylcholine by delaying its metabolism.

Baraka AS, Taha SK, Kawkabani NI. Neuromuscular interaction of sevoflurane—cisatracurium in a myasthenic patient. *Can J Anaesth*. 2000;47:562-565.

de Boer HD, Shields MO, Booij LH. Reversal of neuromuscular blockade with sugammadex in patients with myasthenia gravis: a case series of 21 patients and review of the literature. *Eur J Anaesthesiol*. 2014;31:715-721.

Eisenkraft JB, Book WJ, Mann SM, et al. Resistance to succinylcholine in myasthenia gravis: a dose-response study. *Anesthesiology*. 1988;69:760-763.

Eisenkraft JB, Book WJ, Papatestas AE. Sensitivity to vecuronium in myasthenia gravis: a dose-response study. *Can J Anaesth*. 1990;37:301-306.

Kopman AF. Sugammadex: a revolutionary approach to neuromuscular antagonism. *Anesthesiology*. 2006;104(4):631-633.

Unterbuchner C, Fink H, Blobner M. The use of sugammadex in a patient with myasthenia gravis. *Anaesthesia*. 2010;65:302-305.

C.5. Should the MG patient who is in remission be managed differently?

Although it is well established that MG patients are sensitive to nondepolarizing and resistant to depolarizing neuromuscular blocking drugs, there is no consensus on the response to these drugs during a remission. It is therefore prudent to manage the patient as if he or she had active disease and titrate neuromuscular blocking drugs to effect while monitoring the responses.

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Basaranoglu G, Erden V, Delatioglu H. Anesthesia of a patient with cured myasthenia gravis. *Anesth Analg*. 2003;96:1842-1843.

Wainwright AP, Brodrick PM. Suxamethonium in myasthenia gravis. *Anaesthesia*. 1987;42:950-957.

D. Postoperative Management

D.1. What factors will help you predict this patient's need for continued intubation or other postoperative ventilatory support?

MG places the patient at an increased risk of respiratory failure after general anesthesia. Several studies have attempted to identify specific characteristics of MG patients undergoing surgery that could help predict increased likelihood of postoperative respiratory failure relative to other MG patients. Most of these studies have focused on MG patients undergoing thymectomy. Predictive factors that have been suggested include coexisting respiratory disease not caused by MG (e.g., chronic obstructive pulmonary disease [COPD], asthma), increased pyridostigmine dose (>750 mg per day, although one study utilized 250 mg per day as a benchmark) onset of MG greater than 6 years prior to surgery, and preoperative MG-related respiratory compromise as indicated by vital capacity <4 mL per kg or maximal inspiratory pressure less than -25 cm H_2O on pulmonary function tests. Maximum static expiratory pressure has also been suggested as a marker because expiratory effort necessarily determines the ability to clear respiratory secretions. A more recent scoring system to predict postoperative myasthenic crisis and need for ventilatory support has been proposed which cites as its chief risk factors advanced staging of the patient's MG (bulbar involvement and rapid progression conferring greater risk), BMI >28 kg per m^2, history of prior myasthenic crisis, duration of symptoms >2 years, and association with a pulmonary resection. More invasive surgery increases risk of respiratory failure (transsternal vs. transcervical thymectomy, open abdominal procedure vs. peripheral surgery), as does evidence of recent MG exacerbation (e.g., patient is currently on steroids). Although a definitive risk stratification system has not yet been validated, it is important to assess each patient on a case-by-case basis and engage in frank preoperative discussions regarding risk of postoperative myasthenic crisis and possible need for prolonged ventilatory support.

Eisenkraft JB, Papatestas AE, Kahn CH, et al. Predicting the need for postoperative mechanical ventilation in myasthenia gravis. *Anesthesiology*. 1986;65:79-82.

Leuzzi G, Meacci E, Cusumano G, et al. Thymectomy in myasthenia gravis: proposal for a predictive score of postoperative myasthenic crisis. *Eur J Cardiothorac Surg*. 2014;45:e76-e88.

Mori T, Yoshioka M, Watanabe K, et al. Changes in respiratory condition after thymectomy for patients with myasthenia gravis. *Ann Thorac Cardiovasc Surg*. 2003;9:93-97.

D.2. How will you determine if this patient can be safely extubated?

Postoperative weakness is the greatest contributing factor to perioperative respiratory failure in MG patients. As such, it is important to establish that the patient is fully awake and alert prior to attempting extubation and that any residual neuromuscular blockade has been completely reversed. Adequate respiratory effort should be confirmed by ability to generate a negative inspiratory pressure of at least -20 cm H_2O. Although thymectomy patients often experience improvement in respiratory function and other MG symptoms postoperatively, it is more difficult to predict response to surgeries unrelated to MG. After extubation, it is essential to monitor the patient closely for signs of fatigue, weakness, or evidence of deteriorating respiratory status (hypercarbia, hypoxia, tachypnea). If the patient was taking pyridostigmine preoperatively, oral dosing should be reestablished as soon as possible after extubation; if necessary, alternative anticholinesterase medications such as neostigmine or edrophonium may be used as a bridging measure. The dosage equivalents are shown in Table 53.1.

Care should be taken to ensure that somnolence related to opioid administration does not place the patient at increased

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risk of hypoventilation. In addition, vigilance is required to ensure that impending myasthenic crisis is not masked by intraoperative reversal agents that may wear off in the postanesthesia care unit.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56:17-22.

D.3. How will you manage postoperative analgesia?

MG patients are especially sensitive to the central respiratory depressive effects of parenteral opioid administration. On the other hand, inadequately treated pain related to abdominal or

thoracic surgery can inhibit ventilatory effort and thus can also worsen respiratory status. Nonopioid pain regimens should be considered whenever possible, including neuraxial anesthesia where appropriate because a greatly reduced total dose of opioid compared to parenteral administration may be used to achieve an equivalent analgesic effect. Intravenous nonsteroidal anti-inflammatory drug (NSAID) regimens have also been effective in controlling pain in MG patients without causing respiratory depression. If oral or parenteral opioids are used, the dose should be reduced for MG patients receiving anticholinesterase therapy because these medications have been reported to increase the efficacy of opioids.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56:17-22.

Su C, Su Y, Chou CW, et al. Intravenous flurbiprofen for post-thymectomy pain relief in patients with myasthenia gravis. *J Cardiothorac Surg*. 2012;7:98.

D.4. How will you define and manage postextubation ventilatory failure in this patient?

The postsurgical state is uniquely perilous to the MG patient for respiratory decompensation after extubation; indeed, cases have been reported in which previously undetected MG was diagnosed as a result of unexpected respiratory failure in the postoperative period. Suggested criteria for reintubation have included tachypnea (respiratory rate greater than 40 breaths per minute), respiratory acidosis not due to narcotics, or vital capacity ≤8 mL per kg.

In the MG patient experiencing postoperative respiratory distress, it is crucial to differentiate cholinergic crisis from myasthenic crisis because the precipitating events and appropriate therapies are different. Each may present as muscle weakness, salivation, and sweating. However, although myasthenic crisis is thought to result from surgical stress leading to a decreased responsiveness to anticholinesterase therapy, cholinergic crisis results from an overdose of anticholinergic medications. The two conditions may be differentiated from one another using the Tensilon test, that is, 10 mg of edrophonium administered intravenously. The patient in myasthenic crisis will respond with an improvement in respiratory muscle strength, whereas the patient in cholinergic crisis will exhibit no change or a worsening of symptoms. The treatment for myasthenic crisis is anticholinesterase therapy titrated to effect; in contrast, the treatment for cholinergic crisis may incorporate antimuscarinic drugs to treat salivation and sweating but is mostly supportive and may require mechanical ventilation until the crisis resolves.

Antevil JL, Carroll CG, Roberts PF, et al. Myasthenia gravis—an unexpected cause of respiratory failure and reversible left ventricular dysfunction after cardiac surgery. *J Card Surg*. 2010;25:662-664.

Cheng S, Liu S, Chou C, et al. An uncommon cause of postthyroidectomy respiratory failure. *Thyroid*. 2009;19:1129-1130.

Gorback MS, Moon RE, Massey JM. Extubation after transsternal thymectomy for myasthenia gravis: a prospective analysis. *South Med J*. 1991;84:701-706.

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Chapter 54
Malignant Hyperthermia

Robert Brislin
Mary Theroux
Henry Rosenberg
Vinod Malhotra

A 7-year-old boy with mild/moderate kyphoscoliosis was scheduled for ambulatory surgery for repair of strabismus under general anesthesia. Previous anesthetic history included an uneventful sevoflurane and nitrous oxide anesthesia for bilateral myringotomy. The mother was very nervous because a first cousin of the boy had died under anesthesia in Wisconsin the previous year.

A. Medical Disease and Differential Diagnosis

1. What was the problem of concern in this case?
2. What is malignant hyperthermia (MH)?
3. What are the clinical features of a susceptible patient?
4. Does the history of previous uneventful sevoflurane anesthesia reasonably exclude the patient's susceptibility to MH?
5. What are the clinical features of the syndrome?
6. What are the laboratory findings during an acute crisis of MH?
7. What is the incidence of this syndrome?
8. What is the mode of inheritance of the disease? Does MH skip generations?
9. What genetic disorder results in MH susceptibility?
10. What is the pathophysiology of the syndrome?
11. What laboratory tests can further substantiate the susceptibility of the patient to MH?
12. What is neuroleptic malignant syndrome?

B. Preoperative Evaluation and Preparation

1. How would you prepare this patient for anesthesia and surgery?
2. Is dantrolene prophylaxis indicated?
3. What laboratory tests would you obtain before surgery?
4. Is outpatient surgery appropriate for this patient?
5. In anticipation of general anesthesia, what preparations would you make?

C. Intraoperative Management

1. What anesthetic techniques and agents would you employ?
2. Should body (core) temperature be monitored during general anesthesia lasting more than a short time?
3. What anesthetic agents are contraindicated?
4. If the surgeon wants to use local anesthesia for a procedure, what agents will you recommend?
5. What is the significance of masseter muscle spasm occurring after succinylcholine administration?

6. Twenty minutes into the procedure with sevoflurane anesthesia, the patient developed increasing tachycardia with

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ventricular premature beats and mottled skin. What emergency measures would you take?

7. What modalities would you monitor closely during management of the crisis?
8. What steps should be taken to avoid major morbidity from MH?
9. How does the new formulation of dantrolene (Ryanodex) compare with the existing formulation of dantrolene (Dantrium or Revonto)?

D. Postoperative Management

1. What complications may follow this syndrome?
2. What would be your follow-up in this case?
3. What would you advise the patient and the family?
4. What precautions should an MH-susceptible patient take out of the operating room (OR)?

A. Medical Disease and Differential Diagnosis

A.1. What was the problem of concern in this case?

The patient was a 7-year-old boy with kyphoscoliosis and strabismus and a history of an anesthetic-related death in the family in Wisconsin. Therefore, in addition to the respiratory problems associated with kyphoscoliosis, he presented a likelihood of susceptibility to MH syndrome. The supporting factors for strong suspicion were the family history, kyphoscoliosis, and geographic location. There is a high density of MH-susceptible families in the state of Wisconsin.

Li G, Brady JE, Rosenberg H, et al. Excess comorbidities associated with malignant hyperthermia diagnosis in pediatric hospital discharge records. *Paediatr Anaesth*. 2011;21(9):958-963.

Rosenberg H, Sambuughin N, Riazi S, et al. Malignant hyperthermia susceptibility. In: Pagon RA, Adam MP, Ardinger HH, et al, eds. *GeneReviews*® [Internet]. Seattle, WA: University of Washington, Seattle; 1993. http://www-ncbi-nlm-nih-gov.proxy1.lib.tju.edu/books/NBK1146/. Accessed September 9, 2015.

A.2. What is malignant hyperthermia (MH)?

MH, first described by Denborough and Lovell in 1960, is an inherited clinical syndrome characterized by elevated core temperature, tachycardia, tachypnea, hypercarbia, muscle rigidity and rhabdomyolysis, acidosis, and hyperkalemia. The underlying abnormality relates to an uncontrolled elevation of intracellular calcium in skeletal muscle cells leading to activation of muscle contractile elements and hypermetabolism. These changes are reversed with the administration of dantrolene, but in the absence of timely treatment, death is likely. In almost every instance, the clinical syndrome occurs in a susceptible patient when a “triggering” anesthetic agent is employed. There are several documented instances where an apparent MH crisis has occurred in humans in the absence of anesthetic drugs.

Denborough MA, Lovell RRH. Anaesthetic deaths in a family [letter]. *Lancet*. 1960;2:45.

Groom L, Muldoon SM, Tang ZZ, et al. Identical de novo mutation in the type 1 ryanodine receptor gene associated with fatal, stress-induced malignant hyperthermia in two unrelated families. *Anesthesiology*. 2011;115(5):938-945.

Lavezzi WA, Capacchione JF, Muldoon SM, et al. Case report: death in the emergency department: an unrecognized awake malignant hyperthermia-like reaction in a six-year-old. *Anesth Analg*. 2013;116(2):420-423.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1287-1300.

A.3. What are the clinical features of a susceptible patient?

A family history, if present, particularly in a first-degree relative, is a strong indicator of MH susceptibility. Epidemiologic studies have demonstrated that certain comorbidities such as scoliosis and muscle disorders are more frequent in MH-

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susceptible individuals. However, only a few diseases involving skeletal muscle are known to be associated with MH susceptibility. They include central core disease, King-Denborough syndrome, multiminicore

disease, centronuclear myopathy, congenital fiber-type disproportion, and Native American myopathy (Table 54.1). Nevertheless, many patients susceptible to MH do not have obvious musculoskeletal disorders or a positive family history.

TABLE 54.1 Associated Musculoskeletal Disorders/Signs in Patients Susceptible to Malignant Hyperthermia

Central core disease
Multiminicore disease
King-Denborough syndrome
Native American myopathy
Centronuclear myopathy
Congenital fiber type disproportion
Exercise-induced rhabdomyolysis

Confusion often exists among some anesthesia providers regarding Duchenne or Becker muscular dystrophy and whether such patients need a nontriggering anesthetics. The concern about Duchenne or Becker dystrophy is related to the use of volatile anesthetics resulting in rhabdomyolysis and hyperkalemia due to the direct damage to the muscle cells. However, the pathophysiology of this adverse reaction is apparently not similar to that of MH. MH triggers, especially succinylcholine, should be avoided.

Brislin RP, Theroux MC. Core myopathies and malignant hyperthermia susceptibility: a review. *Paediatr Anaesth*. 2013;23(9):834-841.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110:498-507.

Larach MG, Rosenberg H, Gronert GA, et al. Hyperkalemic cardiac arrest during anesthesia in infants and children with occult myopathies. *Clin Pediatr (Phila)*. 1997;36(1):9-16.

McCarthy TV, Quane KA, Lynch PJ. Ryanodine receptor mutations in malignant hyperthermia and central core disease. *Hum Mutat*. 2000;15:410-417.

Rosenberg H, Pollock N, Schiemann A, et al. Malignant hyperthermia: a review. *Orphanet J Rare Dis*. 2015;10:93.

A.4. Does the history of previous uneventful sevoflurane anesthesia reasonably exclude the patient's susceptibility to MH?

No, it does not. Cases may occur during a second or subsequent anesthetic course. A notable case is one described in the case report, of an 8-month-old infant born at 24 weeks of gestation who died unexpectedly 12 hours after his ninth uneventful general anesthetic. The authors have personal experience with similar cases where uneventful anesthetics with triggering agents preceded fulminant episode of MH at a later anesthetic exposure.

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Bendixen D, Skovgaard LT, Ording H. Analysis of anaesthesia in patients suspected to be susceptible to malignant hyperthermia before diagnostic in vitro contracture test. *Acta Anaesthesiol Scand*. 1997;41:480-484.

Newmark JL, Voelkel M, Brandom BW, et al. Delayed onset of malignant hyperthermia without creatine kinase elevation in a geriatric, ryanodine receptor type 1 gene compound heterozygous patient. *Anesthesiology*. 2007;107(2):350-353.

A.5. What are the clinical features of the syndrome?

The clinical features of MH are the result of an uncontrolled, exaggerated, hypermetabolic state triggered by the use of potent inhalation anesthetic agents and/or succinylcholine. In humans, MH-like events have occurred in association with heat and exercise. Some of those patients harbor MH causative mutations in the ryanodine receptor 1 (*RYR1*) gene. Common manifestations of MH include the following:

Specific for malignant hyperthermia

- Increase in end-tidal carbon dioxide during constant ventilation (the most sensitive and specific sign)

- Generalized rigidity (extremely high specificity)
- Masseter muscle rigidity (not as specific as generalized rigidity and also sometimes difficult to distinguish from tight jaw due to “light anesthesia” and a normal increase in masseter muscle tension when succinylcholine is used.)
- Increased temperature (not uncommonly higher than 40°C); formerly considered a late sign of MH but now recognized as a sign often occurring early during the course of MH

Nonspecific

- Tachycardia (the earliest and most consistent clinical sign, although not specific)
- Tachypnea
- Arrhythmias
- Skin mottling
- Profuse sweating
- Altered blood pressure

Hyperkalemic Cardiac Arrest

Sudden hyperkalemic cardiac arrest has been reported after the administration of MH trigger agents in children with undiagnosed myopathy, especially the dystrophinopathies, Duchenne or Becker muscular dystrophy. This response is not a result of pathophysiologic changes typical for MH but rather muscle membrane destruction leading to hyperkalemia. The pathways leading to the abnormal response is not clear.

The treatment is similar to treatment for hyperkalemia, that is, glucose and insulin, calcium chloride or gluconate, and hyperventilation.

Gurnaney H, Brown A, Litman RS. Malignant hyperthermia and muscular dystrophies. *Anesth Analg*. 2009;109:1043-1048.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110:498-507.

Larach MG, Localio AR, Allen GC, et al. A clinical grading scale to predict malignant hyperthermia susceptibility. *Anesthesiology*. 1994;80:771-779.

Larach MG, Rosenberg H, Gronert GA, et al. Hyperkalemic cardiac arrest during anesthesia in infants and children

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with occult myopathies. *Clin Pediatr (Phila)*. 1997;36(1):9-16.

Van der Spek AF, Fang WB, Ashton-Miller JA, et al. The effects of succinylcholine on mouth opening. *Anesthesiology*. 1987;67(4):459-465.

A.6. What are the laboratory findings during an acute crisis of MH?

The laboratory values reflect changes of a hypermetabolic state and muscle tissue damage (Table 54.2). Hence, hypercarbia, respiratory and metabolic acidosis, hyperkalemia, elevated creatine kinase, myoglobinemia, and coagulopathy are common findings. Disseminated intravascular coagulation syndrome may result in cases of extreme (>105°F) hyperthermia.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110:498-507.

Litman RS, Rosenberg H. Malignant hyperthermia: update on susceptibility testing. *JAMA*. 2005;293:2918-2924.

A.7. What is the incidence of this syndrome?

The incidence of clinical MH is difficult to measure because many clinical syndromes resemble MH, and often, the anesthetic management is altered when initial signs suggesting MH are detected. The incidence also depends on the prevalence in a population of genetic mutations causal for MH as well as the prevalence of use of MH trigger agents.

One of the earliest epidemiologic studies of MH was conducted in Denmark, where an estimate of the incidence of fulminant MH was noted to be 1 in 260,000 general anesthetics and 1 in 60,000 anesthetics where succinylcholine was used. The incidence was even higher, that is, 1 in 5,000 anesthetics, when such signs as masseter muscle rigidity, unexplained tachycardia, and unexplained fever were included.

Genetic studies as well as studies of discharge diagnoses after surgery have suggested that the prevalence as opposed to incidence of MH is much higher. Mutations causal for MH have

been found in 1 in 3,000 people in France and in Japan. A recent study in the United States documented a prevalence of genetic changes associated with MH close to 1 in 500 people.

TABLE 54.2 The Laboratory Findings of Acute Malignant Hyperthermia

METABOLIC AND RESPIRATORY ACIDOSIS

Arterial blood gases

↓↓ pH

↑↑↑ PCO_2

Mild decreases in PO_2

Electrolytes

↑ K

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↑ Ca or decreased

↑ Mg

Serum

↑ Lactate

↑ Pyruvate

↑ Creatine kinase

↑ Lactate dehydrogenase

↑ Aldolase

↑ Myoglobin

Increased international normalized ratio, increased fibrin split products increased prothrombin time, increased partial thromboplastin time.

It is generally acknowledged that MH is more common in children than adults. In addition, the incidence in males is higher than in females. Two recent studies of coded hospital discharge data showed that the prevalence of MH is 1 in 100,000 hospital discharges for adults and 4 per 100,000 discharges for children.

Brady JE, Sun LS, Rosenberg H, et al. Prevalence of malignant hyperthermia due to anesthesia in New York State, 2001-2005. *Anesth Analg*. 2009;109:1162-1166.

Gonsalves SG, Ng D, Johnston JJ, et al. Using exome data to identify malignant hyperthermia susceptibility mutations. *Anesthesiology*. 2013;119(5):1043-1053.

Li G, Brady JE, Rosenberg H, et al. Excess comorbidities associated with malignant hyperthermia diagnosis in pediatric hospital discharge records. *Paediatr Anaesth*. 2011;21(9):958-963.

Monnier N, Krivosic-Horber R, Payen JF, et al. Presence of two different genetic traits in malignant hyperthermia families: implication for genetic analysis, diagnosis, and incidence of malignant hyperthermia susceptibility. *Anesthesiology*. 2002;97(5):1067-1074.

Rosero EB, Adesanya AO, Timaran CH, et al. Trends and outcomes of malignant hyperthermia in the United States, 2000 to 2005. *Anesthesiology*. 2009;110:89-94.

A.8. What is the mode of inheritance of the disease? Does MH skip generations?

MH is inherited in humans in an autosomal dominant fashion with reduced penetrance and variable expressivity. It is heterogenetic with up to seven gene loci implicated, but only three are confirmed to be causal for MH.

More than 70% of MH cases are linked to the *RYR1* located on chromosome 19. Less than 2% are related to mutations in the gene coding for dihydropyridine receptor (*DHPR*) known as *CACNA1s*. Over 300 mutations have been found in the *RYR1* gene with at least 35 mutations documented to be causal for the syndrome by the European Malignant Hyperthermia Group (EMHG.org).

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Because MH is inherited in an autosomal dominant manner, the susceptibility to it does not “skip” generations. Nevertheless, because of the low penetrance, not all of those with MH mutations display the syndrome on exposure to trigger agents.

In MH-susceptible pigs, the inheritance is autosomal recessive with only one DNA change noted to account for all cases.

Litman RS, Rosenberg H. Malignant hyperthermia: update on susceptibility testing. *JAMA*. 2005;293:2918-2924.

McCarthy TV, Healey JM, Heffron JJ, et al. Localization of the malignant hyperthermia susceptibility locus to human chromosome 19q12-13.2. *Nature*. 1990;343:562-564.

Rosenberg H, Rueffert H. Clinical utility gene card for: malignant hyperthermia. *Eur J Hum Genet*. 2011;19. doi:10.1038/ejhg.2010.248.

Sambuughin N, Holley H, Muldoon S, et al. Screening of the entire ryanodine receptor type 1 coding region for sequence variants associated with malignant hyperthermia susceptibility in the North American population. *Anesthesiology*. 2005;102:515-521.

Stamm DS, Aylsworth AS, Stajich JM, et al. Native American myopathy: congenital myopathy with cleft palate, skeletal anomalies, and susceptibility to malignant hyperthermia. *Am J Med Genet A*. 2008;146A(14):1832-1841.

Stewart SL, Hogan K, Rosenberg H, et al. Identification of the Arg1086His mutation in the alpha subunit of the voltage-dependent calcium channel (CACNA1S) in a North American family with malignant hyperthermia. *Clin Genet*. 2001;59:178-184.

A.9. What genetic disorder results in MH susceptibility?

The most common genetic defect is a defective calcium channel located in the membrane of the sarcoplasmic reticulum of skeletal muscle. This channel is termed the *RYR1* because it binds the plant alkaloid ryanodine.

The channel is closely associated with other proteins and structures, such as the *DHPR* calcium channel that mediates transfer of voltage change to the *RYR1*. Other proteins associated with the *RYR1* include calsequestrin, triadin, and FK506-binding protein (FKB-12). Mutations in the *RYR1* gene are associated with MH susceptibility in more than 65% of patients and their families. Nevertheless, only about 30% of patients with MH harbor a mutation *proven* to lead to increased intracellular calcium on exposure to caffeine or MH trigger anesthetics, the critical criteria to confirm the pathophysiology of MH. Over 300 additional mutations have yet to be characterized regarding the effects on calcium movements. One reason for the slow progress in deciphering the significance of these many mutations is that, unlike many other conditions, there are many private mutations that predispose to MH. No single mutation accounts for more than about 10% of MH cases. The *CACNA1S* gene coding for the α1 subunit of the *DHPR* is also involved in intracellular calcium control and has been associated with susceptibility in 1% to 2% of MH-susceptible families. More recently, a variant in the *STAC3* gene was associated with MH susceptibility in Native American myopathy seen in the Lumbee Native American population. There are probably other genes that may lead to MH susceptibility but are much less common than those associated with the *RYR1* and the *CACNA1S* genes.

Of interest is the observation that mutations associated with central core disease and multiminicore disease, two myopathies that also predispose to MH, are located on the *RYR1* gene as well. In central core disease, the sarcoplasmic reticulum is depleted of calcium to a significant extent because of the increased permeability of the *RYR1*. With a depletion of calcium, muscle contraction is weakened when the muscle is activated.

Recently, genetically engineered mice were developed that include one or more of the mutations causal for MH in the mouse genome. The mice display signs typical of MH during exposure to trigger agents and also on exposure to raised environmental temperature. The number of identified genetic mutations and variants that may contribute to MH susceptibility is rapidly increasing due to much attention to the role of the Ryanodine receptor gene in the pathophysiology of other myopathies.

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Brislin RP, Theroux MC. Core myopathies and malignant hyperthermia susceptibility: a review. *Paediatr Anaesth*. 2013;23(9):834-841.

Chelu MG, Goonasekera SA, Durham WJ, et al. Heat- and anesthesia-induced malignant hyperthermia in a RyR1 knock-in mouse. *FASEB J*. 2006;20:329-330.

Dlamini N, Voermans NC, Lillis S, et al. Mutations in RYR1 are a common cause of exertional myalgia and rhabdomyolysis. *Neuromuscul Disord*. 2013;23(7):540-548.

Sambuughin N, Holley H, Muldoon S, et al. Screening of the entire ryanodine receptor type 1 coding region for sequence variants associated with malignant hyperthermia susceptibility in the North American population. *Anesthesiology*. 2005;102:515-521.

A.10. What is the pathophysiology of the syndrome?

The MH syndrome results from an abnormal and uncontrolled elevation of intracellular calcium levels in skeletal muscle. During normal muscle contraction, the process of calcium release from the sarcoplasmic reticulum begins with depolarization of the sarcolemma that is transmitted via the T tubules to the *DHPR*, which in turn activates the calcium channel termed the *RYR1* to release calcium. The elevated calcium removes the inhibition of actin and myosin interaction that leads to mechanical force generation. Reuptake of calcium returns the intracellular cytoplasmic concentration of calcium to normal, and muscle relaxation takes place. Reuptake is mediated via a calcium adenosine triphosphate (ATP)ase pump mechanism. A variety of intermediate proteins also regulate the intrasarcoplasmic reticulum concentration of calcium, such as calsequestrin, a calcium-binding protein. Genetically engineered mice that do not express calsequestrin have been shown to develop clinical signs of MH on exposure to trigger anesthetics. It is thought that in the absence of the calcium buffer, intracellular calcium levels increase significantly but only on exposure to MH triggers. Thus, the control of calcium release is a highly regulated process that involves a variety of energy-consuming steps requiring ATP breakdown and heat production.

During an MH episode, the *RYR1* calcium channel is locked in an open position, leading to an uncontrolled release of calcium with elevation of intracytoplasmic calcium levels and continuous muscle activation as well as ATP breakdown. The sarcoplasmic reticulum calcium pump is unable to resequester the calcium. ATP breakdown during this process aggravates heat production further. Fortunately, dantrolene reverses these changes.

Energy-consuming processes take place through glycolysis as well as oxidative phosphorylation. Eventually, ATP levels are insufficient to maintain sarcolemmal integrity and potassium leaks from the cell resulting in hyperkalemia. Myoglobinemia occurs for the same reason as does an increase of a number of enzymes, including creatine kinase.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1287-1300.

Protasi F, Paolini C, Dainese M. Calsequestrin-1: a new candidate gene for malignant hyperthermia and exertional/environmental heat stroke. *J Physiol*. 2009;587(pt 13):3095-3100.

Rosenberg H, Pollock N, Schiemann A, et al. Malignant hyperthermia: a review. *Orphanet J Rare Dis*. 2015;10:93.

Rosenberg H, Sambuughin N, Riazi S, et al. Malignant hyperthermia susceptibility. In: Pagon RA, Adam MP, Ardinger HH, et al, eds. *GeneReviews*® [Internet]. Seattle, WA: University of Washington, Seattle; 1993. http://www-ncbi-nlm-nih-gov.proxy1.lib.tju.edu/books/NBK1146/. Accessed September 9, 2015.

A.11. What laboratory tests can further substantiate the susceptibility of the patient to MH?

The most accurate diagnostic test for MH is the exposure of biopsied skeletal muscle to halothane, caffeine, and, more recently, ryanodine or chlorocresol. In this test, approximately 1 g of muscle is harvested from the thigh under regional or, in the case of a child, general anesthesia. Strips or fascicles of muscle weighing 100 to 200 mg are suspended in a water

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bath at 37°C, and exposure is made to halothane, caffeine, ryanodine, or chlorocresol in specific graded concentrations. The isometric contracture, *not contraction*, response to muscle is measured via strain gauge following specific guidelines. The threshold and height of the contracture is measured, and a diagnosis of MH is made based on the contracture threshold and strength exceeding specific values.

The test is highly sensitive, close to 100%, but as many as 20% of positive results are false-positives. Nevertheless, the value of the test resides in ruling out MH susceptibility with certainty.

The test is invasive and costly and requires strict adherence to specific protocols. Currently, there are only five testing centers in North America. There are over 20 in Europe and others in Brazil, New Zealand, Australia, and Japan. The testing protocols in North America and Europe employ the same drugs and techniques for muscle harvest, but there are slight differences in exposure to caffeine and halothane and threshold for determining a positive response. The biopsy center director must carefully evaluate the patient and history before recommending the test in order to enhance accuracy.

Molecular Genetic Testing for Malignant Hyperthermia Susceptibility

The era of DNA testing for MH susceptibility began in 1990 when a mutation in the *RYR1* gene was shown to be causal for MH in pigs. In humans, several genes have been associated with MH, although the *RYR1* gene is probably responsible for most cases. At present, 34 mutations in the *RYR1* gene have been proven to be causal for MH based on strict criteria related to in vitro calcium release or clinical MH in several generations and families. Unfortunately, no mutation accounts for more than a small percentage of all patients with MH susceptibility. The chief advantage of genetic testing is that all that is required is a blood sample, and the specimen may be shipped to the laboratory. The main limitation of genetic testing is the sensitivity of approximately 30%. Undoubtedly, the sensitivity will improve as more mutations are identified and tested for their ability to alter the structure and/or the function of the *RYR1*. On the other hand, genetic testing is very specific.

Patients should consider genetic testing if:

1. They have had a positive contracture test.
2. A family member has had a positive contracture test.
3. They have suffered a very likely MH episode but have not had a contracture test.
4. A family member has been found to have a causal mutation.

In those patients who are tested and a causal mutation identified, those with the mutation are MH-susceptible (high specificity), but those without the mutation *cannot* be considered MH-negative because they may harbor another mutation.

At present, there are two clinical testing laboratories for diagnosing MH susceptibility: Prevention Genetics (https://www.preventiongenetics.com) and the DNA diagnostic laboratory at the University of Pittsburgh (http://path.upmc.edu/divisions/mdx/diagnostics.html). Other laboratories are beginning to offer testing but may not test the entire *RYR1* gene. We suggest checking with MHAUS or a genetic counselor before ordering. You may contact Malignant Hyperthermia Association of the United States website (http://www.mhaus.org/) to help answer questions.

The decision to undergo genetic testing is complex because the test, although requiring only a blood sample, costs approximately $900 for the search for the most common mutations. Once a mutation is found, the cost for screening family members is $200 each. This compares to an approximate cost of $6,000 for the contracture test. The pros and cons of testing should be discussed with either an MH expert or a genetic counselor.

Allen GC, Larach MG, Kunselman AR. The sensitivity and specificity of the caffeine-halothane contracture test: a report from the North American Malignant Hyperthermia Registry. *Anesthesiology*. 1998;88:579-588.

Girard T, Treves S, Voronkov E, et al. Molecular genetic testing for malignant hyperthermia susceptibility. *Anesthesiology*. 2004;100:1076-1080.

Hopkins PM, Rüffert H, Snoeck MM, et al. European Malignant Hyperthermia Group guidelines for investigation of malignant hyperthermia susceptibility. *Br J Anaesth*. 2015;115(4):531-539.

Litman RS, Rosenberg H. Malignant hyperthermia: update on susceptibility testing. *JAMA*. 2005;293:2918-2924.

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A.12. What is neuroleptic malignant syndrome?

The neuroleptic malignant syndrome is also a hypermetabolic syndrome characterized by hyperthermia, rigidity, rhabdomyolysis, acidosis, and tachycardia—features that mimic MH. However, neuroleptic malignant syndrome is precipitated by a variety of neuroleptic drugs, including haloperidol; the atypical antipsychotics, phenothiazines; and other centrally acting drugs.

This syndrome differs from MH in that central dopamine depletion is responsible for the clinical picture. The mainstays of treatment are benzodiazepines and a dopamine agonist such as bromocriptine. Patients also respond symptomatically to dantrolene therapy. A recent report identified *RYR1* mutations in a small percentage of patients manifesting neuroleptic malignant syndrome. Perhaps many more also have these mutations.

A variety of other drug-induced hyperthermic syndromes resemble MH such as the serotonin syndrome. A common situation for the serotonin syndrome is the administration of meperidine in a patient on monoamine oxidase inhibitor drugs. Serotonin syndrome also may occur in patients on antidepressants, especially the antidepressants that prevent serotonin reuptake.

Ecstasy and other methylenedioxymethamphetamine agonists also produce hyperthermia. Again, the signs may resemble MH, but the pathophysiology is very different.

Anesthesiologists may encounter neuroleptic malignant syndrome, serotonin syndrome, and other drug-induced MH-like syndromes in the intensive care unit and emergency room settings.

Shah NN, Fless KG, Litinski M, et al. Atypical neuroleptic malignant syndrome: pitfalls and challenges in the delirious substance abuser. *Open J Anesthesiol*. 2012;2:53-57.

Strawn JR, Keck PE Jr, Caroff SN. Neuroleptic malignant syndrome. *Am J Psychiatry*. 2007;164:870-876.

B. Preoperative Evaluation and Preparation

B.1. How would you prepare this patient for anesthesia and surgery?

Preoperative preparation should include a detailed medical history, assessment of the patient's physical status, evaluation of laboratory findings including creatine kinase, and specific investigations to determine the susceptibility of the patient to MH. Four possible scenarios are as follows:

- The caffeine-halothane contracture test result is normal. The patient should be considered not susceptible to MH, and the anesthetic should be nonrestrictive.
- The caffeine-halothane contracture test is abnormal, implying MH susceptibility. Or, a mutation associated with MH is identified. In this case, trigger-free anesthetic agents should be employed, and all preparations should be made to quickly treat the syndrome if it develops.
- The caffeine-halothane contracture test is not available. This is very frequently the case because this test is done in only a few centers in the country. In such situations, the patient should be treated as MH-susceptible, and all appropriate steps should be followed.
- Patient has a disease known to predispose him or her to MH; a classic example is central core disease. These patients should be treated as MH-susceptible, and all appropriate steps should be followed.

Allen GC, Rosenberg H, Fletcher JE. Safety of general anesthesia in patients previously tested negative for malignant hyperthermia susceptibility. *Anesthesiology*. 1990;72:619-622.

Brislin RP, Theroux MC. Core myopathies and malignant hyperthermia susceptibility: a review. *Paediatr Anaesth*. 2013;23(9):834-841.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1287-1300.

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B.2. Is dantrolene prophylaxis indicated?

If a nontriggering anesthetic is administered with appropriate monitoring to an MH-susceptible patient, dantrolene prophylaxis is not necessary.

With the judicious use of trigger-free anesthetics, MH is extremely unlikely. A very rare case or two have been reported of MH occurring during an anesthetic without trigger agents; nevertheless, because many syndromes may mimic it, it is not at all clear whether any of the cases were really MH.

The side effects of dantrolene include nausea, vomiting, pain at the injection site, and depression of the twitch response. In patients with preexisting muscle weakness, dantrolene may cause respiratory insufficiency in the postoperative period.

Brandom BW, Larach MG, Chen MS, et al. Complications associated with the administration of dantrolene 1987 to 2006: a report from the North American Malignant Hyperthermia Registry of the Malignant Hyperthermia Association of the United States. *Anesth Analg*. 2011;112:1115-1123.

Lichtman AD, Oribabor C. Malignant hyperthermia following systemic rewarming after hypothermic cardiopulmonary bypass. *Anesth Analg*. 2006;102:372-375.

B.3. What laboratory tests would you obtain before surgery?

There is no routine laboratory testing indicated for strabismus surgery in this child. Serum creatine kinase level is of value as a baseline test and should be obtained.

B.4. Is outpatient surgery appropriate for this patient?

With the use of trigger-free anesthetics and appropriate monitoring, surgery normally performed in an outpatient setting is acceptable. Postoperative admission to the hospital solely on the basis of MH susceptibility is not warranted. When MH occurs, it is usually in the immediate postoperative period and not beyond 2 hours postoperatively. The current recommendation is to observe the patient for up to 2 hours in the postanesthesia care unit (PACU) and then discharge the patient if there are no signs of MH and the patient is otherwise doing well. All ambulatory surgery and office-based surgery settings should have a plan for managing MH and transferring the patient to a hospital.

Brandom BW. Ambulatory surgery and malignant hyperthermia. *Curr Opin Anaesthesiol*. 2009;22(6):744-747.

Larach MG, Dirksen SJ, Belani KG, et al. Special article: creation of a guide for the transfer of care of the malignant hyperthermia patient from ambulatory surgery centers to receiving hospital facilities. *Anesth Analg*. 2012;114(1):94-100.

Pollock N, Langton E, McDonnell N, et al. Malignant hyperthermia and day stay surgery. *Anaesth Intensive Care*. 2006;34:40-45.

Schleelein LE, Litman RS. Hyperthermia in the pediatric intensive care unit—is it malignant hyperthermia? *Paediatr Anaesth*. 2009;19(11):1113-1118.

B.5. In anticipation of general anesthesia, what preparations would you make?

A satisfactory preparation for administering anesthesia to this patient should include measures to prevent and treat an acute crisis of MH. The following should be available:

Equipment

- Drain, remove, or disable vaporizers.
- Fresh circuit, reservoir bag, and soda lime
  - For newer anesthesia work stations, the washout period with 10 L per minute oxygen flow may be prolonged

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up to 60 to 90 minutes. The manufacturers' guidelines for machine preparation should be followed.
    - Activated charcoal filter placed on the inspiratory and expiratory limb of the machine will significantly hasten the anesthesia machine inhalation agent washout period.
- Routine monitors as recommended by the American Society of Anesthesiologists including the following:
    - Pulse oximeter
    - Capnometer
    - Core temperature monitor
    - Electrocardiogram and blood pressure monitors

Items to have available

Cooling aids

- Hypothermia blanket
- Crushed ice
- Cold saline for irrigation and intravenous infusion
- Nasogastric tube and Foley catheter for cavity cooling. This is rarely necessary due to the above measures alone cooling the patient rapidly enough.

Drugs

- Sodium bicarbonate, mannitol, furosemide, dantrolene (intravenous), sterile water, antiarrhythmics, insulin, 50% dextrose, and calcium chloride
- *Avoid* calcium channel blockers because of interaction with dantrolene, possibly resulting in cardiac arrest.

Birgenheier N, Stoker R, Westenskow D, et al. Activated charcoal effectively removes inhaled anesthetics from modern anesthesia machines. *Anesth Analg*. 2011;112:1363-1370.

Kim TW, Nemergut ME. Preparation of modern anesthesia workstations for malignant hyperthermiasusceptible patients: a review of past and present practice. *Anesthesiology*. 2011;114(1):205-212.

San Juan AC Jr, Wong KC, Port JD. Hyperkalemia after dantrolene and verapamil-dantrolene administration in dogs. *Anesth Analg*. 1988;67:759-762.

C. Intraoperative Management

C.1. What anesthetic techniques and agents would you employ?

Potent inhalation agents and succinylcholine (excluding nitrous oxide) are to be avoided. If possible, local or regional anesthesia is preferred. Anesthesia may be induced with a barbiturate, benzodiazepine, or hypnotic agent and the patient ventilated with 100% oxygen. Fentanyl or other opioid may be added to ensure adequate depth of anesthesia. Topical anesthesia of the larynx and vocal cords may be achieved with a local anesthetic spray. The trachea is intubated with or without the use of a nondepolarizing muscle relaxant. Anesthetic maintenance can be achieved using a total intravenous anesthetic with a nondepolarizing muscle relaxant if needed. Nitrous oxide is not a triggering agent of MH and may be used as an adjuvant as needed. Vital signs are monitored with very close attention to capnography.

C.2. Should body (core) temperature be monitored during general anesthesia lasting more than a short time?

Definitely. Although temperature elevation is often not the first sign of MH, it is one of the common early signs of the syndrome. Therefore, core temperature should be monitored for all procedures lasting more than 30 minutes. Skin crystalline temperature monitors are not recommended because they do not adequately track rapidly changing temperatures. In addition, temperature monitoring is also important in detecting hypothermia.

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Brandom BW, Larach MG, Chen MS, et al. Complications associated with the administration of dantrolene 1987 to 2006: a report from the North American Malignant Hyperthermia Registry of the Malignant Hyperthermia Association of the United States. *Anesth Analg*. 2011;112:1115-1123.

Larach MG, Brandom BW, Allen GC, et al. Malignant hyperthermia deaths related to inadequate temperature monitoring, 2007-2012: a report from the North American Malignant Hyperthermia Registry of the Malignant Hyperthermia Association of the United States. *Anesth Analg*. 2014;119(6):1359-1366.

Shafer SL, Dexter F, Brull SJ. Deadly heat: economics of continuous temperature monitoring during general anesthesia. *Anesth Analg*. 2014;119(6):1235-1237.

C.3. What anesthetic agents are contraindicated?

In general, the anesthetic agents to be avoided include potent inhalation agents and depolarizing muscle relaxants. Of the agents commonly employed today, the following have been implicated in triggering MH:

- Inhalation agents: halothane, enflurane, isoflurane, desflurane, and sevoflurane
- Muscle relaxants: succinylcholine

Rosenberg H, Pollock N, Schiemann A, et al. Malignant hyperthermia: a review. *Orphanet J Rare Dis*. 2015;10:93.

Visoiu M, Young MC, Wieland K, et al. Anesthetic drugs and onset of malignant hyperthermia. *Anesth Analg*. 2014;118(2):388-396.

C.4. If the surgeon wants to use local anesthesia for a procedure, what agents will you recommend?

Both ester and amide local anesthetics are now considered safe for use in patients with MH syndrome.

D'Ambrosio J, Adragna MG. Guidelines for the use of local anesthetics in the dental treatment of patients who are susceptible to malignant hyperthermia. *Spec Care Dentist*. 1988;8:61-63.

Maccani RM, Wedel DJ, Melton A, et al. Femoral and lateral femoral cutaneous nerve block for muscle biopsies in children. *Paediatr Anaesth*. 1995;5:223-227.

C.5. What is the significance of masseter muscle spasm occurring after succinylcholine administration?

Rigidity of the jaw muscles after administration of succinylcholine is referred to as *masseter muscle rigidity* (MMR) or trismus. MMR presages clinical MH in up to 30% of cases. Even in

the absence of clinical MH, myoglobinuria following succinylcholine-induced MMR is common postoperatively. MMR probably occurs in individuals of all ages, although MMR is more common in children, particularly following induction with volatile anesthetics.

MMR has been reported in 1% of children after halothane and succinylcholine induction and in adults after succinylcholine administration. Should MMR occur, elective surgery should be postponed, and the patient observed in an intensive care unit setting for 24 hours seeking myoglobinuria specifically. The patient should be followed until creatine kinase levels normalize.

In the case of emergency surgery, the anesthetic should be converted to a “nontrigger” technique and the patient observed for early signs of MH. Dantrolene and other treatment procedures for MH should be made ready.

The patient and/or family should be advised to be evaluated for MH susceptibility.

The incidence of MMR and MH episodes in children has recently decreased as a result of recommendations that the use

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of succinylcholine in children be reserved for emergency situations.

Other causes of succinylcholine-induced MMR include any form of myotonia or periodic paralysis.

Gronert GA. Management of patients in whom trismus occurs following succinylcholine. *Anesthesiology*. 1988;68:653-655.

O'Flynn RP, Schutak JG, Rosenberg H, et al. Masseter muscle rigidity and malignant hyperthermia susceptibility in pediatric patients. An update on management and diagnosis. *Anesthesiology*. 1994;80:1228-1233.

Parness J, Bandschapp O, Girard T. The myotonias and susceptibility to malignant hyperthermia. *Anesth Analg*. 2009;109:1054-1064.

Rosenberg H. Trismus is not trivial. *Anesthesiology*. 1987;67:453-455.

C.6. Twenty minutes into the procedure with sevoflurane anesthesia, the patient developed increasing tachycardia with ventricular premature beats and mottled skin. What emergency measures would you take?

Although tachycardia may arise from other, more common causes, such as a light plane of anesthesia or hypovolemia, its association with dysrhythmia in this patient raises the suspicion that an MH crisis may be starting. End-expiratory carbon dioxide should be monitored, and if it is rising despite increasing minute ventilation after ruling out equipment problems, the diagnosis of MH should be strongly considered. Time is of the essence, and this constitutes a critical emergency, so the following steps should be taken:

- Stop all anesthetics and surgery (if possible).
- Hyperventilate the patient with 100% oxygen.
  - Obtain help and assistance through the MH hotline of the Malignant Hyperthermia Association of the United States (MHAUS; 1-800-MH-HYPER).
- Administer specific drug therapy: Start dantrolene sodium early while muscle perfusion is still present. An initial intravenous dose of 2.5 mg per kg should be followed by repeated doses of 1 to 2 mg per kg to a total of 10 mg per kg depending on the patient's response. More dantrolene may be administered if clinically indicated.
- Initiate aggressive cooling immediately for rapidly increasing temperatures and for those higher than 40°C. Methods for cooling include surface cooling with the patient on a cooling blanket and with ice packs placed on the groin and axillae. These measures are usually sufficient and gastric, rectal, or peritoneal lavage with iced saline is rarely used or necessary in practice. Cooling should be stopped when the patient's temperature falls to lower than 38°C to prevent inadvertent hypothermia.
- Treat acidosis with sodium bicarbonate (2 mEq per kg initial dose and titrate as necessary).
- Treat hyperkalemia with hyperventilation, sodium bicarbonate, insulin, 50% dextrose, and calcium chloride/gluconate.
- Treat arrhythmias with standard antiarrhythmics and avoid calcium channel blockers if dantrolene has been given.
- An arterial line and Foley catheter should be inserted in all cases of *fulminant* MH. Central venous catheterization should be considered for unstable patients or where aggressive therapy is needed.

- Maintain urine output with mannitol or furosemide.
- Follow creatine kinase levels every 12 hours.
- Check electrolytes and coagulation parameters.
- Register the patient and the event with the North American Malignant Hyperthermia Registry.

Forms may be obtained through MHAUS. Access to the North American Malignant Hyperthermia Registry is through the MHAUS website (http://www.mhaus.org/) or the North American MH Registry website “mhreg.org”.

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Rosenberg H, Pollock N, Schiemann A, et al. Malignant hyperthermia: a review. *Orphanet J Rare Dis*. 2015;10:93.

C.7. What modalities would you monitor closely during management of the crisis?

The modalities that should be monitored closely include the following:

- End-tidal carbon dioxide
- Arterial blood gases/electrolytes (especially K+)/coagulation
- Core temperature
- Creatine kinase levels
- Myoglobin levels: urine and serum
- Urine output (**quantity and color**)

C.8. What steps should be taken to avoid major morbidity from MH?

All sites where general anesthesia is administered should have 36 vials of dantrolene available within about 10 minutes. Recently, a new formulation of dantrolene from Eagle Pharmaceuticals Inc. (Woodcliff Lake, NJ) named Ryanodex was released. The concentration of this new formulation is 250 mg of dantrolene per vial and is mixed with 5 mL of sterile bacteriostatic water. Current MHAUS recommendations advise MH carts be stocked with three vials of Ryanodex if institutions are using this dantrolene formulation. In addition, when using the Ryanodex formulation, mannitol must also be given because it does not contain the mannitol as in the older formulation.

All patients undergoing general anesthesia for more than 30 minutes should have core temperature monitored.

All OR should have an MH drill each year. This drill should involve all OR personnel, going through the steps of alerting the team, obtaining dantrolene, mixing dantrolene, simulating blood draw, cooling the patient, and discussing the episode with family members.

In addition, nonhospital sites should ensure that a hospital is designated to receive a patient who is experiencing an MH episode. The facility should have a plan regarding who will accompany the patient and what drugs and monitors will accompany the transport personnel. The local hospital personnel must ensure dantrolene is in stock as well as be familiar with treating the syndrome.

Larach MG, Dirksen SJ, Belani KG, et al. Special article: creation of a guide for the transfer of care of the malignant hyperthermia patient from ambulatory surgery centers to receiving hospital facilities. *Anesth Analg*. 2012;114(1):94-100.

C.9. How does the new formulation of dantrolene (Ryanodex) compare with the existing formulation of dantrolene (Dantrium or Revonto)?

Present formulations of dantrolene (Dantrium and Revonto) are lyophilized, freeze dried, and dispensed as dantrolene sodium (DS) 20 mg in a 70-mL vial and contain 3,000 mg of mannitol. It should be reconstituted by adding 60 mL of sterile water without a bacteriostatic agent, and the vial needs to be shaken until clear. Warming the sterile water to 40°C immediately prior to mixing can speed up the process and also help drawing the drug in a syringe because the solution is fairly viscous. One may require 4 to 7 vials to start the treatment and may go up to 36 vials in an adult achieving maximum dosage. This can be a tedious and time-consuming process.

Recent formulation of dantrolene (Ryanodex) is a nanocrystalline dantrolene sodium suspension (DSS) that allows for a much larger dose of 250 mg to be dispensed in a vial that requires only 5 mL of sterile water to dissolve it in solution. It offers the advantage of rapid reconstitution and administration. In one animal study, the time for preparation for DSS (less than 60 seconds) was 10- to 15-fold shorter compared with DS (658 to 1,062 seconds), and the time taken to inject was a 100-fold faster. It contains only 125 mg of mannitol; hence, mannitol needs to be given separately. Because the diluent is in small amounts of water, fluid load is not as significant as in case of existing formulations. This becomes especially significant in pediatric patients.

The cost of DSS (required supply of three vials) is close to $7,000 in United States. It has a shelf life of 24 months. DS

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has a shelf life of 36 months and costs less than half as much (required supply of 36 vials). The cost of DSS may be substantially reduced when DSS is purchased for several locations within the same organization.

Rosenberg H, Pollock N, Schiemann A, et al. Malignant hyperthermia: a review. *Orphanet J Rare Dis*. 2015;10:93.

Schütte JK, Becker S, Burmester S, et al. Comparison of the therapeutic effectiveness of a dantrolene sodium solution and a novel nanocrystalline suspension of dantrolene sodium in malignant hyperthermia normal and susceptible pigs. *Eur J Anaesthesiol* . 2011;28(4):256-264.

D. Postoperative Management

D.1. What complications may follow this syndrome?

Disseminated intravascular coagulation is a major complication of MH, especially when the patient's temperature exceeds 41°C. The highest temperature achieved has a direct correlation to the probability of death as an outcome. Abnormal clotting studies (prothrombin and partial thromboplastin times) as well as decrease in platelet count are seen early even when profound disseminated intravascular coagulation (DIC) may not be yet evident. Other complications include renal failure, hyperkalemia, and compartment syndrome. As a result of massive muscle breakdown, the patient may be weak for days and also complain of muscle cramps and pain for a prolonged period of time. A study examining MH events voluntarily submitted to the North American Malignant Hyperthermia Registry of MHAUS in United States reported a 2.7% cardiac arrest rate and a 1.4% mortality rate.

Lack of or inadequate temperature monitoring increases the mortality rate. Larach et al. reported the mortality from an MH event as a function of temperature monitoring: 30%, 21%, and 2% for no monitoring, skin temperature monitoring only, and core temperature monitoring, respectively (P = .0012). The relative risk (lower bound) for no probe versus core probe was 13.8 (2.1). The relative risk (lower bound) for skin probe versus core probe was 9.7 (1.5).

Larach MG, Brandom BW, Allen GC, et al. Malignant hyperthermia deaths related to inadequate temperature monitoring, 2007-2012: a report from the North American Malignant Hyperthermia Registry of the Malignant Hyperthermia Association of the United States. *Anesth Analg*. 2014;119(6):1359-1366.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110:498-507.

D.2. What would be your follow-up in this case?

The vigorous therapy started in the OR should be continued in the immediate postoperative period into the postanesthesia care unit or the intensive care unit. Dantrolene administration of 1 mg per kg intravenously every 4 to 6 hours should be continued until the following parameters are met: Potassium and core temperature normalize and do not trend upward, carbon dioxide normalizes, and creatinine kinase levels start to decrease. These parameters are usually accomplished in 36 to 48 hours. Often, a transient period of hypothermia is observed due to vigorous cooling of the patient, but the temperature will rise again even though typically not to the critical level once dantrolene has been started.

Other laboratory values that should be followed until normalized include the following:

- Arterial blood gases
- Electrolytes
- Coagulation profile

Body temperature should be monitored along with other vital signs. Recrudescence of MH occurs in approximately 25% of treated cases; therefore, the patient should be watched in an intensive care unit setting for at least 36 hours following an episode.

Anesthetic maintenance can be achieved using a total intravenous anesthetic with a nondepolarizing muscle relaxant if needed. Nitrous oxide is not a triggering agent of MH and may be used as an adjuvant as needed

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Burkman JM, Posner KL, Domino KB. Analysis of the clinical variables associated with recrudescence after malignant hyperthermia reactions. *Anesthesiology*. 2007;106(5):901-906.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1287-1300.

D.3. What would you advise the patient and the family?

The patient and his family should be warned of the dangerous nature of this syndrome and should be advised to carry an identification band at all times. The pedigree of the family should be prepared, and the members should be investigated for susceptibility to this syndrome and issued medical identification bracelets or pendants accordingly.

The MHAUS has been active since 1981 and offers current information and advice on patient management and a variety of materials for health care professionals. The following is some useful contact information:

Emergency hotline: 1-800-MH-HYPER

Address: MHAUS, P.O. Box 1069, Sherburne, NY 13815

Phone: 1-800-98-MHAUS

Website: http://www.mhaus.org/

In addition, the patient and his family should consult with one of the MH diagnostic centers to discuss further evaluation. A complete listing is available on the MHAUS website.

The patient should be registered with the North American Malignant Hyperthermia Registry.

Forms may be obtained through MHAUS.

The website for the North American Malignant Hyperthermia Registry is http://www.mhreg.org/or through MHAUS directly.

The phone number is 1 (888) 274-7899.

The Registry is located at Mercy Hospital of the University of Pittsburgh. The director is Dr. Barbara Brandom.

Patient identification bracelets are available through the Medic Alert Foundation at www.medicalert.org; 1-800-432-5378. MedicAlert Foundation 2323 Colorado Avenue. Turlock, CA 95382.

D.4. What precautions should an MH-susceptible patient take out of the operating room (OR)?

In general, MH-susceptible patients should be cognizant of their response to heat and exercise. As for any patient, excess exposure to heat and humidity, especially with exercise, should be limited or avoided. Although it is true that a few cases of what appears to be MH have been reported without anesthesia, these are very rare. At present, there is no way to predict which patients may have an adverse response to environmental conditions.

Fiszer D, Shaw MA, Fisher NA, et al. Next-generation sequencing of RYR1 and CACNA1S in malignant hyperthermia and exertional heat illness. *Anesthesiology*. 2015;122(5):1033-1046.

Lavezzi WA, Capacchione JF, Muldoon SM, et al. Case report: death in the emergency department: an unrecognized awake malignant hyperthermia-like reaction in a six-year-old. *Anesth Analg*. 2013;116(2):420-423.

Muldoon S, Deuster P, Voelkel M, et al. Exertional heat illness, exertional rhabdomyolysis, and malignant hyperthermia: is there a link? *Curr Sports Med Rep*. 2008;7(2):74-80.

Tobin JR, Jason DR, Challa VR, et al. Malignant hyperthermia and apparent heat stroke. *JAMA*. 2001;286:168-169.

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Chapter 55

Postoperative Residual Neuromuscular Weakness and Prolonged Apnea

David J. Kopman

Aaron F. Kopman

A healthy 35-year-old, 65-kg female was scheduled for an elective abdominal hysterectomy. Anesthesia was induced with propofol 2.0 mg per kg, fentanyl 2.0 μg per kg, and rocuronium 1.2 mg per kg. Anesthesia, which lasted 90 minutes, was maintained with desflurane 5.0% end-tidal and supplemented with fentanyl as needed. At the termination of surgery, residual neuromuscular block was not antagonized because the tidal volume was deemed to be adequate and the train-offour count (TOFC) using facial nerve stimulation was four with no detectable fade. Upon arrival in the postanesthesia care unit (PACU), the patient was tachypneic, had uncoordinated and floppy arm movements, and appeared to be agitated and in distress. Arterial oxygen saturation on room air was 89%.

A. Medical Diseases and Differential Diagnosis

1. What is the differential diagnosis for postoperative apnea?
2. How is residual neuromuscular block diagnosed?
3. Do all voluntary muscles respond similarly to nondepolarizing relaxants?
4. If this was an emergency surgery, anesthesia was induced with a rapid sequence technique including succinylcholine. The patient remained apneic not only throughout the procedure but also in the PACU. What was the possible diagnosis? How would you confirm it? How would you manage the patient?
5. What are acetylcholinesterase and serum cholinesterase?
6. What is the incidence of atypical cholinesterase activity?
7. What is the significance of the dibucaine number?
8. What are some factors that can lower pseudocholinesterase (PChE) levels?
9. What are the side effects of succinylcholine?

B. Intraoperative Management

1. How is the choice among muscle relaxants made?
2. How much do individuals vary in their sensitivity to nondepolarizing relaxants?
3. What are the characteristics of nondepolarizing block?
4. What is a train-of-four (TOF) stimulus?
5. Why is the TOF ratio of clinical importance?
6. How do we define adequate recovery of neuromuscular function?
7. Are there useful and/or trustworthy clinical tests of neuromuscular recovery?
8. How accurate are subjective estimates of the TOF ratio?
9. What is double burst stimulation (DBS)?
10. What is the posttetanic count (PTC)?
11. What function does the conventional peripheral nerve stimulator (PNS) serve?

12. How can the TOF ratio be measured quantitatively?
13. What are the limitations of anticholinesterase antagonists?
14. Is there anything wrong with administering neostigmine when the TOFC is less than 3?
15. Is reversal of residual block always necessary?
16. Is there any way to rapidly antagonize a profound nondepolarizing block?

C. Postoperative Management

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1. What is the incidence of residual neuromuscular block in the PACU?
2. Does undetected postoperative residual neuromuscular block (PORB) have clinical consequences?

A. Medical Diseases and Differential Diagnosis

A.1. What is the differential diagnosis for postoperative apnea?

The differential diagnosis for postoperative apnea includes the following:

- Residual anesthetic agent
- Residual narcotic
- Residual muscle relaxant
- Hypocarbia
- Occurrence of some medical complication during anesthesia, such as stroke or embolism

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:2660.

A.2. How is residual neuromuscular block diagnosed?

This patient showed clear signs of residual neuromuscular weakness upon arrival in the PACU. TOF stimulation at the ulnar nerve showed a TOFC of only 2 at the adductor pollicis (thumb). A provisional diagnosis of residual nondepolarizing block was made and the patient received neostigmine 0.05 mg per kg plus an appropriate dose of glycopyrrolate (0.01 mg per kg). Seven minutes later, the TOFC was 4 with no evidence of fade on palpation of the thumb, and all signs of residual block had abated.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:995-996, 2660.

A.3. Do all voluntary muscles respond similarly to nondepolarizing relaxants?

Although facial nerve stimulation is widely used by clinicians to judge the adequacy of block and recovery, this practice can be very misleading. At a time when the TOFC at the orbicularis oculi or corrugator supercilii muscles shows good recovery from nondepolarizing block, the response at the hand may be almost nonexistent. Thus, facial nerve stimulation may give the clinician a false sense of security about the adequacy of neuromuscular recovery at the end of a case.

Similarly, in the intubated patient breathing spontaneously, a normal tidal volume and maintenance of an acceptable PCO_2 do not necessarily indicate adequate neuromuscular recovery. The diaphragm is the first muscle to recover from nondepolarizing block and requires significantly higher plasma levels of relaxants to maintain paralysis. The muscles which protect the upper airway are far more sensitive to nondepolarizing relaxants. Thus, a patient who may be able to maintain adequate respiratory exchange while intubated may experience complete airway obstruction when extubated.

Donati F. Neuromuscular monitoring: more than meets the eye. *Anesthesiology*. 2012;117:934-936.

Donati F, Bejan DR. Not all muscles are the same. *Br J Anaesth*. 1992;68:235-236.

Thilen SR, Hansen BE, Ramaiah R, et al. Intraoperative neuromuscular monitoring site and residual paralysis. *Anesthesiology*. 2012;117:964-972.

A.4. If this was an emergency surgery, anesthesia was induced with a rapid sequence technique including succinylcholine. The patient remained apneic not only throughout the procedure but also in the PACU. What was the possible diagnosis? How would you confirm it? How would you manage the patient?

The easiest possibility to exclude is residual neuromuscular block. In the given patient, stimulation of the ulnar nerve with a PNS resulted in no response of the muscles of the hand. Hence, the diagnosis of a prolonged response to succinylcholine was established. Extreme prolongation in succinylcholine's duration of effect is usually a manifestation of an atypical genotype. Following a 1.0 mg per kg dose of succinylcholine, in patients homozygous for the most common atypical butyrylcholinesterase (BChE) genotypes, apnea generally lasts upward of an hour, and it may take as much as 3 hours for adequate respiratory efforts to return. However, the duration of apnea is highly dependent on the BChE variant in question

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Traditionally, identification of the human BChE variant has been performed by biochemical analysis. These tests, which have been used for decades, consist of the measurement of plasma cholinesterase activity with different substrates and of testing the degree of inhibition of this activity with a well-known inhibitor, such as dibucaine, fluoride, or R02-0683. These tests have identified multiple genes that can reside at the same allelic site, such as the atypical, silent, fluoride-resistant, J, K, H, and Newfoundland variants. However, biochemical testing often leads to equivocal results. More recently, molecular biologic techniques have been applied to identifying a patient's exact genotype.

Once the diagnosis of an atypical response to succinylcholine is ascertained, treatment is entirely supportive and symptomatic. Since the duration of residual block is hard to predict, the patient should remain intubated, artificially ventilated, and sedated. Only after a strong, sustained response to indirect tetanic stimulation at the wrist can be demonstrated should sedation be terminated and an attempt made to wean the patient off controlled ventilation. Patients recovering from prolonged succinylcholine induced block usually exhibit a “dual” or “phase II” block during recovery (fade on repetitive stimulation). While neostigmine or edrophonium can under certain circumstances antagonize this block, this approach is risky when dealing with prolonged succinylcholine apnea. If significant plasma levels of succinylcholine are still present, the administration of an acetylcholinesterase may be counterproductive.

The patient should obviously be informed that she had a prolonged episode of muscular weakness and that the presumptive cause was an atypical reaction to succinylcholine. The patient should be urged to have this diagnosis confirmed and she should be directed to an appropriate laboratory. If an atypical genotype is confirmed, she should encourage her family members to be tested as well. Finally, the patient should be assured that this diagnosis has no adverse health consequences but that in the future when surgery is planned, her anesthesiologist needs to be informed of this diagnosis.

Cerf C, Mesguish M, Gabriel I, et al. Screening patients with prolonged neuromuscular blockade after succinylcholine and mivacurium. *Anesth Analg*. 2002;94:461-466.

Levano S, Ginz H, Siegemund M, et al. Genotyping the butyrylcholinesterase in patients with prolonged neuromuscular block after succinylcholine. *Anesthesiology*. 2005;102:531-535.

Levano S, Keller D, Schobinger E, et al. Rapid and accurate detection of atypical and Kalow variants in the butyrylcholinesterase gene using denaturing high performance liquid chromatography. *Anesth Analg*. 2008;106:147-151.

A.5. What are acetylcholinesterase and serum cholinesterase?

Acetylcholinesterase is a relatively specific enzyme that hydrolyzes acetylcholine (ACh) faster than it does other choline esters. It is found in red blood cells, the central nervous system, and at the neuromuscular junction. It is responsible for hydrolyzing and inactivating the ACh produced during normal neuromuscular transmission. It does not hydrolyze succinylcholine.

Serum cholinesterase, also called *cholinesterase*, *pseudocholinesterase (PChE)*, *butyrylcholinesterase (BChE)*, and *nonspecific cholinesterase*, hydrolyzes many choline esters, including

succinylcholine. It is found in many human tissues but not in the red blood cell. It is synthesized in the liver. Its physiologic function is unknown, but it may hydrolyze choline esters, such as propionylcholine and butyrylcholine, which may be formed by bacterial action in the gut and by the enzyme systems responsible for the formation of ACh.

Massoulié J, Bon S. The molecular forms of cholinesterase and acetylcholinesterase in vertebrates. *Ann Rev Neurosci*. 1982;5:57-106.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:958-994.

Pantuck EJ. Plasma cholinesterase: gene and variations. *Anesth Analg.* 1993;77:380-386.

Taylor P, Schumacher M, MacPhee-Quingley K, et al. The structure of acetylcholinesterase: relationship to its function and cellular disposition. *Trends Neurosci*. 1987;10:93-95.

A.6. What is the incidence of atypical cholinesterase activity?

The incidence of atypical cholinesterase activity varies with the population studied, but it is approximately 1 of 2,800 in the general population of the United States with a 1:1 male/female ratio.

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Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:958-994.

A.7. What is the significance of the dibucaine number?

The dibucaine number (DN) is the percentage of PChE enzyme activity that is inhibited by dibucaine. Together, the DN and the PChE enzyme activity results can help identify individuals at risk for prolonged paralysis following the administration of succinylcholine. Decreased PChE enzyme activity in conjunction with a DN less than 30 suggests high risk for prolonged paralysis. Normal to decreased PChE enzyme activity in conjunction with a DN 30 to 79 suggests variable risk. The relation between the DN and the duration of succinylcholine neuromuscular blockade is shown in Table 55.1.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:958-994.

A.8. What are some factors that can lower pseudocholinesterase (PChE) levels?

Reduced PChE activity may be associated with the following:

- Abnormal genotype
- Normal physiologic variation (e.g., pregnancy). However, until BChE activity is reduced to <30% of normal, only modest increases in the duration of succinylcholine are to be expected.
- Liver disease
- Malnutrition
- End-stage renal disease
- Burns
- Plasmapheresis

TABLE 55.1 Relation between Dibucaine Number and Duration of Succinylcholine Neuromuscular Blockade

TYPE OF PSEUDOCHOLINESTERASE	GENOTYPE	FREQUENCY	DIBUCAINE NUMBER[a]	RESPONSE TO SUCCINYLCHOLINE OR MIVACURIUM
Homozygous typical	EuEu	Normal	70-80	Normal
Heterozygous	EuEa	1/480	50-60	Slightly prolonged
Homozygous atypical	EaEa	1/3,200	20-30	Markedly prolonged

[a] The dibucaine number indicates the percentage of enzyme inhibited.

- Noncompetitive cholinesterase inhibitors (e.g., pesticides, certain nerve gases)
- Competitive cholinesterase inhibitors (e.g., neostigmine)

These include liver disease, advanced age, malnutrition, pregnancy, burns, oral contraceptives, monoamine oxidase inhibitors, echothiophate, cytotoxic drugs, neoplastic disease, anticholinesterase drugs, tetrahydroaminacrine, hexafluorenium, and metoclopramide.

Davis L, Britten JJ, Morgan M. Cholinesterase. Its significance in anaesthetic practice. *Anaesthesia*. 1997;52:244-260.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:958-994.

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A.9. What are the side effects of succinylcholine?

The most common untoward side effect seen after succinylcholine administration is muscle pain occurring in the first 24 to 48 hours postoperatively. Women and patients undergoing ambulatory surgery appear most susceptible to this phenomenon. The reported incidence of succinylcholine-induced myalgia is quite variable but probably occurs in 25% to 50% of patients. Discomfort is typically characterized as being similar to the muscle soreness that occurs after heavy or unusual exercise. It has been postulated that the etiology of the phenomenon is related to muscle damage caused by asynchronous contractions during the initial muscle depolarization that precedes paralysis. Defasciculating doses of nondepolarizing relaxants (10% of the ED_{95}) given 2 to 5 minutes prior to succinylcholine have been shown to reduce the incidence of myalgia by as much as 50%. Pretreatment with nonsteroidal antiinflammatory drugs has also been shown to reduce the incidence of muscle pain following succinylcholine administration.

Succinylcholine may also be associated with various cardiac dysrhythmias including bradycardia, tachycardia, and junctional and ventricular dysrhythmias. Stimulation of nicotinic receptors at sympathetic and parasympathetic ganglion and muscarinic receptors at the sinus node are believed to be involved in this phenomenon. Infants and children may be more likely to manifest clinically significant bradycardia following succinylcholine administration secondary to their relatively high degree of resting vagal tone as compared to adults. Pretreatment with atropine is effective in preventing succinylcholine-induced bradycardia and is recommended when succinylcholine is to be used in this patient population. Sinus bradycardia in adults is more commonly seen when a second dose of succinylcholine is given approximately 5 minutes after the first. Pretreatment with atropine can prevent this as well. Junctional rhythms following succinylcholine administration are also relatively common. The postulated mechanism of action is muscarinic stimulation of the sinus node that results in diminished sinus activity and the subsequent emergence of the atrioventricular node as the dominant pacemaker. Various mechanisms have been postulated to explain ventricular dysrhythmias that sometimes occur after succinylcholine administration including potassium release from skeletal muscle, succinylcholine mediated sensitivity to catecholamines, and profound sinus and atrioventricular node slowing.

The most serious complication associated with succinylcholine administration is severe and potentially lethal levels of hyperkalemia in at-risk individuals. When succinylcholine is administered to an otherwise healthy patient during the induction of anesthesia, plasma potassium levels typically increase by 0.5 mEq per L as potassium ions move from the intracellular to extracellular space. The increase is transient and is typically tolerated well by most patients. In at-risk patients, however, the efflux of potassium from the intracellular space can be in excess of 3.5 mEq per L, enough to induce malignant dysrhythmias and cardiac arrest. The list of susceptible patients includes those with congenital muscular dystrophies, upper or lower motor neuron defects, prolonged chemical denervation (e.g., muscle relaxants, magnesium, clostridial toxins), direct muscle trauma or inflammation, extensive burns, and disuse atrophy. In the event that succinylcholine is inadvertently given to an at-risk patient and an exaggerated hyperkalemic response is suspected, prompt treatment with calcium chloride (1 to 2 g), hyperventilation, sodium bicarbonate (1 mEq per kg), regular insulin, and dextrose should be initiated to prevent severe dysrhythmias and cardiac arrest.

Succinylcholine also causes increases in intraocular, intragastric, and intracranial pressures (ICP). The increase in intraocular pressure (IOP) caused by succinylcholine begins rapidly after drug administration. Peak pressures may rise as much as 5 to 15 mm Hg before returning to baseline levels about 6 minutes after drug dosing. The etiology of this phenomenon is unclear, but detachment of the intraocular muscles from the globe fails to prevent the pressure rise, which is suggestive of an intraocular mechanism. It has been suggested that succinylcholine use should be avoided in the setting of open-eye injuries, although there is scant evidence that its administration has led to extrusion of intraocular contents or blindness. The increase in intragastric pressure (IGP) caused by succinylcholine is likely related to fasciculations of the abdominal skeletal musculature. A defasciculating dose of a nondepolarizing muscle relaxant given prior to succinylcholine administration can prevent any increase in IGP. Succinylcholine can also cause a transient increase in ICP.

The increase in ICP after succinylcholine administration correlates with muscle fasciculations, increased electroencephalogram (EEG) activity, and elevated cerebral blood flow. Prior administration of a nondepolarizing muscle relaxant can attenuate or even prevent this pressure increase. The use of succinylcholine in the setting of intracranial hypertension is probably best limited to emergency situations where the benefits of rapid airway control outweigh the risks of a transient increase in ICP.

Lastly, it should be remembered that succinylcholine is a potent trigger of malignant hyperthermia (MH). Its use should be restricted to settings where prompt recognition and treatment of MH are possible.

Martyn JA, Richtsfeld M. Succinylcholine-induced hyperkalemia in acquired pathologic states: etiologic factors and molecular mechanisms. *Anesthesiology*. 2006;104:158-169.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:958-994.

B. Intraoperative Management

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B.1. How is the choice among muscle relaxants made?

A muscle relaxant can be chosen based on onset characteristics, duration of action, and method of metabolism (Table 55.2). Muscle relaxants can be characterized as short, intermediate, and long duration. Metabolism may or may not be dependent on liver and kidney function.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:958-994.

B.2. How much do individuals vary in their sensitivity to nondepolarizing relaxants?

In any group of healthy patients, there exists a wide variability in the sensitivity to the effects of neuromuscular blocking agents (NMBAs). The potency of these drugs is expressed as the agent's ED_{50} or ED_{95} (i.e., the dose which will produce 50% or 95% depression of a single twitch [T1] in an average individual). The coefficient of variation (the standard deviation as a percentage of the mean value) for the ED_{95} of most agents approximates 20% to 25%. Thus, if the ED_{95} for drug X is 1.0 mg per kg, in 5% of normal individuals, the ED_{95} may be <0.60 mg per kg. Because of the shape of the dose-response curve of nondepolarizing relaxants, this modest difference in drug requirement may have large consequences as to the depth of block. In these individuals, a plasma level that produces only 50% block of T1 in the average subject may produce >90% instead.

Similarly, the duration of effect of administered relaxants is quite variable. For example: Following a 1.2 mg per kg dose, the clinical duration of rocuronium (time to 25% T1 recovery) in a sample size of only 12 averaged 67 minutes; however, the range in responses went from 39 to 118 minutes.

Following a dose 2 × the ED_{95} of a blocker of intermediate duration (e.g., vecuronium), 30% of individuals will still need pharmacologic antagonism 2 hours later.

TABLE 55.2 Characteristics of Commonly Used Muscle Relaxants

DRUG	ED_{95} UNDER N_2O/O_2 (mg/kg)	DOSE FOR INTUBATION (mg/kg)	INTUBATION TIME (sec)	CLINICAL DURATION (min)	METABOLISM (%)	ELIMINATION	
						KIDNEY (%)	LIVER (%)
Ultrashort acting							
Succinylcholine	0.5	1.0	60	5-10	Plasma cholinesterase (98-99)	<2	0
Short acting							
Mivacurium	0.08	0.2-0.25	120	12-15	Plasma cholinesterase (95-99)	<5	0
Intermediate acting							
Vecuronium	0.05	0.1-0.2	120	45-60	Liver (30-40)	40-50	50-60
Rocuronium	0.3	0.6-1.0	90	45-55	None	<10	>70
Cisatracurium	0.05	0.15-0.2	120	45-60	Hofmann elimination (77)	16	—
Long acting							

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α-Tubocurarine	0.5	0.5-0.6	150	100-120	None	80	20
Pancuronium	0.07	0.08-0.12	150	100-120	Liver (10-20)	85	15
Pipecuronium	0.05	0.08-0.10	180	100-120	10	>90	>10
Doxacurium	0.025	0.05-0.08	240	120-150	None	>90	>10

From Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2010:872-880.

In the aged or in patients with renal or hepatic disease, this variability is even more pronounced. This is especially true of aminosteroid blockers, such as vecuronium or rocuronium, when compared to atracurium or cisatracurium.

Arain SR, Kern S, Ficke DJ, et al. Variability of duration of action of neuromuscular-blocking drugs in elderly patients. *Acta Anaesth Scand*. 2005;49:312-315.

Heier T, Feiner JR, Wright PM, et al. Sex-related differences in the relationship between acceleromyographic adductor pollicis train-of-four ratio and clinical manifestations of residual neuromuscular block: a study in healthy volunteers during near steady-state infusion of mivacurium. *Br J Anaesth*. 2012;108:444-451.

Kopman AF, Kahn NA, Neuman GG. Precurarization and priming: a theoretical analysis of safety and timing. *Anesth Analg*. 2001:93:1253-1256.

B.3. What are the characteristics of nondepolarizing block?

The distinguishing feature of nondepolarizing block is fade on repetitive stimulation. For example, consider a situation in which the amplitude of twitch height (T1) is reduced by 50% with a nondepolarizing blocker when stimuli are delivered at 0.10 Hz (1 every 10 seconds). If the rate of stimulation is increased to 1 Hz, the height of T1 may fall to <20% of control, and at 2 Hz to about 10% of control. This fade is most easily appreciated subjectively when tetanic stimuli (rates ≥30 Hz) are delivered.

Lee C, Katz RL. Fade of neurally evoked compound electromyogram during neuromuscular block by d-tubocurarine. *Anesth Analg*. 1977;56:271-275.

B.4. What is a train-of-four (TOF) stimulus?

A “train-of-four” consists of four stimuli delivered at half-second intervals (2 Hz). The TOF ratio is the height of the fourth indirectly elicited response divided by the amplitude of the first response. This ratio in unparalyzed individuals normally approximates a value of 1.0 when measured by mechanomyography (MMG), electromyography (EMG), or kinemyography but may exceed a value of 1.10 when measured by acceleromyography (AMG) (see the following text). As the depth of block increases, this ratio becomes smaller and eventually the fourth, then the third, and so on responses “drop out.” If only two responses to a TOF stimulus are present, we speak of a TOF count of 2.

Ali HH, Utting JE, Gray C. Stimulus frequency in the detection of neuromuscular block in humans. *Br J Anaesth*. 1970;42:967-978.

B.5. Why is the TOF ratio of clinical importance?

The TOF fade is a far more sensitive index of residual block than single twitch depression. In addition, the TOF ratio is useful because each TOF sequence serves as its own control. It is not necessary to know the amplitude of the evoked response prior to relaxant administration or to worry about baseline drift over time.

Traditionally, the TOF ratio is measured at the hand by noting the response of thumb adduction. While clinicians are much more interested in the neuromuscular function of the diaphragm, masseter, and laryngeal adductors, correlations with adductor pollicis muscle function have over time served as useful clinical surrogates for the muscles we really care about.

Ali HH, Utting JE, Gray TC. Quantitative assessment of residual antidepolarizing block. I. *Br J Anaesth*. 1971;43:473-477.

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Kopman AF. Surrogate endpoints and neuromuscular recovery. *Anesthesiology*. 1997;87:1029-1031.

B.6. How do we define adequate recovery of neuromuscular function?

Once the TOF ratio at the adductor pollicis has recovered to a value of 0.70, tests of mechanical respiratory reserve such as vital capacity and peak expiratory flow rate have usually recovered to within 90% of control. At a TOF value of 0.70, recovery of single twitch to control height and a sustained response to tetanic stimulation at 50 Hz for 5 seconds is usually present.

The studies done in the 1970s thus suggested that a TOF ratio of 0.70 was synonymous with adequate neuromuscular recovery and this was the accepted standard for the next two decades. However, by the late 1990s, this assumption was questioned. Work in awake volunteers demonstrated that at a TOF ratio of 0.70, grip strength was decreased by more than

40%. At a TOF ratio of 0.70, the vast majority of subjects had difficulty apposing their incisor teeth and could not sip water from a straw because they could not make a tight seal around the straw with their lips. All individuals had double vision at TOF ratio <0.90. It was clear that these health volunteers were not “street ready” until their TOF ratios reached or exceeded a value of 0.90. In addition, other volunteer studies revealed even more alarming data. At a TOF ratio of 0.70, there is a decreased response in the ventilatory response to hypoxia (via a mechanism at the carotid body), and the swallowing mechanism is disorganized. Partial paralysis (a TOF of 0.70) causes pharyngeal dysfunction, and there is an increased risk for aspiration with mechanical adductor pollicis TOF ratios <0.90. Pharyngeal function is not normalized until an adductor pollicis TOF ratio of >0.90 is reached. Thus, the current standard for adequate neuromuscular recovery is a TOF of 0.90 or better.

Heier T, Caldwell JE, Feiner JR, et al. Relationship between normalized adductor pollicis train-of-four ratio and manifestations of residual neuromuscular block: a study using acceleromyography during near steadystate concentrations of mivacurium. *Anesthesiology*. 2010;113:825-832.

Kopman AF, Yee PS, Neuman GG. Relationship of the train-of-four fade ratio to clinical signs and symptoms of residual paralysis in awake volunteers. *Anesthesiology*. 1997;86:765-771.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:958-994.

B.7. Are there useful and/or trustworthy clinical tests of neuromuscular recovery?

The first commercially available PNS did not appear until the mid-1960s and units capable of delivering TOF stimuli did not arrive for another decade. Even today, devices that can quantify or measure the TOF ratio in real time are not widely distributed. Thus, clinicians have been reluctant to abandon clinical tests of neuromuscular recovery first suggested half a century ago: tidal volume, negative inspiratory force, grip strength, the 5-second head lift, the ability to protrude the tongue, and so on. Unfortunately, most of these tests share one fundamental weakness. They require an awake and cooperative patient. Ideally, we would like to know the state of neuromuscular recovery prior to awakening the patient and certainly prior to tracheal extubation.

The most widely cited test, the 5-second head lift, is clearly not a sensitive test of residual block. At a TOF ratio of 0.50, the majority of patients may still pass this test. Other widely mentioned tests are no better and may actually be very misleading. Traditional “bedside” tests of residual muscle weakness lack sensitivity and must be considered unreliable.

Heier T, Caldwell JE, Feiner JR, et al. Relationship between normalized adductor pollicis train-of-four ratio and manifestations of residual neuromuscular block: a study using acceleromyography during near steadystate concentrations of mivacurium. *Anesthesiology*. 2010;113:825-832.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:958-994.

B.8. How accurate are subjective estimates of the TOF ratio?

Unfortunately, visual or tactile estimations of the TOF ratio are notoriously inaccurate. Once the TOF ratio exceeds a value of 0.40 to 0.50, a majority of experienced anesthetists are unable to detect the presence of any fade at all. Thus, failure to detect fade made indicates a true value anywhere from 0.50 to 1.0. Accurate assessment of the TOF ratio requires an objective or quantitative monitor (see later in this chapter).

Viby-Mogensen J, Jensen NH, Engbaek J, et al. Tactile and visual evaluation of the response to train-of-four nerve

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stimulation. *Anesthesiology*. 1985;63:440-443.

B.9. What is double burst stimulation (DBS)?

Because of the limitations in subjective interpretation of TOF fade, other patterns of stimulation have been investigated. A somewhat more sensitive test is the response to DBS. This sequence consists of a very brief tetanic pulse (3 stimuli at 50 Hz), a 0.75-second pause, and another brief tetanus. The observer feels two strong twitches. Most observers lose the ability to detect DBS fade at a TOF ratio of about 0.60.

Engbaek J, Ostergaard D, Viby-Mogensen J. Double burst stimulation (DBS): a new pattern of nerve stimulation to identify residual neuromuscular block. *Br J Anaesth*. 1989;62:274-278.

B.10. What is the posttetanic count (PTC)?

As the level of neuromuscular block is progressively deepened, the TOFC eventually falls to zero. No response to TOF stimulation can be elicited. Because posttetanic potentiation is a prominent feature of nondepolarizing block, it is still possible, however, to get additional information about the depth of block. The following sequence is employed: a 5-second 50-Hz tetanus, a 3-second pause, and then 20 single-twitch stimuli at 1 Hz. The number of responses elicited is referred to as the PTC. Generally, when the count approximates a value of 10, the first response to TOF stimulation appears.

Viby-Mogensen J, Howardy-Hansen P, Chraemmer-Jørgensen B, et al. Posttetanic count (PTC): a new method of evaluating an intense nondepolarizing block. *Anesthesiology*. 1981;55:458-461.

B.11. What function does the conventional peripheral nerve stimulator (PNS) serve?

Since subjective estimates of the TOF ratio are so unreliable, one may ask does intraoperative TOF stimulation serve any purpose. The answer is a resounding yes. The only satisfactory method of determining the degree of neuromuscular block is to stimulate a motor nerve with an electric current and observe the contraction of the muscles innervated by that nerve. The TOFC (the number of evoked responses at the thumb that can be detected) gives a useful estimate of the depth of neuromuscular block. A rough rule of thumb (no pun) follows: A TOFC of 1 equals T1 5% recovery, TOFC of 2 = 15% recovery, TOFC of 3 = 25% recovery, and TOFC of 4 (with fade) ≥ 35% recovery. This information allows the clinician to judge the need for additional increments of blocking drug and the point in time when antagonism of residual block with an anticholinesterase is likely to be effective.

Kopman AF. Tactile evaluation of train-of-four count as an indicator of reliability of antagonism from vecuronium- or atracurium-induced neuromuscular blockade. *Anesthesiology*. 1991;75:588-593.

B.12. How can the TOF ratio be measured quantitatively?

Prior to the current decade, the vast bulk of clinical research on neuromuscular function was done by measuring either evoked mechanical force (MMG) or summated electrical action potentials (EMG) at the adductor pollicis. While these techniques represent gold standards for reliability, they are unfortunately cumbersome to use in daily practice. In addition, at present, there are no commercially available free-standing MMG or EMG monitors designed for use in the operating room. However, using a different method of measurement (AMG), it is now possible to obtain a real-time display of the TOF ratio using a small handheld device, which is relatively easy to set up and has a user-friendly interface. The rationale for AMG is based on Newton's second law of motion which states that force is equal to mass times acceleration. Presumably, the mass of the thumb remains constant so that acceleration is directly proportional to force. For measurement of acceleration, a piezoelectric ceramic wafer is fixed to the thumb. When an evoked mechanical response of the thumb is elicited, an electrical signal proportional to the acceleration is generated in the ceramic transducer. This signal can then be digitized, processed, and electronically displayed in real time. Thus, it is now finally possible for the clinician to accurately and easily determine the extent of neuromuscular block (the TOF ratio) in real time. An excellent review of the pros, cons, and limitations of AMG may be found in the following references.

Claudius C, Viby-Mogensen J. Acceleromyography for use in scientific and clinical practice: a systematic review of the evidence. *Anesthesiology*. 2008;108:1117-1140.

Fuchs-Buder T, Schreiber JU, Meistelman C. Monitoring neuromuscular block: an update. *Anaesthesia*. 2009;64(1):82-89.

Hemmerling TM, Le N. Brief review: neuromuscular monitoring: an update for the clinician. *Can J Anaesth*. 2007;54:58-72.

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Loughnan T, Loughnan AJ. Overview of the introduction of neuromuscular monitoring to clinical anaesthesia. *Anaesth Intensive Care*. 2013;41(1):19-24.

Stewart PA, Freelander N, Liang S, et al. Comparison of electromyography and kinemyography during recovery from non-depolarising neuromuscular blockade. *Anaesth Intensive Care*. 2014;42:378-384.

B.13. What are the limitations of anticholinesterase antagonists?

Nondepolarizing neuromuscular block is competitive in nature. Molecules of an NMBA compete with molecules of Ach for access to nicotinic binding sites or receptors at the myoneural junction. The NMBA-receptor or Ach-receptor binding is very evanescent in duration (millisecond). Thus, the relative concentration of NMBA versus Ach determines which molecule is most likely to succeed in the contest for receptor access. Anticholinesterases such as neostigmine affect antagonism by preventing Ach degradation and thus increasing the concentration of Ach in the synaptic cleft. However, there is a ceiling to this effect. Once the cholinesterase enzyme is completely inhibited, the addition of additional neostigmine or edrophonium will have no further effect. In contrast, there is no limit to the concentration of NMBA that may exist at the receptor if excessive doses of relaxant are administered. In practical terms, the maximum depth of block that can be rapidly antagonized by anticholinesterases approximately corresponds to the reappearance of the fourth response to TOF stimulation. To achieve rapid (within 10 minutes) reversal to a TOF ratio of 0.7 in more than 87% of patients, three or four tactile responses should be present at the time of neostigmine administration. It was not possible within 30 minutes to achieve a TOF ratio of 0.9 in all patients, regardless of the number of tactile responses present at neostigmine administration.

Beemer GH, Goonetilleke PH, Bjorksten AR. The maximum depth of an atracurium neuromuscular block antagonized by edrophonium to effect adequate recovery. *Anesthesiology*. 1995;82:852-858.

Kirkegaard H, Heier T, Caldwell JE. Efficacy of tactile-guided reversal from cisatracurium-induced neuromuscular block. *Anesthesiology*. 2002;96:45-50.

B.14. Is there anything wrong with administering neostigmine when the TOFC is less than 3?

As noted earlier, when the TOFC is only 1 or 2, anticholinesterases cannot be counted on to achieve satisfactory reversal in a timely manner. The peak effect of the antagonist is followed by a plateau phase that represents the balance between diminishing anticholinesterase activity and spontaneous recovery. The latter becomes the major determinant at profound levels of neuromuscular block. However, even at a TOFC of 1 to 2, it may be possible to achieve a TOF ratio >0.40 within 10 minutes. The problem for the clinician is that further recovery may be quite slow, and unless an objective monitor of neuromuscular function is being used, the clinician is likely to have the false impression that adequate recovery has been achieved as subjective detection of fade at TOF ratios >0.40 is highly unreliable.

Kopman AF, Kopman DJ, Ng J, et al. Antagonism of profound cisatracurium and rocuronium block: the role of objective assessment of neuromuscular function. *J Clin Anesth*. 2005;17:30-35.

B.15. Is reversal of residual block always necessary?

If a quantitative monitor of neuromuscular function is used, the answer to this question is simple. If the TOF ratio approximates a value of 0.90 or better, anticholinesterase administration is pointless and is best avoided. Neostigmine, edrophonium, atropine, etc., all have their own side effects and should not be administered unnecessarily. Similarly, if the TOFC is less than 4 or 4 with obvious fade, then anticholinesterase administration is indicated. However, objective monitors are still not widely available. What should be done when the TOFC is 4 with no detectable fade?

Many clinicians base the decision of whether to reverse or not on the time interval since the last dose of relaxant. Unfortunately, this is often an unreliable way to proceed. Two hours after a single dose of an intermediate-duration blocker, 30% of individuals may have TOF ratios <0.90, and 10% will still not have returned to a value of 0.70.

Therefore, in the absence of objective evidence that the TOF ratio is >0.85 to 0.90, an antagonist should be administered. However, when no fade to TOF stimulation can be subjectively detected, the dose of neostigmine can be safely reduced to only 0.02 mg per kg.

Caldwell JE. Reversal of residual neuromuscular block with neostigmine at one to four hours after a single intubating dose of vecuronium. *Anesth Analg*. 1995;80:1168-1174.

Fuchs-Buder T, Meistelman C, Alla F, et al. Antagonism of low degrees of atracurium-induced neuromuscular

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blockade: dose-effect relationships for neostigmine. *Anesthesiology*. 2010;112:34-40.

B.16. Is there any way to rapidly antagonize a profound nondepolarizing block?

A radically new approach to reversal now presents itself with the introduction of sugammadex. This drug was recently approved by the United States Food and Drug Administration for use to reverse the effects of neuromuscular blockade induced by rocuronium bromide and vecuronium bromide. Sugammadex is a γ-cyclodextrin. It acts by strongly binding with monoquaternary aminosteroid blocking agents (rocuronium and vecuronium) and thus lowers the free plasma concentrations of these drugs, allowing the agents to diffuse away from the myoneural junction. (Note: Sugammadex is not an effective antagonist of benzylisoquinolinium-based relaxants such as cisatracurium.) To give just one example of its efficacy, rocuronium is given in a dose of 1.2 mg per kg. Five minutes later, sugammadex 12 mg per kg is administered. In less than 2 minutes, the TOF ratio returned to a value of 0.90.

de Boer H, Driessen JJ, Marcus MA, et al. Reversal of rocuronium-induced (1.2 mg/kg) profound neuromuscular block by sugammadex: a multicenter, dose-finding and safety study. *Anesthesiology*. 2007;107:239-244.

Geldner G, Niskanen M, Laurila P, et al. A randomised controlled trial comparing sugammadex and neostigmine at different depths of neuromuscular blockade in patients undergoing laparoscopic surgery. *Anaesthesia*. 2012; 67:991-998.

Lemmens HJ, El-Orbany MI, Berry J, et al. Reversal of profound vecuronium-induced neuromuscular block under sevoflurane anesthesia: sugammadex versus neostigmine. *BMC Anesthesiol*. 2010;10:15.

Naguib M, Brull SJ. Sugammadex: a novel selective relaxant binding agent. *Expert Rev Clin Pharmacol*. 2009;2:37-53.

C. Postoperative Management

C.1. What is the incidence of residual neuromuscular block in the PACU?

Numerous reports since 2000 make clear that even with agents of intermediate duration, undetected residual weakness in the postoperative period is not a rare event. Large studies from Europe, where routine reversal with cholinesterase inhibitors were not administered, report that 20% to 40% of patients arrived in their PACU with TOF values <0.70.

As might be expected when a TOF ratio of 0.90 is set as the standard of adequate antagonism, the incidence of PORB approaches 40%. The incidence of PORB is highly variable from institution to institution and very dependent on individual practice patterns. Diligent intraoperative monitoring and routine antagonism of residual block can result in dramatic reductions in the incidence of PORB. In a study from France between 1995 and 2004, quantitative measurement and reversal of neuromuscular block in the operating room of one institution increased from 2% to 60% and from 6% to 42%, respectively. During the same time, the incidence of residual neuromuscular block, defined as a TOF ratio less than 0.9, decreased from 62% to 3%.

Unfortunately, the lessons vividly demonstrated by these authors are far from universally understood or applied. A recent survey of North American and European clinical practices indicates that even in the year 2009, 10% of clinicians rarely or never monitor neuromuscular function with even the simplest of PNS, and the routine administration of antagonists is even less common.

Naguib M, Kopman AF, Lien CA, et al. A survey of current neuromuscular practice in the United States and Europe. *Anesth Analg*. 2010;111:110-119.

Todd MM, Hindman BJ, King BJ. The implementation of quantitative electromyographic neuromuscular monitoring in an academic anesthesia department. *Anesth Analg*. 2014;119:323-331.

Yip PC, Hannam JA, Cameron AJ, et al. Incidence of residual neuromuscular blockade in a post-anaesthetic care unit. *Anaesth Intensive Care*. 2010;38:91-95.

C.2. Does undetected postoperative residual neuromuscular block (PORB) have clinical consequences?

In North America, in excess of 20 million patients each year receive an anesthetic. The size of the subgroup that receives a nondepolarizing blocking agent is unknown but obviously still numbers in the millions. As indicated previously, the exact

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incidence of PORB probably varies greatly from institution to institution. Nonetheless, even if it is as low as 5% overall

(highly optimistic), the number of individuals who arrive in the PACU with suboptimal neuromuscular recovery is substantial. Nevertheless, outcome studies that suggest that this a major public health risk are few and far between, and few clinicians perceive residual block as an important safety issue. In truth, the majority of patients who arrive in the PACU with TOF ratios <0.90 do not experience complications. However, not all individuals are so fortunate. Undetected PORB is clearly associated with potentially adverse respiratory events and increased morbidity. A recent prospective case-controlled study of critical respiratory events (CREs) (e.g., episodes of hypoxia, signs of airway obstruction, need for reintubation) in a university hospital's PACU is instructive. Sixty-one patients with CREs were identified. Their mean TOF ratio as measured by AMG was 0.62. The TOF value in 42 matched controls was 0.98. The same authors in a separate study were also able to demonstrate a lower frequency of residual neuromuscular blockade in the PACU (4.5%) (TOF ratio ≤0.9) in cases where intraoperative AMG was employed compared with the cases where conventional PNS were used (30%). During transport to the PACU, fewer AMG patients developed arterial oxygen saturation values, measured by pulse oximetry, of less than 90% (0%) or airway obstruction (0%) compared with subjective monitoring (21.1% and 11.1%, respectively). The incidence, severity, and duration of hypoxemic events during the first 30 minutes of PACU admission were less in the AMG group (all $P < .0001$). These findings add credence to the hypothesis that incomplete neuromuscular recovery is an important contributing factor in the development of adverse respiratory events in the PACU.

Brull SJ, Murphy GS. Residual neuromuscular block: lessons unlearned. Part II: methods to reduce the risk of residual neuromuscular blockade. *Anesth Analg*. 2010;111:129-140.

Butterly A, Bittner EA, George E, et al. Postoperative residual curarization from intermediate-acting neuromuscular blocking agents delays recovery room discharge. *Br J Anaesth*. 2010;105:304-309.

Kopman AF, Brull SJ. Is postoperative residual neuromuscular block associated with adverse clinical outcomes? What is the evidence? *Curr Anesthesiol Rep*. 2013; 3:114-121.

Kumar GV, Nair AP, Murthy HS, et al. Residual neuromuscular blockade affects postoperative pulmonary function. *Anesthesiology*. 2012;117:1234-1244.

Murphy GS, Brull SJ. Residual neuromuscular block: lessons unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. *Anesth Analg*. 2010;111:120-128.

Murphy GS, Szokol JW, Marymount JH, et al. Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. *Anesthesiology*. 2008;109:389-398.

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Chapter 56
Burns

Shreyajit R. Kumar
Anup Pamnani
Michael Tjeuw

A 45-year-old man, who was smoking in bed, sustained 40% second- and thirddegree burns over his face, neck, chest, and upper extremities. He had a history of hypertension, angina, and angioplasty of the right coronary artery 1 year ago. He has smoked three packs of cigarettes per day for 20 years, and he drinks alcohol daily. He is scheduled for tangential excision of eschar on the third post-burn day. His blood pressure is 190/100 mm Hg with a heart rate of 120 beats per minute, and he weighs 110 kg.

A. Medical Disease and Differential Diagnosis

1. How do you classify the burn injury?
2. How do you express the extent of the burn injury?
3. Should the “rule of nines” be used in children?
4. What is the definition and etiologies of a major burn according to the American Burn Association?
5. What functions does the skin perform?
6. What pathophysiologic changes accompany major thermal injury?
7. Name some of the known mediators released with thermal injury. What are the responses to those mediators?
8. What is the prognosis for this patient? What major factors affect his prognosis?
9. What are the most common causes of death?
10. Does this patient have a smoke inhalation burn? How do you make the diagnosis?
11. What is carbon monoxide poisoning? How do you diagnose and treat carbon monoxide poisoning?
12. What resuscitative measure would you institute immediately in this patient with 40% burns?
13. What fluid formula would you use?
14. What cardiovascular changes typify the burn injury?
15. What hematologic changes occur in burn injury?
16. What changes occur in liver function? What are the anesthetic implications of such changes?
17. What are Curling ulcers? How can they be prevented?
18. What complications are associated with electrical burns?

B. Preoperative Evaluation and Preparation

1. What preoperative preparations would you order? What are particular concerns in this patient?
2. What are the various operative and management options available for severely burned patients?

3. What are the advantages and disadvantages of early tangential excision splitthickness skin grafting (TE/STSG)?
4. What is this patient's mean arterial blood pressure? How do you calculate it?
5. Are you concerned about this patient's blood pressure? What treatment would you institute?
6. This patient was ventilated with respirator settings of tidal volume, 800 mL; respiratory rate, 20 breaths per minute;

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FIO_2, 60%; and positive end-expiratory pressure, 10 cm H_2O. Arterial blood gas analyses showed the following: pH, 7.24; PO_2, 56 mm Hg; PCO_2, 60 mm Hg; and O_2 saturation, 80%. How would you interpret these arterial blood gas analysis results? What are the possible causes of high PCO_2 and low PO_2?

7. How do you calculate oxygen content and oxygen delivery? What factors govern the oxygen delivery to the tissues?
8. What are the symptoms and signs of alcohol withdrawal? Are you concerned that this patient could develop delirium tremens?
9. How would you prevent the adverse effects of alcohol withdrawal?

C. Intraoperative Management

1. What monitors would you use in the operating room?
2. What information can be obtained from an arterial line and a pulmonary artery catheter? How are these calculations performed?
3. If the patient had not been intubated, how would you proceed with the anesthetic induction?
4. Why is awake intubation considered the safest?
5. What anesthetic agents would you use? Discuss inhalation versus intravenous agents.
6. Why are you concerned about the patient's body temperature? What is normothermia for a burned patient?
7. How is temperature best maintained?
8. What derangements occur with hypothermia?
9. What muscle relaxant would you use?
10. Why is succinylcholine contraindicated in burned patients? For how long should it be avoided?
11. What other adverse effects are associated with succinylcholine?
12. How are the doses of nondepolarizing muscle relaxants affected by burn injury?
13. How are the muscle relaxants such as succinylcholine, atracurium, cisatracurium, vecuronium, pancuronium, rocuronium, and curare metabolized and eliminated? Which of them has significant histamine release?
14. What is the difference between metabolism and elimination of drugs?

D. Postoperative Management

1. How would you monitor this patient during transport?
2. What is meant by diffusion hypoxia? How do you prevent it?
3. Why do patients often shiver in the recovery room on emergence from anesthesia?
4. Discuss the causes of oliguria in the recovery room.

A. Medical Disease and Differential Diagnosis

A.1. How do you classify the burn injury?

Burns classification is based on both depth and degree of tissue injury. First-degree burns are superficial and confined to epidermal injury. Second-degree burns are partial-thickness, involving the epidermis and dermis. Second-degree burns are subdivided into superficial

and deep dermal burns. Third-degree burns are full-thickness and characterized by irreversible destruction of all dermal and epidermal elements. Fourth-degree burns involve injury to underlying tissue structures—muscle, fascia, tendon, and bone (Table 56.1).

TABLE 56.1 Classification of Burn Depth

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CLASSIFICATION	BURN DEPTH	OUTCOME
Superficial		
First degree	Confined to epidermis	Heals spontaneously
Partial thickness		
Second degree		
Superficial dermal burn	Epidermis and upper dermis	Heals spontaneously
Deep dermal burn	Epidermis and deep dermis	Requires excision and grafting for rapid return of function
Full thickness		
Third degree	Destruction of epidermis and dermis	Wound excision and grafting required Some limitation of function and scar formation
Fourth degree	Muscle, fascia, bone	Complete excision required, limited function

From MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749-770, with permission.

MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749-770.

Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:521-547.

A.2. How do you express the extent of the burn injury?

Extent of burn injury is expressed as a total body surface area (TBSA) percentage. Burn size is estimated by the “rule of nines” (Fig. 56.1). In adults, each upper extremity and the head and neck are 9% of TBSA. The lower extremities and anterior and posterior trunk are 18% each, and the perineum is approximately 1% of the TBSA. The burn proportions are additive, yielding a TBSA burn.

MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749-770.

Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:521-547.

A.3. Should the “rule of nines” be used in children?

The “rule of nines” will not estimate TBSA burns in children because the head and neck comprise a relatively larger portion of the body surface area and a smaller surface area in the lower extremities. The Lund and Browder chart represents a precise method, accounting for the changing proportions of the TBSA from infancy to adulthood (Fig. 56.2).

MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749-770.

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Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:521-547.

A.4. What is the definition and etiologies of a major burn according to the American Burn Association?

The American Burn Association defines a Brunicardi burn as follows:

- Full-thickness burns more than 10% TBSA
- Partial-thickness burns more than 25% in adults or 20% at extremes of age
- Burns involving face, hands, feet, or perineum

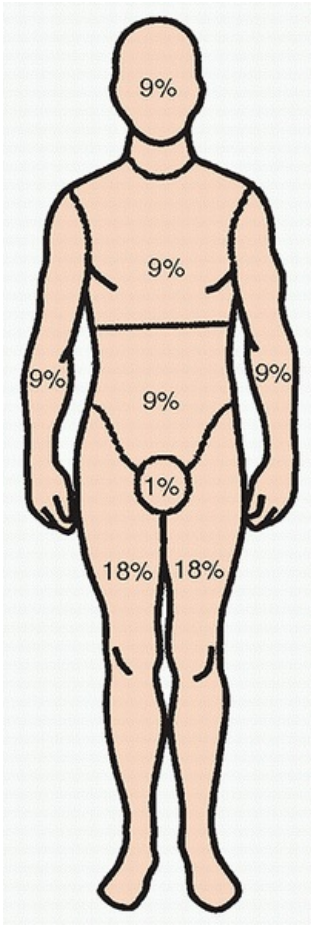


FIGURE 56.1 The rule of nines for determining the percentage of body surface area burned in adults. (Adapted from MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749-770.)

The American Burn Association accounts for the following etiologies of burn injury:

- Flame—from superheated oxidized air
- Scaled—from hot liquid
- Contact—from hot or cold solid materials
- Chemicals—from noxious chemicals
- Electricity—conduction of current through tissues

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Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:521-547.

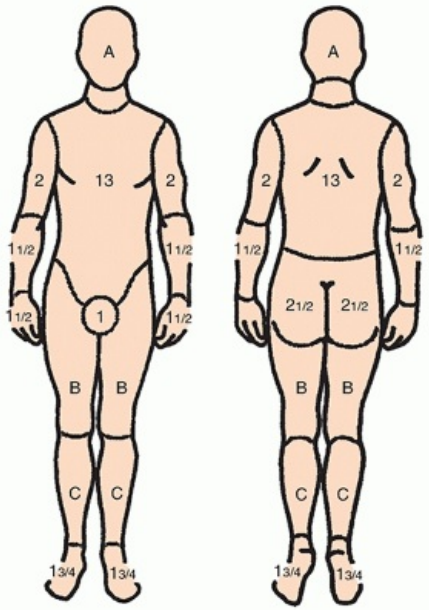
A.5. What functions does the skin perform?

The skin is the largest organ of the body with a surface area ranging from 1.5 to 2.0 m^2 in the adult. It is the primary immune barrier, protecting against microorganism invasion. The skin provides thermal regulation, fluid and electrolytes homeostasis, vitamin D metabolism, and sensation (touch, temperature, pain).

Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:125-126, 209.

A.6. What pathophysiologic changes accompany major thermal injury?

The pathophysiologic alterations that accompany major thermal injury are complex. Destruction of the skin—the largest organ of the body—has a profound systemic impact. Thermal regulation, fluid and electrolyte homeostasis, and protection against bacterial infection are all lost. Inflammatory mediators released from burn injury result in a leaky capillary syndrome; fluid and albumin are sequestered from the intravascular compartment into the burn wound, causing hemoconcentration and hypoalbuminemia. Increased secretion of antidiuretic hormone may cause oliguria or anuria.



Relative percentages of areas affected by growth

	AGE IN YEARS					
AREA	0	1	5	10	15	Adult
A: half of head	9½	8½	6½	5½	4½	3½
B: half of thigh	2¾	3¼	4	4¼	4½	4¾
C: half of leg	2½	2½	2¾	3	3¼	3½

FIGURE 56.2 Diagram and table for determining the percentage of body surface area burned in children. (Adapted from MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749-770.)

The metabolic rate is markedly increased after the burn injury. Depending on the size of the burn, the increase in metabolic rate can be doubled or tripled with a proportionate increase in oxygen consumption and carbon dioxide production. This hypermetabolic state will continue for weeks or months until full skin coverage is achieved and the tissue repair processes are complete.

Cardiac output (CO) is often decreased in patients with major burns. This decrease is partially due to a rapid reduction in circulating blood volume as well as an upregulation of circulating myocardial-depressant factor.

Changes in vascular integrity occur in other areas remote from the injury site. The entire vascular compartment becomes permeable to circulating macromolecules, manifesting as edema. Severe pulmonary edema can be life-threatening. Airway edema is the impetus for early intubation.

Pulmonary function is significantly altered. A reduction occurs in all of functional residual capacity, lung capacity, and chest

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wall compliance. Increases occur of the alveolar-arterial oxygen gradient (PAO_2-PaO_2) and minute ventilation (as high as 40 L per minute; normal, 6 L per minute).

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:227-326.

Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:103-115.

MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749-770.

A.7. Name some of the known mediators released with thermal injury. What are the responses to those mediators?

After a thermal injury, mediators released from the burn wound contribute to local inflammation and edema. Local mediators include histamine, prostaglandins, thromboxane, bradykinin, nitric oxide, serotonin, catecholamine, and platelet aggregation factor.

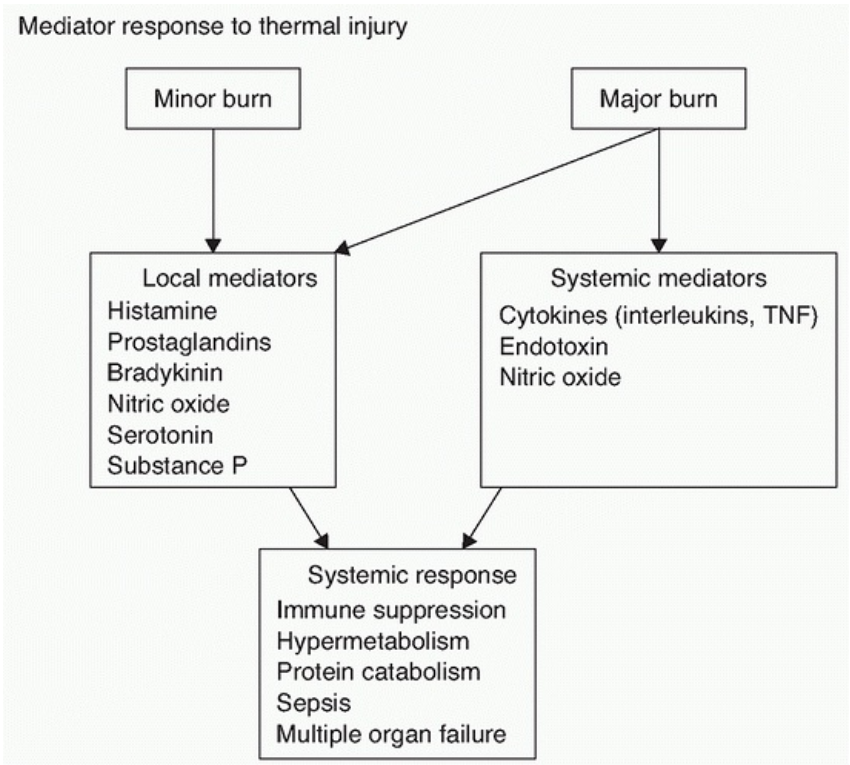


FIGURE 56.3 Mediators released with thermal injury and the response to their release. TNF, tumor necrosis factor. (From MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89: 749-770, with permission.)

In minor burns, the inflammatory process is limited to the wound itself. In major burns, local injury triggers the release of circulating (systemic) mediators, resulting in a systemic response. This response is characterized by hypermetabolism, immune suppression, and the systemic inflammatory response syndrome (protein catabolism, sepsis, multiple organ failures).

The systemic mediators are cytokines (interleukins), endotoxin, and nitric oxide (Fig. 56.3).

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:227-326.

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Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:103-115.

MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749-770.

A.8. What is the prognosis for this patient? What major factors affect his prognosis?

The prognosis for this patient is very poor. Statistical survival based on TBSA alone would predict a less than 50% chance of survival. Other factors that affect his prognosis are age, size and depth of burn, associated pulmonary injury, and preexisting medical disease. In this patient with a history of angioplasty for coronary artery disease, hypertension, heavy smoking, and obesity, the risk of myocardial infarction is greatly increased.

A.9. What are the most common causes of death?

The major early cause of death is asphyxia. The most common cause of long-term mortality is septic complications. Hypovolemic shock is no longer common in the United States due to a better understanding of early goal-directed resuscitation.

A.10. Does this patient have a smoke inhalation burn? How do you make the diagnosis?

The patient probably sustained a smoke inhalation burn. Smoke inhalation should be highly suspected in patients who were burned in an enclosed space, received burns of the face, were burned while under the influence of alcohol or drugs, or lost consciousness at the time of the accident.

A patient with smoke inhalation often exhibits no physical signs or symptoms during the first 24 hours after the burn—the "lucid period." The early symptoms and signs of respiratory tract

injury include burned nasal mucosa/lips/mouth, singed nasal hair, hoarseness, wheezing, and soot in the sputum. The posterior pharynx may appear red, and the larynx may appear edematous. Radiographic findings are usually negative immediately after injury. Laboratory tests include blood gas analysis, carboxyhemoglobin concentration, xenon scans, and fiberoptic bronchoscopy.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:227-326.

Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:229-239.

A.11. What is carbon monoxide poisoning? How do you diagnose and treat carbon monoxide poisoning?

Carbon monoxide is the leading cause of hypoxia in survivors of burn injuries; it is liberated from the incomplete combustion of carbon-containing substrates (wood, coal, and gasoline). Carbon monoxide has a 250 times greater affinity for hemoglobin than oxygen, displacing oxygen from its hemoglobin-binding sites. CO-oximetry is necessary for diagnosis of carbon monoxide poisoning, as the arterial blood gas PaO_2 will be falsely normal.

Expeditious oxygen therapy will displace carbon monoxide from hemoglobin moieties. The standard half-life of carbon monoxide elimination is 4 to 6 hours at room air. This is reduced to 40 to 80 minutes with 100% oxygen and 15 to 30 minutes with hyperbaric oxygen therapy.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:227-326.

Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:229-239.

A.12. What resuscitative measure would you institute immediately in this

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patient with 40% burns?

Early and aggressive fluid resuscitation will combat the distributive, third-spacing hypovolemia. Judicious fluid administration will ensure end-organ perfusion and adequate urine output. If an upper airway burn is involved, endotracheal intubation is indicated to prevent edematous airway compromise.

A.13. What fluid formula would you use?

The Parkland formula will guide the initial resuscitation in hypovolemic shock after burn injury. It has been adopted as the standard of practice at most burn centers due to its simplicity, reduced cost, and equivalent outcome when compared to other calculations for fluid administration.

Other formulas differ widely in the colloid/crystalloid ratio and in the rate of fluid administration. Although much controversy still surrounds the use of “the solution” for resuscitation in burn shock, scientific investigation supports the need for both crystalloid and colloid solutions (Table 56.2). Current sentiment supports the Parkland calculation as a resuscitation “starting point.” Emphasis should then be placed on factors used to guide resuscitation; urine output of 0.5 to 1.0 mL/kg/hr is the important parameter.

TABLE 56.2 Fluid Resuscitation for Adults with Major Burns

CRYSTALLOID REGIMENS		
Parkland	Lactated Ringer's	4 mL/kg/% burn
Modified Brooke	Lactated Ringer's	2 mL/kg/% burn
COLLOID REGIMENS		
Evans	Normal saline	1 mL/kg/% burn
	Colloid	1 mL/kg/% burn
	5% Dextrose	2,000 mL/24 hr
Brooke	Lactated Ringer's	1.5 mL/kg/% burn
	Colloid	0.5 mL/kg/% burn
	5% Dextrose	2,000 mL/24 hr

Parkland Formula

First 24 hours

- *Electrolyte solution* (*lactated Ringer's*)—4 mL/kg/percentage of body area with second- and third-degree burn
- *Administration rate*—half the solution given in the first 8 hours, one-quarter in the second 8 hours, one-quarter in the third 8 hours
- *Urine output*—maintain at 0.5 to 1.0 mL/kg/hr

Second 24 hours

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- *Glucose in water*—to replace evaporated water loss and maintain serum sodium concentration of 140 mEq per L
- *Colloid solutions (e.g., albumin)*—amount proportional to burn
  - *30% to 50% burn*: 0.3 mL/kg/percentage of burn
  - *50% to 70% burn*: 0.4 mL/kg/percentage of burn
  - *Larger than 70% burn*: 0.5 mL/kg/percentage of burn
- *Urine output*—maintain at 0.5 to 1.0 mL/kg/hr

Blumetti J, Hunt JL, Arnoldo BD, et al. The Parkland formula under fire: is the criticism justified? *J Burn Care Res*. 2008;29(1):180-186.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery* . 10th ed. New York: McGraw-Hill; 2015:227-326.

Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:115-125.

A.14. What cardiovascular changes typify the burn injury?

Microvascular destruction of capillary membranes results in acute fluid sequestration from intravascular compartment to interstitial spaces. Decreased plasma volume leads to depressed CO and hypotension. Catecholamine release triggers vasoconstriction, which may further compromise tissue perfusion. Ventricular dysfunction is attributed to myocardialdepressant factor present in lymphatic fluid.

Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:361-369.

Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:521-547.

A.15. What hematologic changes occur in burn injury?

Hematologic changes can be seen in erythrocytes (red blood cells [RBCs]), platelets, and the coagulation mechanism.

Erythrocytes (*RBCs*). Hemoconcentration occurs immediately after the injury, from the initial third spacing of plasma. Anemia results from secondary fluid resuscitation and from hemolysis during thermal injury. Erythrocyte production is altered from circulating inhibitory factors.

Platelets. Dilutional thrombocytopenia occurs from initial resuscitation. Thrombocytopathia results from microaggregate formation in the skin and smoke-damaged lung. The platelet level will normalize by the end of the first week unless sepsis or multiple system organ failure occurs.

Coagulation. Thrombotic and the fibrinolytic mechanisms are activated, and clotting factors decrease. Disseminated intravascular coagulopathy may occur in fourth-degree burns involving structures deep to the skin.

Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:277-289.

Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:521-547.

A.16. What changes occur in liver function? What are the anesthetic implications of such changes?

Decreased circulating volume during the initial burn phase may result in shock liver and restrict hepatic detoxification capacity. Albumin levels will decrease, which may increase the free fraction levels of benzodiazepines and phenytoin. In contrast, a rise in the acute-phase

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reactant α_1-acid-glycoprotein increases the binding of pH basic drugs, such as lidocaine, propranolol, and muscle relaxants.

Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:301-313.

Martyn JAJ. The use of neuromuscular relaxants in burn patients. In: Rupp SM, ed. *Problems in Anesthesia*. Philadelphia, PA: JB Lippincott; 1989:482.

A.17. What are Curling ulcers? How can they be prevented?

A Curling ulcer is a gastric or duodenal stress ulcer resulting from a systemic thermal injury. Without treatment, the incidence is as high as 80%. Atrophy of the small bowel mucosa occurs within 12 hours of injury and is proportional to burn extent. Additional decreases in intestinal blood flow exacerbate the gastric injury. Curling ulcers can be prevented prophylactically with antacids, H_2-antagonists, and early enteral feeding.

Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:521-547.

A.18. What complications are associated with electrical burns?

Electrical burns result in small skin area necrosis, with large amounts of damage to deep tissue structures—muscles, tendons, blood vessels, and nerves. Thus, the fluid losses are greater than predicted from Parkland calculation. The total injury is determined by the duration of current flow, the resistance of the tissue, and the area of contact. Muscle necrosis may cause myoglobinuria and acute tubular necrosis. Thrombotic phenomena may manifest late. Cardiac conduction abnormalities, ectopy, and congestive heart failure may all be secondary to electrical injury.

Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:433-441.

B. Preoperative Evaluation and Preparation

B.1. What preoperative preparations would you order? What are particular concerns in this patient?

A thorough medical history and physical examination should be conducted, with a focus on this patient's salient risk factors. In this patient, hypertension, ischemic heart disease, angioplasty of left main coronary artery, and the history of heavy smoking and heavy alcohol consumption are of particular concern. The following laboratory tests should be ordered: complete blood count, basic metabolic profile (“chem-10”), venous lactate, coagulation profile, liver function tests, electrocardiogram, urinalysis, chest radiograph, and arterial blood gas. With respect to this patient's left main coronary artery disease, cardiac enzymes would be beneficial. Any concern about a tenuous cardiac status should prompt involvement by a cardiologist.

Urine output, central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), CO, and cardiac index (CI) will all be beneficial in assessing the adequacy of fluid volume resuscitation.

B.2. What are the various operative and management options available for severely burned patients?

Early tangential excision of burn tissue and early wound closure, primarily by skin grafting, has significantly improved mortality among the severely burned population. Eschar, or burned skin, is an active medium for bacterial propagation, and topical antibiotic creams—silver sulfadiazine—should be applied for infection control.

Early removal of injured tissue prevents wound infection and decreases systemic inflammatory response. A widely adopted strategy involves a 48-hour period of initial resuscitation to achieve hemodynamic stability, followed by TE/STSG. The extent of escharotomy is limited to 20% of TBSA and repeated every 2 days until excision is complete.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery* . 10th ed. New York: McGraw-

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Hill; 2015:227-326.

Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:521-547.

B.3. What are the advantages and disadvantages of early tangential excision splitthickness skin grafting (TE/STSG)?

The expeditious escharotomy—within 2 days—will remove the bacterial load, reduce the risk of bacteremia and sepsis, and shorten the recovery phase and overall hospital length of stay. Very early excision—within 24 hours—has the disadvantage of a major operative stress during the resuscitative phase of the injury. The patient is not optimized, and there is an increase in anesthetic risk.

Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:157-173.

Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:521-547.

B.4. What is this patient's mean arterial blood pressure? How do you calculate it?

This patient's mean arterial blood pressure (MAP) can be calculated from his blood pressure of 190/100 mm Hg; his MAP is 130 mm Hg. The equation is MAP = two-third of diastolic pressure + one-third of the systolic pressure. An equivalent calculation is MAP = diastolic pressure + one-third of the pulse pressure; the pulse pressure is the difference between systolic and diastolic pressure.

B.5. Are you concerned about this patient's blood pressure? What treatment would you institute?

Yes, given this patient's history of angina and coronary artery disease requiring left main coronary angioplasty, his blood pressure should be maintained in the normal range.

β-Blockers (labetalol, Lopressor), calcium channel blockers (nicardipine), angiotensinconverting enzyme inhibitors (Vasotec), and hydralazine are all intravenous vasodilators that may be utilized.

This tachycardic patient—heart rate 120 beats per minute—would benefit from *β*-blockade with labetalol or Lopressor. Reduction of afterload and tachycardia will decrease overall myocardial oxygen demand and reduce his risk of infarction.

Adequacy of volume resuscitation should be assessed. Measuring CVP, PAOP, CO, CI, and systemic vascular resistance (SVR) will aid in treatment initiation.

B.6. This patient was ventilated with respirator settings of tidal volume, 800 mL; respiratory rate, 20 breaths per minute; FIO_2, 60%; and positive end-expiratory pressure, 10 cm H_2O. Arterial blood gas analyses showed the following: pH, 7.24; PO_2, 56 mm Hg; PCO_2, 60 mm Hg; and O_2 saturation, 80%. How would you interpret these arterial blood gas analysis results? What are the possible causes of high PCO_2 and low PO_2?

Arterial blood gas analysis demonstrates an abnormal respiratory acidosis with a substantial hypoxic alveolar-arterial (A-a) gradient. This patient was hypoventilated with high PCO_2 of 60 mm Hg (normal PCO_2 is 35 to 45 mm Hg). He has an uncompensated respiratory acidosis.

The etiology of this patient's hypercarbia may be a hypermetabolic state with marked increase in CO_2 production.

The most common cause of hypoxemia with an increased A-a gradient is a ventilation/perfusion mismatch. Atelectasis,

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pneumonia, pulmonary edema, or malposition of endotracheal tube with single-lung ventilation will increase dead space or shunt fractionation, resulting in ventilation/perfusion mismatch.

B.7. How do you calculate oxygen content and oxygen delivery? What factors govern the oxygen delivery to the tissues?

The oxygen content of arterial blood (CaO_2) is the sum of two components, the oxygen dissolved in plasma and the oxygen bound to hemoglobin (Hgb). It is expressed as:

CaO_2 (mL/dL) = 1.31 × Hgb (g/dL) × SaO_2 (%) + 0.003 × PaO_2

Normal arterial oxygen content: CaO_2 = 20.73 mL per 100 mL

Oxygen delivery (DO_2) is directly proportional to the CO and arterial oxygen content:

$DO_2 = CO \times CaO_2 = CO \times [(1.31 \times Hgb\ (g/dL) \times SaO_2\ (\%) + 0.003 \times PaO_2]$

Thus, the three main factors that govern the oxygen delivery to tissues are CO, Hgb, and arterial oxygen saturation.

Criner GJ, Barnette RE, D'Alonzo GE, eds. *Critical Care Study Guide: Text and Review*. 2nd ed. New York: Springer; 2010:493-494.

B.8. What are the symptoms and signs of alcohol withdrawal? Are you concerned that this patient could develop delirium tremens?

Minor withdrawal symptoms peak within 10 to 30 hours of the last drink and include restlessness, insomnia, tremors, disorientation, convulsions, and hallucinations. Major withdrawal symptoms—*delirium tremens*—occur 3 to 10 days after cessation of drinking and are characterized by severe autonomic hyperactivity (tachycardia and hypertension), agitation, fever, diaphoresis, and global convulsions. This patient is at great risk of withdrawal syndrome, and early treatment should be initiated.

B.9. How would you prevent the adverse effects of alcohol withdrawal?

Benzodiazepines are effective in preventing the alcohol withdrawal syndrome symptoms. If autonomic hyperactivity occurs, *β*-blockers will attenuate the tachycardia and dysrhythmias.

C. Intraoperative Management

C.1. What monitors would you use in the operating room?

All standard monitors, noninvasive blood pressure, electrocardiogram (ECG) (leads II and V), pulse oximetry, capnography, and temperature should be used in this patient. A Foley catheter is essential for assessing urine output and volume status. An indwelling arterial line may be helpful if the standard blood pressure cuff interferes with the surgical field. A pulmonary artery catheter with CVP monitoring will be beneficial in this severely burned patient with ischemic heart disease.

C.2. What information can be obtained from an arterial line and a pulmonary artery catheter? How are these calculations performed?

The arterial line displays beat-to-beat continuous blood pressure measurements. This is most useful in fluctuating hypotensive or hypertensive situations. During dysrhythmias such as atrial fibrillation or ventricular tachycardia, variations in ventricular response or blood pressure will be recognized instantly. The morphology of the waveform can also provide information about arterial resistance (i.e., a narrow waveform is suggestive of both a reduced stroke volume and an increased SVR), stroke volume (area under the curve), and preload (pulse pressure variation, particularly in response to mechanical positive pressure ventilation). In addition, it serves as ready vascular access for blood sampling (e.g., arterial blood gas analyses, electrolytes, hematocrit, and blood sugar levels).

A pulmonary artery catheter allows the measurement of PAOP, a surrogate of left atrial pressures. Left atrial pressure reflects left ventricular end-diastolic pressure, which is helpful in assessing the preload status of the left ventricle. CVP, although useful as a rough estimate of preload, does not correlate with left ventricular end-diastolic pressure when either isolated right-sided or left-sided cardiac dysfunction occurs. The multilumen pulmonary artery catheters are capable of

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measuring CVP and CO through the thermodilution method. It also permits sampling of mixed venous blood. These measurements permit calculation of many hemodynamic variables.

$$CI = \frac{CO}{\text{Body surface area}} \qquad \text{(normal 2.8 to 4.2 L/min/m}^2\text{)}$$

$$\text{Stroke volume (SV)} = \frac{CO}{\text{Heart rate}} \qquad \text{(normal 60 to 80 mL/beat)}$$

$$\text{Stroke index (SI)} = \frac{CI}{\text{Heart rate}} \qquad \text{(normal 40 to 65 mL/beat/m}^2\text{)}$$

$$SVR = \frac{\text{Mean BP} - \text{CVP}}{CO} \times 80 \qquad \text{(normal 900 to 1,400 dynes/sec/cm}^5\text{)}$$

$$PVR = \frac{\text{Mean PAP} - \text{PCWP}}{CO} \times 80 \qquad \text{(normal 150 to 250 dynes/sec/cm}^5\text{)}$$

Mixed venous blood samples are needed for shunt calculations:

$$\frac{Q_s}{Q_t} = \frac{(Cc_{O_2} - Ca_{O_2})}{(Cc_{O_2} - C\bar{v}_{O_2})}$$

Cc_{O_2} = pulmonary capillary oxygen content

Ca_{O_2} = artery oxygen content

$C\bar{v}_{O_2}$ = mixed venous oxygen content

A low mixed venous oxygen level (<30 mm Hg) is suggestive of inadequate tissue perfusion.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:1315-1344.

C.3. If the patient had not been intubated, how would you proceed with the anesthetic induction?

This patient has a facial burn, which portends a difficult intubation. Burns on the face may cause severe airway and facial edema; careful assessment of the mouth opening, pharynx, and larynx is warranted. The safest way to secure the airway is to perform an awake intubation with topical anesthesia and mild sedation; it can be achieved by either direct or fiberoptic-guided intubation. If prolonged postoperative intubation is anticipated, the nasotracheal route is more easily secured, provides optimal patient comfort, and permits better oral hygienic care. Phenylephrine drops will achieve nasal mucosa vasoconstriction. Alternatively, a tracheostomy should be considered early in those patients with acute lung injury who will require prolonged mechanical ventilation.

C.4. Why is awake intubation considered the safest?

Awake intubation is the safest modality to secure an airway because when the patient is breathing spontaneously, the patient retains airway protective reflexes, is at lower risk for upper airway obstruction, and is less likely to have oxygen desaturation. This precludes the need for mask ventilation and avoids the risk of stomach distention.

When the patient is breathing spontaneously and maintains adequate oxygenation, the anesthesiologist has more time to do laryngoscopy. Identifying the passage of air from the glottis may be helpful in blind intubation.

C.5. What anesthetic agents would you use? Discuss inhalation versus intravenous agents.

For the severely burned patient, once the airway is secured, a high-dose narcotic-muscle relaxant technique would be preferred because this technique confers intraoperative hemodynamic stability and optimal postoperative analgesia.

The narcotics, such as morphine, meperidine (Demerol), fentanyl, or sufentanil, do not interfere with myocardial contractility, whereas potent inhalation agents will depress the myocardium. If inhalation agents are chosen, the concentration should be carefully titrated to prevent hemodynamic embarrassment.

C.6. Why are you concerned about the patient's body temperature? What is normothermia for a burned patient?

Massive burn injury with loss of skin integrity will lead to considerable evaporative fluid losses and the risk of profound intraoperative hypothermia. This tendency is exacerbated by

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the vasodilatory effects of general anesthesia on central thermoregulatory centers and by the cool arid operating room milieu. The infusion of large volume intravenous fluids at room temperature also contributes to the development of hypothermia.

Normothermia for a burned patient is approximately 38.5°C. The stress of thermal injury results in a resetting of the hypothalamic thermostat.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:227-326.

Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:173-199.

Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:521-547.

C.7. How is temperature best maintained?

Hypothermia is a chief concern from loss of the insulator effect of the skin organ. Heat losses occur through convection, conduction, evaporation, and radiation. Methods to maintain normothermia should involve active warming and prevention of heat loss. Crystalloid and blood transfusions must be administered through the blood- and/or fluid-warming device. A prewarmed thermal mattress, such as a Bear-Hugger, is placed under a single-layer sterile sheet on the operating table. Warming the operating room to temperatures between 24°C (75.2°F) and 27°C (80.6°F) with a relative humidity higher than 50% is particularly effective. The nonsurgical areas of the patient's body must be covered. Heated, humidified airway circuits are most effective in minimizing the heat loss from ventilation with cold anesthetic gases.

C.8. What derangements occur with hypothermia?

Hypothermia causes many physiologic changes. Hypothermia decreases metabolism, heart rate, CO, and blood pressure. At temperatures less than 28°C (82.4°F), atrial pacing becomes irregular and ventricular ectopy increases. Ventricular fibrillation occurs between 25°C (77°F) and 30°C (86°F) in the human adult.

Decreasing the rate of metabolism can prolong the duration of many anesthetic drugs. Decreased hepatic blood flow could slow the delivery of drugs to the site of metabolism.

Hypothermia alone shifts the oxygen dissociation curve to the left, resulting in a less liberation of oxygen by hemoglobin.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:1622-1646.

C.9. What muscle relaxant would you use?

A nondepolarizing muscle relaxant should be used. Depolarizing relaxants, that is, succinylcholine, should be avoided. In general, the choice of muscle relaxant should be based on the duration of the operation and the presence of any coexisting diseases affecting drug elimination. Muscle relaxants without histamine release would be preferred, such as vecuronium and rocuronium.

C.10. Why is succinylcholine contraindicated in burned patients? For how long should it be avoided?

Succinylcholine is contraindicated in burned patients because it may cause a significant transient increase in serum potassium levels as high as 13 mEq per L, resulting in ventricular fibrillation and cardiac arrest. This hyperkalemic response begins approximately 5 to 15 days after the burn and persists for 2 to 3 months or longer, irrespective of degree and size of burn injury.

The exact mechanism responsible for this response is not known. Gronert and Theye postulated that the abrupt release of potassium is from the hypersensitive muscle membranes. Extrajunctional acetylcholine receptors are located on the muscle membranes of burned patients. Stimulation of these receptors may mediate a potentially lethal efflux of potassium.

The exact time for this hypersensitivity is unclear. Most authors advocate against succinylcholine use from 24 to 48 hours after the burn injury until complete healing has

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occurred. A hyperkalemic response has been reported in a patient after 480 days. The recommended limit now is extended to approximately 2 years after the burned skin has healed.

Gronert GA, Theye RA. Pathophysiology of hyperkalemia induced by succinylcholine. *Anesthesiology*. 1975;43:89-99.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:958-975.

Schaner PJ, Brown RL, Kirksey TD, et al. Succinylcholine-induced hyperkalemia in burned patients. 1. *Anesth Analg*. 1969;48:764-770.

Tolmie JD, Joyce TH, Mitchell GD. Succinylcholine danger in the burned patient. *Anesthesiology*. 1967;28:467-470.

C.11. What other adverse effects are associated with succinylcholine?

The adverse effects of succinylcholine are many. Its side effects are as follows:

- Hyperkalemia, particularly following burns, spinal cord injuries, and generalized major trauma: a single case report of a marked hyperkalemic response to succinylcholine in a patient with a closed head injury without peripheral paralysis
- Increased intracranial and intraocular pressures: the practical importance of which is controversial
- Increased intragastric pressure: counterbalanced by the increase in lower esophageal pressure, which reduces or eliminates the increased risk of regurgitation
- Muscle pains: more likely to concern the patient with minor injuries who ambulates soon after surgery
- Prolonged paralysis in patients with atypical pseudocholinesterase
- Cardiac arrhythmias, particularly bradycardia after repeated doses
- Trigger for malignant hyperthermia

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:962-975.

C.12. How are the doses of nondepolarizing muscle relaxants affected by burn injury?

In general, burn patients show great resistance to the nondepolarizing relaxants. Martyn et al. first reported that burn patients required a five times higher plasma concentration of D-tubocurarine to attain a given percentage of twitch depression compared with healthy subjects. The dose of pancuronium is increased by 2.5 times.

This increased requirement appears secondary to an upregulation of and altered affinity for junctional receptors. The burn patient also has increased plasma protein binding of nondepolarizing relaxants.

Martyn JA, Liu LM, Szyfelbein SK, et al. The neuromuscular effects of pancuronium in burned children. *Anesthesiology*. 1983;59:561-564.

Martyn JA, Szyfelbein SK, Ali HH, et al. Increased D-tubocurarine requirement following major thermal injury. *Anesthesiology*. 1980;52:352-355.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:988-989.

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C.13. How are the muscle relaxants such as succinylcholine, atracurium, cisatracurium, vecuronium, pancuronium, rocuronium, and curare metabolized and eliminated? Which of them has significant histamine release?

See Table 56.3.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:978.

C.14. What is the difference between metabolism and elimination of drugs?

Drug metabolism is the chemical modification of a substance. There are two phases: Phase I metabolism involves the chemical reactions of oxidation, reduction, and hydrolysis. Many are catalyzed by the cytochrome P450 system in the liver. Phase II metabolism involves

conjugations, the combining of endogenous substances with drugs. This is also known as *the synthetic mode of biotransformation*. Hepatic conjugation to a glucuronide moiety allows for metabolite solubility and elimination in urine.

TABLE 56.3 The Metabolism, Elimination, and Histamine Release of Muscle Relaxants

	ELIMINATION			
RELAXANT	**KIDNEY (%)**	**LIVER (%)**	**PLASMA METABOLISM (%)**	**HISTAMINE RELEASE**
Succinylcholine	<2	0	98	Slight
Atracurium	10-40	0	60-90	Slight
Cisatracurium	16	?	77	None
Vecuronium	40	60	0	None
Pancuronium	85	15	0	None
Rocuronium	25	70	0	None
D-Tubocurarine	80	20	0	Moderate

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:978.

Drug elimination involves all the processes that lead to removal from the body—hepatobiliary metabolism and conjugation, renal diuresis, and pulmonary excretion (i.e., CO_2, inhaled anesthetics).

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill

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Livingstone; 2015:530-540.

D. Postoperative Management

D.1. How would you monitor this patient during transport?

This patient was most likely intubated, paralyzed, apneic, and still under the influence of general anesthetic. Monitoring should be directed toward respiration, oxygenation, and hemodynamics. These can be achieved by utilizing a transport monitor capable of monitoring ECG, blood pressure, CVP, and pulse oximeter. During transport, ventilation should be controlled with positive pressure ventilation via an Ambu bag with supplemental oxygen.

D.2. What is meant by diffusion hypoxia? How do you prevent it?

In 1954, Fink et al. first reported diffusion hypoxia during recovery from nitrous oxide-oxygen anesthesia. A mild degree of hypoxia may develop for more than 10 minutes after cessation of a nitrous oxide-oxygen anesthetic if the patient is breathing room air. The arterial oxygen saturation may fall 5% to 10% and often reaches values less than 90% (PaO_2 <60 mm Hg). This desaturation occurs upon rapid nitrous oxide elimination. Nitrous oxide is 35 times more soluble in blood than nitrogen. Alveolar oxygen is diluted by the high nitrous oxide concentration diffusing from blood. Diffusion hypoxia can be prevented by the administration of a high fractional inspired oxygen for several minutes before allowing the patient to breathe room air.

Fink BR. Diffusion anoxia. *Anesthesiology*. 1955;16:511-519.

Fink R, Carpenter SL, Holaday DA, et al. Diffusion anoxia during recovery from nitrous oxide-oxygen anesthesia. *Fed Proc*. 1954;13:354.

D.3. Why do patients often shiver in the recovery room on emergence from anesthesia?

Postanesthetic shivering is commonly observed in the recovery room after emergence from inhalational general anesthetics. It is postulated that inhalation agents inhibit central hypothalamic thermoreceptors and that shivering is a thermoregulatory response to intraoperative heat loss. Shivering will produce energy to maintain normothermia. Secondarily,

tremors may be the result of anesthetic-induced disinhibition of descending spinal reflexes. Similar nonthermoregulatory tremors have been seen in women during labor after neuroaxial anesthesia.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Churchill Livingstone; 2015:1624-1636.

D.4. Discuss the causes of oliguria in the recovery room.

Oliguria is arbitrarily defined as the production of less than 400 mL of urine in 24 hours. It is the functional manifestation of *acute renal failure* (ARF). The syndrome of ARF may be classified into the following three groups:

- *Prerenal ARF (hypovolemic)* . A reduction of renal blood flow decreases both the filtration rate and the overall urinary flow. There is no structural damage to the kidney. Prerenal azotemia is reversible with volume expansion. However, if untreated, it can progress to the ischemic form of acute tubular necrosis.
- *Renal ARF (acute tubular necrosis)* . Ischemia or nephrotoxic substances result in structural damage to the renal tubules.
- *Postrenal ARF (obstruction of urinary outflow)* . Obstruction occurs distal to the kidney, at the level of the ureter, bladder, or urethra. Pus, tubular debris, blood clots, nephrolithiasis, tumor burden, prostatic hypertrophy, or a nonfunctioning Foley catheter can cause mechanical cessation of urinary flow.

Determining the underlying etiology of oliguria is essential, as management strategies vary greatly. To identify the cause of oliguria, one must make a careful assessment of the urinary sediment. Presence of renal tubular cells, renal tubular cell

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casts, and pigmented granular casts is strong evidence supporting acute tubular necrosis. Normal urinary sediment is consistent with prerenal azotemia. Other data, such as CVP and PAOP, provides valuable information about the state of hydration. Postrenal etiologies of ARF are supported by bladder ultrasonography (demonstrating an enlarged, distended bladder) or an elevated pressure on bladder manometry (supporting intra-abdominal hypertension).

Perazella MA, Coca SG, Kanbay M, et al. Diagnostic value of urine microscopy for differential diagnosis of acute kidney injury in hospitalized patients. *Clin J Am Soc Nephrol*. 2008;3:1615-1619.

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Chapter 57
Trauma

Andrew Sosa
Jaideep K. Malhotra
Ralph L. Slepian

A 31-year-old man sustained multiple stab wounds to the left upper quadrant of his abdomen and to his left hemithorax. Vital signs were as follows: blood pressure, 85/60 mm Hg; heart rate, 130 beats per minute; respiratory rate, and 32 breaths per minute; temperature, 34.5°C (94.1°F). His hematocrit was 27%. He was emergently brought to the operating room for an exploratory laparotomy and possible thoracotomy.

A. Medical Disease and Differential Diagnosis

1. How is trauma classified?
2. What are the injuries associated with thoracic trauma?
3. What are the injuries associated with cardiac trauma?
4. What are the complications of acute pericardial tamponade?
5. What are the anesthetic implications for treating cardiac tamponade?
6. How is the initial assessment and management of the trauma patient performed?
7. What constitutes a primary survey and what is its objective?
8. What constitutes a secondary survey, and what is its objective?
9. What are the signs and symptoms of a hemothorax? What is the definition of massive hemothorax?
10. What are the indications for a thoracotomy to treat a hemothorax?
11. How are pneumothoraces categorized?
12. What is an occult pneumothorax?
13. If the patient has a widened mediastinum on chest radiograph, what are your concerns?
14. What are the most commonly injured organs in blunt abdominal trauma?
15. What is a focused abdominal sonography for trauma (FAST) examination?
16. What is diagnostic peritoneal lavage?
17. Why was diagnostic peritoneal lavage not performed for this patient?
18. Define shock.
19. What are the four types of shock?
20. List the signs and symptoms of shock.
21. What is the pathophysiology of hypovolemic shock?
22. How would you classify hemorrhage?
23. What is the initial treatment of hemorrhagic shock?
24. Would you choose crystalloid or colloid therapy to treat hypovolemic shock?
25. Is there a place for dextran or hetastarch (Hespan) in treating hypovolemic shock?
26. Is there a place for hypertonic saline in the treatment of hypovolemic shock?

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B. Preoperative Evaluation and Preparation

1. What premedication would you order?
2. What preoperative testing would you order?

C. Intraoperative Management

1. How would you monitor this patient?
2. How would you induce anesthesia?
3. What technique could you use if single-lung ventilation was indicated?
4. What agents would you choose to maintain anesthesia?
5. What muscle relaxant would you choose?
6. What can be done to decrease the incidence of intraoperative awareness?
7. Five minutes after intubation, the peak airway pressure increased from 20 to 40 cm H_2O. What are the possible causes?
8. How would you make a diagnosis of tension pneumothorax?
9. What is the treatment of tension pneumothorax?
10. The patient's blood loss was continuing, and the hematocrit was 18%. What type of blood would you give if the type and crossmatch are not completed?
11. What precautions should be taken if more than 2 units of type O Rh-negative uncrossmatched whole blood is given?
12. What are the complications associated with any blood transfusion?
13. What is considered a massive transfusion?
14. What are the complications associated with a massive transfusion?
15. Can the shift of the oxygen-hemoglobin dissociation curve be quantitated?
16. How is hypothermia defined?
17. What are the adverse effects of hypothermia?
18. What is the treatment of hypothermia?
19. What are the effects of blood transfusion on the immune system?
20. What are the guidelines for transfusion of blood products?
21. What are the guidelines for the ratio of plasma/platelet transfusion to packed red blood cells in a massive transfusion?
22. If a patient were a member of the Jehovah's Witness religious sect, would you give a blood transfusion?
23. If a child is a Jehovah's Witness and suffered from hemorrhagic shock, what would you do?
24. What are the concentrated factors available for bleeding patients?
25. What is thromboelastography and thromboelastometry? How can they guide transfusion?

D. Postoperative Management

1. What is acute respiratory distress syndrome (ARDS)? What is acute lung injury?
2. How is ARDS treated?
3. In the recovery room, you are called to see this patient because of oliguria. How would you evaluate and treat this patient?
4. If this patient had a crush injury and low urine output, what other concerns might you have? What if the patient has dark or “tea-colored” urine?

A. Medical Disease and Differential Diagnosis

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A.1. How is trauma classified?

Trauma is usually separated into two distinct categories: penetrating and blunt trauma. Both can cause havoc on the body's vascular, visceral, musculoskeletal, and nervous systems.

A.2. What are the injuries associated with thoracic trauma?

Penetrating injuries associated with thoracic trauma are typically associated with stabbings and gunshot wounds. The latter causes far more destruction because of the large amount of kinetic energy transferred to the thoracic cavity from the impact of the bullet. As a result, gunshot wounds to the thorax are diffuse and much more likely to be fatal when compared to stabbings.

Blunt injuries to the chest are far more common than penetrating injuries. The most common causes of blunt injuries are deceleration injuries (as a result of motor vehicle accidents) and crush injuries. These can range from relatively minor injuries such as rib fractures to more severe ones such as lung contusion, tracheobronchial tears, flail chest, pneumothorax, hemothorax, injuries to the great vessels, and traumatic ruptures of the esophagus or diaphragm.

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:379-402.

A.3. What are the injuries associated with cardiac trauma?

Penetrating cardiac injuries often lead to immediate cardiovascular collapse, and patients rarely survive to reach the operating room. Injuries associated with penetrating cardiac trauma include pericardial tamponade, cardiac perforation, rupture of a chamber, and fistula formation.

Blunt cardiac trauma injuries include cardiac contusion (most common), pericardial ruptures, rupture of a chamber, valvular tears, coronary artery injuries, and ventricular aneurysms.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1509-1510.

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:379-402.

A.4. What are the complications of acute pericardial tamponade?

The primary complication of pericardial tamponade is a decrease in cardiac output secondary to pericardial pressure causing severe diastolic dysfunction. Unstable patients with acute pericardial tamponade present with hypotension, tachycardia, and tachypnea. The diagnosis can be made by the presence of Beck triad (hypotension, distended neck veins, and muffled heart sounds) and pulsus paradoxus; these signs can be easily missed on a hypovolemic trauma patient. Definitive diagnosis of cardiac tamponade can be made with transthoracic echocardiography. If the diagnosis of acute pericardial tamponade is made and the patient is unstable, immediate evacuation of the pericardium via a pericardiocentesis or a pericardial window is required (also see Chapter 12).

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1509-1510.

A.5. What are the anesthetic implications for treating cardiac tamponade?

The anesthetic goal for treating acute cardiac tamponade is to maintain intrinsic sympathetic tone. These patients are extremely dependent on intrinsic sympathetic tone, and therefore, maintenance of heart rate and preload are of utmost importance. A preinduction intra-arterial catheter and large-bore intravenous access are essential. Ketamine and etomidate are considered appropriate agents for induction. A rapid sequence induction with succinylcholine or an awake intubation can be performed. If possible, preinduction sedation should be avoided. Inotropes such as epinephrine should be readily available and can be given in small doses to avoid bradycardia and hypotension. Induction should be delayed until after patient preparation and draping is completed. In the event the patient becomes hemodynamically unstable, the effusion can then be drained as quickly as possible (also see Chapter 12).

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Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1509-1510.

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:310-312, 379-402.

A.6. How is the initial assessment and management of the trauma patient performed?

A systematic and organized approach to the assessment and management of the trauma patient has been developed by the American College of Surgeons and is taught as Advanced Trauma Life Support. Initial evaluation and management as stated by Advanced Trauma Life Support consists of five components:

1. The primary survey
2. Resuscitation
3. The secondary survey
4. Continued monitoring and reevaluation
5. Definitive care

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:379-402.

A.7. What constitutes a primary survey and what is its objective?

The assessment of the trauma patient consists of the primary and secondary survey. The function of the primary survey is to identify and treat immediately life-threatening injuries. The life-threatening injuries associated with chest trauma are the following:

- Lost airway
- Tension pneumothorax
- Massive hemothorax
- Open pneumothorax
- Cardiac tamponade
- Flail chest

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:379-402.

Chest trauma: initial evaluation. http://www.trauma.org/archive/thoracic/CHESTintro.html. February 2004. Accessed October 20, 2015.

A.8. What constitutes a secondary survey, and what is its objective?

The secondary survey is a more detailed examination aimed at identifying other non-life-threatening injuries, planning further laboratory and radiographic studies, and forming a workable differential diagnosis. Examples of chest injuries identified on secondary survey are the following:

- Simple pneumothorax or hemothorax
- Rib fractures
- Pulmonary contusion
- Non-life-threatening blunt myocardial injury

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Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:379-402.

Chest trauma: initial evaluation. http://www.trauma.org/archive/thoracic/CHESTintro.html. February 2004. Accessed October 20, 2015.

A.9. What are the signs and symptoms of a hemothorax? What is the definition of massive hemothorax?

The signs and symptoms of a hemothorax include diminished breath sounds on the affected side, hemorrhagic shock, and mediastinal shift. A massive hemothorax is defined as a rapid accumulation of greater than 1,500 mL of blood in the thoracic cavity.

Reed AP, Yudkowitz FS. *Clinical Cases in Anesthesia*. 4th ed. London: Elsevier Saunders; 2014:395-410.

A.10. What are the indications for a thoracotomy to treat a hemothorax?

Hemothorax, if severe enough, can lead to hemorrhagic shock. Therefore, timely diagnosis and treatment are of utmost importance. After a chest tube is placed, if drainage of blood is greater than 1,200 mL or if drainage is greater than 200 mL per hour for over 4 hours, a thoracotomy is indicated. Alternatively, if the patient is older than 60 years, then if drainage is

greater than 100 mL per hour for over 4 hours, a thoracotomy is also indicated. If the patient does not meet these criteria but is still hemodynamically unstable or if ventilation is difficult, emergent surgery should be performed.

Reed AP, Yudkowitz FS. *Clinical Cases in Anesthesia*. 4th ed. London: Elsevier Saunders; 2014:395-410.

A.11. How are pneumothoraces categorized?

Pneumothoraces are categorized into three broad categories: open, closed, and tension pneumothorax. Pneumothoraces, like hemothoraces, can cause severe hypoxemia, impair venous return, and cause a severe mediastinal shift.

Open pneumothoraces are a result of penetrating wounds and allow intrathoracic pressure to equalize with atmospheric pressure. The result is introduction of outside air every time the patient takes a breath. Definitive treatment is to close the wound and placement of a chest tube.

Closed pneumothoraces can result from both blunt and penetrating trauma to the chest. It is defined as the presence of air in the pleural space. Diagnosis can be made radiographically, via a chest radiograph or computed tomography (CT), although in many trauma situations, the patients' condition precludes obtaining a chest radiograph. In such cases, diagnosis can be made by physical examination, that is, by percussion or by diminished or absent breath sounds. In addition, a diagnosis can be made by ultrasound examination of the chest. Recent studies have suggested that using ultrasound detection of a pneumothorax can be a faster and more sensitive test than a supine chest radiograph. Treatment for a pneumothorax is the placement of a chest tube if the patient is unstable or if the pneumothorax is greater than 10% of the pleural cavity.

Tension pneumothorax is the progressive build-up of air within the pleural space that cannot escape. Essentially, it is a “one-way valve” that is exacerbated by positive pressure ventilation. This progressive build-up of air can cause a mediastinal shift, an acute rise in airway pressures, and obstruction of venous return. All of these factors can result in a sudden and dramatic cardiovascular collapse.

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:382-383.

Pneumothorax: an overview of pneumothoraces-diagnosis & management. http://www.trauma.org/index.php/main/article/393/. Published May 9, 2009. Accessed May 2, 2015.

Wilkerson RG, Stone MB. Sensitivity to bedside ultrasound and supine anteroposterior chest for the identification of

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pneumothorax after blunt trauma. *Acad Emerg Med*. 2010;17:11-17.

A.12. What is an occult pneumothorax?

An occult pneumothorax is a pneumothorax that is diagnosed by CT but was not identified previously on the chest radiograph. In many cases, this type of pneumothorax is managed conservatively and resolves over time, without requiring placement of a chest tube. Frequently, a trauma patient with an occult pneumothorax will require general anesthesia and positive pressure ventilation. Whether these patients should have a chest tube placed preemptively is currently debated. For now, the decision should be made on a case-by-case basis.

When any trauma patient is placed on positive pressure ventilation, a history of a negative chest radiograph alone does not rule out the presence of an occult pneumothorax. As many as 50% of all pneumothoraces are occult, with an overall incidence of 5% in all trauma patients.

Ball CG, Kirkpatrick AW, Feliciano DV. The occult pneumothorax: what have we learned? *Can J Surg*. 2009;52:E173-E179.

Ouellet JF, Trottier V, Kmet L, et al. The OPTICC trial: a multi-institutional study of occult pneumothoraces in critical care. *Am J Surg*. 2009;197:581-586.

A.13. If the patient has a widened mediastinum on chest radiograph, what are your concerns?

A chest radiograph revealing a widened mediastinum may indicate the presence of a thoracic aortic injury. These types of injuries are often life-threatening, necessitating immediate identification and intervention. Blunt aortic injury is associated with high-speed deceleration and

is the second leading cause of death in trauma patients, accounting for 16% of all traumarelated deaths. Open surgical repair requires a double-lumen tube, single-lung ventilation, and clamping of the proximal aorta while taking measures to protect the spinal cord. In patients with coexisting injuries, such as increased intracranial pressure, profound bleeding, or hypoxemia, this procedure may be contraindicated. These patients may be medically managed with blood pressure control until these other issues have resolved. They may also be candidates to undergo a less invasive endovascular repair, a technique that has been increasingly used over the last 20 years.

Ekeh AP, Peterson W, Woods RJ, et al. Is chest x-ray an adequate screening tool for diagnosis of blunt thoracic aortic injury? *J Trauma*. 2008;65:1088-1092.

Neschis DG, Scalea TM, Flinn WR, et al. Blunt aortic injury. *N Engl J Med*. 2008;359:1708-1716.

A.14. What are the most commonly injured organs in blunt abdominal trauma?

In blunt abdominal trauma, the most commonly injured organs are the spleen, liver, kidneys, and bowel. Generally, blunt abdominal trauma leads to higher mortality rates than penetrating trauma. The reason is multifactorial and includes greater difficulty in diagnosis and frequent association with other injuries, such as head injury, chest trauma, and fractures.

A.15. What is a focused abdominal sonography for trauma (FAST) examination?

FAST is a rapid ultrasonography examination performed in the trauma resuscitation room. It has been used to determine the presence of fluid (blood) within the peritoneum, pericardium, and thorax. Currently, FAST is particularly helpful in the bedside examination of hemodynamically unstable blunt trauma patients. It may also have a role in some patients with penetrating trauma.

Ng A. Trauma ultrasonography: the FAST and beyond. http://www.trauma.org/archive/radiology/FASTintro.html. December 2001. Accessed October 20, 2015.

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Rozycki GS, Root HD. The diagnosis of intraabdominal visceral injury. *J Trauma*. 2010;68(5):1019-1023.

A.16. What is diagnostic peritoneal lavage?

In penetrating trauma, diagnostic peritoneal lavage allows for rapid identification of a hemoperitoneum and, therefore, the discovery of an intraperitoneal injury. Peritoneal lavage is a procedure performed in the emergency room to help determine whether a patient has internal bleeding that requires an exploratory laparotomy. It is done by performing a minilaparotomy under local anesthesia. A catheter is then placed into the abdomen and is aspirated for gross blood. Aspiration of 10 mL of blood is considered a positive finding. A grossly bloody aspirate is indicative of solid or vascular injury. If less than 10 mL of blood is aspirated, then 1 L of lactated Ringer's solution or normal saline is allowed to drain into the abdomen. The lavage fluid is then allowed to return by gravity and is sent to the laboratory for analysis. Criteria for a positive peritoneal lavage are an erythrocyte count of 100,000 per μL, a white blood cell count of 500 per μL, the presence of bile or food particles, and a fluid amylase concentration of 175 units per dL. The white blood cell level itself should not determine the need for laparotomy. The level of white blood cells also does not rise initially but requires several hours to rise. Alkaline phosphatase and amylase are contained in the small bowel and spill into the abdominal cavity after injury. These levels tend to rise early in injury. Amylase in lavage fluid has been seen as a more accurate marker than alkaline phosphatase. If the peritoneal lavage meets one or more of these criteria, the patient goes to the operating room for an exploratory laparotomy.

Roberts JR, Hedges JR, Custalow CB, et al, eds. Roberts and Hedges' *Clinical Procedures in Emergency Medicine*. Philadelphia, PA: Elsevier Saunders; 2014:852-872.

A.17. Why was diagnostic peritoneal lavage not performed for this patient?

Peritoneal lavage was not done for two reasons. First, it is felt that all penetrating wounds to the abdomen need to be surgically explored. Second, this patient was exhibiting signs of shock and obviously needed to be sent to the operating room without delay.

Before CT and ultrasonography technologies, diagnostic peritoneal lavage was the only diagnostic test available to rapidly evaluate the abdomen for injury. Although diagnostic peritoneal lavage is highly sensitive, it can also result in false-positive results, leading to unnecessary exploratory laparotomies. CT now allows for evaluation of all intraperitoneal organs, the diaphragm, and the retroperitoneum (an area inaccessible to diagnostic peritoneal lavage) while also allowing for identification of the specific organ injured. CT should be used in the evaluation of hemodynamically stable trauma patients.

Rozycki GS, Root HD. The diagnosis of intraabdominal visceral injury. *J Trauma*. 2010;68(5):1019-1023.

A.18. Define shock.

Shock is defined as the circumstance of insufficient oxygen delivery to sustain aerobic metabolism in vital cells of essential organs. Shock of all forms appears to be invariably related to inadequate tissue perfusion. The low-flow state in vital organs seems to be the final common denominator in all forms of shock.

Townsend CM Jr, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:66-119.

A.19. What are the four types of shock?

For a working classification of shock, the following classification offered by Blalock in 1934 is still useful and functional:

- *Hematogenic (hypovolemic, hemorrhagic) shock*: characterized by a loss of circulatory blood volume
- *Cardiogenic shock*: characterized by an inability of the myocardium to pump blood

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- *Vasogenic (septic) shock*: characterized by an infection that causes a decrease in peripheral vascular resistance
- *Neurogenic shock*: characterized by an impairment of the central nervous system-mediated control of vascular tone

Townsend CM Jr, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:66-119.

A.20. List the signs and symptoms of shock.

Tachycardia, hypotension, cool extremities, pallor, oliguria, tachypnea, decreased capillary refill, anxiety, restlessness, and loss of consciousness are signs and symptoms of shock.

A.21. What is the pathophysiology of hypovolemic shock?

Cardiovascular Derangement

An acute decrease in circulating blood volume leads to an increase in sympathetic activity with an outpouring of epinephrine and norepinephrine from the adrenal gland. The α-adrenergic response causes vasoconstriction, which shunts blood from the skin, viscera, and muscle, thereby preserving the coronary and cerebral circulation. With constriction of both precapillary and postcapillary sphincters, a reduction occurs in hydrostatic pressure of the capillary bed, which allows the osmotic pressure to draw fluid back into the vascular space from the interstitial space. This process of hemodilution tends to expand the patient's blood volume. In addition to the vasoconstriction and hemodilution, a tachycardic response may be noted.

Myocardial-depressant factor is a peptide thought to be released from the pancreas during low-flow states. This peptide is thought to be responsible for some of the decreased cardiac performance seen in trauma patients. Pancreatectomy and various myocardial-depressant factor antagonists demonstrate protective myocardial effects during shock in animals.

Acid-Base Disturbance

Metabolic acidosis is almost always seen in association with a shock state. As a result of decreased blood flow or a low rate of perfusion, oxygen delivery to vital organs is reduced, and consequently, a mandatory change occurs from aerobic to anaerobic metabolism. This shift

will lead to the production of lactic acid instead of carbon dioxide as the end product of metabolism. The increase in lactic acid leads to a metabolic acidosis.

Marx JA, Hockberger RS, Walls RM, et al, eds. *Rosen's Emergency Medicine-Concepts and Clinical Practice*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2014:67-74.

Townsend CM Jr, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery* . 19th ed. Philadelphia, PA: Elsevier Saunders; 2012:66-119.

A.22. How would you classify hemorrhage?

Classification of hemorrhage based on blood loss is as follows:

Class I: Blood loss of up to 15% of the blood volume: normal pulse and blood pressure

Class II: Blood loss of up to 30% of the blood volume: tachycardia, decreased urine output, and anxiety

Class III: Blood loss of up to 40% of the blood volume: marked tachycardia, hypotension, tachypnea, oliguria, and anxiety

Class IV: Blood loss of more than 40% of the blood volume: tachycardia and hypotension, tachypnea, anuria, confusion, and lethargy

Dutton RP. Shock and trauma anesthesia. *Anest Clin North Am*. 1999;17:83-95.

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A.23. What is the initial treatment of hemorrhagic shock?

The initial treatment of hemorrhagic shock is to attempt to stabilize hemodynamics by administering intravenous fluids and blood products as needed to maintain tissue perfusion and oxygen delivery. Recently, trauma centers have revised the standard approach to resuscitation for major traumatic hemorrhage requiring massive transfusion. Trauma centers have adapted the practice of initial resuscitation with hemostatic components such as plasma and platelets as well as packed red blood cells. This strategy for treating massive hemorrhage was pioneered from knowledge gained from combat hospitals in Iraq and Afghanistan. This approach involves limiting the total volume of crystalloid and replacing intravascular volume with packed red blood cells and fresh frozen plasma (FFP) in a ratio approaching 1:1. This strategy is geared to avoid the acute coagulopathy associated with major trauma and blood loss and has been shown to decrease mortality rates in combat and civilian injuries requiring massive transfusion.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1509-1510.

Griffee MJ, Deloughery TG, Thorborg PA. Coagulation management in massive bleeding. *Curr Opin Anaesthesiol*. 2010;23:263-268.

A.24. Would you choose crystalloid or colloid therapy to treat hypovolemic shock?

Crystalloid solutions can sustain hemodynamics and deliver adequate oxygenation in healthy patients who have lost as much as 30% of their total blood volume. Still, controversy remains over the use of crystalloid versus colloid therapy for the initial therapy of hypovolemic shock.

Proponents of crystalloid therapy believe that both intravascular and interstitial fluid losses occur in hypovolemic shock and that these can be readily replaced with crystalloids. Another benefit of crystalloids is the decrease in blood viscosity, which may enhance perfusion. A particular advantage to lactated Ringer's solution is that lactate is metabolized to bicarbonate, which may help to buffer the patient's acidosis. Finally, in this age of medical economics, the cost of crystalloid is much less than that of colloid. Because crystalloid leaves the intravascular space and enters the interstitial space, large quantities are needed, and some fear that these quantities may lead to both pulmonary and peripheral edema, although studies have not confirmed this fear.

Proponents of colloid therapy, on the other hand, argue that much less volume of fluid is needed to counteract hypovolemic shock and that early colloid therapy can prevent the complications associated with large-volume crystalloid resuscitation such as dilutional coagulopathy, hyperchloremic acidosis, and edema. Colloids maintain the oncotic pressure and hold the interstitial fluids in the intravascular space, which is felt to possibly prevent pulmonary

edema. If leaky alveolar capillary membranes are seen within the lung, colloids may worsen pulmonary edema.

Choi PT, Yip G, Quinonez LG, et al. Crystalloids vs. colloids in fluid resuscitation: a systematic review. *Crit Care Med*. 1999;27:200-210.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1767-1810.

Orlinsky M, Shoemaker W, Reis ED, et al. Current controversies in shock and resuscitation. *Surg Clin North Am*. 2001;81:1217-1262.

A.25. Is there a place for dextran or hetastarch (Hespan) in treating hypovolemic shock?

Dextran and hetastarch are synthetic polysaccharide solutions with varying mean molecular weights. Dextran 40, dextran 70, and hetastarch have all been used as volume expanders. Dextrans are relatively inexpensive, increase effective blood volume, and decrease blood viscosity. Nevertheless, their negative aspects are considerable. They impair coagulation by coating platelets, and they impair typing and crossmatching by coating red blood cells. In addition, anaphylactic reactions

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have been reported.

A.26. Is there a place for hypertonic saline in the treatment of hypovolemic shock?

Hypertonic saline is now being used for resuscitation at some major centers. Its effects tend to be of short duration, so it is not used alone. It is under investigation as a resuscitative agent, particularly in the prehospital setting, because small volumes may have beneficial cardiovascular effects. If one combines hypertonic saline and dextran, the effective resuscitation will be prolonged. Hypertonic saline is usually supplied as 7.5% NaCl, often combined with a colloid, 6% dextran 70. The optimal dose is thought to be 4 mL per kg.

The potential advantage is that the greater the sodium concentration, the less total volume will be required for resuscitation. A serious potential danger exists in that patients may become hypernatremic, which can lead to brain dehydration. In patients with high intracranial pressure, this brain dehydration may have a potential benefit in lowering it.

Hypertonic saline solutions have been used successfully in hemorrhagic shock resuscitation in animals and humans. This type of fluid resuscitation offers the advantage of requiring smaller volumes for a similar effect (4 to 5 mL per kg), making it especially attractive for use during prehospital resuscitation. Hypertonic saline has been shown to elevate mean arterial pressure and cardiac output and increase renal, mesenteric, total splanchnic, and coronary blood flow. It causes a small and transient rise in circulating volume by transcapillary refill. These beneficial effects after controlled hemorrhage have been established. Its hypertonic nature and small volume usage are particular advantages in traumatic brain injury. Hypertonic saline promotes redistribution of fluid into the vascular compartment and decreases intracranial pressure. It also seems to offer similar advantages to improvement in microcirculatory flow of the spinal cord. Use of these products during uncontrolled hemorrhage, nevertheless, has been strongly questioned.

Marx JA, Hockberger RS, Walls RM, et al, eds. *Rosen's Emergency Medicine-Concepts and Clinical Practice*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2014:67-74.

Orlinsky M, Shoemaker W, Reis ED, et al. Current controversies in shock and resuscitation. *Surg Clin North Am*. 2001;81:1217-1262.

B. Preoperative Evaluation and Preparation

B.1. What premedication would you order?

None. This is a critically ill patient who is coming to the operating room for emergency surgery. Narcotics and sedatives are contraindicated because they could worsen his already tenuous hemodynamic state.

B.2. What preoperative testing would you order?

Because of the emergent nature of the trauma setting, preoperative tests and imaging studies are frequently limited. If the patient is hemodynamically unstable, any preoperative evaluation is aborted, and the patient is taken directly to the operating room.

If the patient is stable, a portable chest radiograph, arterial blood gas, complete blood count, and FAST can be obtained in a relatively short period in the emergency department or operating room before surgery. Often, these tests can be obtained while the patient is being prepared for emergency surgery. This information can be combined with other monitoring adjuncts such as oxygen saturation, invasive blood pressure, and electrocardiogram to evaluate the patient and formulate an appropriate management strategy. Although it is usually not possible to clinically clear the c-spine before surgery, it is important to know the results of any radiologic studies that have been done (e.g., in order to rule out an unstable cervical spine fracture) and to adjust the anesthetic plan accordingly.

C. Intraoperative Management

C.1. How would you monitor this patient?

Routine noninvasive monitor would include electrocardiogram, blood pressure cuff, oxygen monitor, pulse oximeter, end-tidal carbon dioxide, esophageal stethoscope, temperature probe, and Foley catheter.

Invasive monitors for this patient would include an arterial line and a central venous catheter. An arterial line is useful for

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blood sampling and direct blood pressure monitoring. The central venous line is helpful for determining the patient's volume status. A pulmonary artery catheter may be indicated if the patient shows signs of heart failure.

C.2. How would you induce anesthesia?

Because all trauma patients are considered to have a full stomach, the best way to protect the patient's airway is to perform a rapid sequence induction with cricoid pressure while maintaining in-line cervical immobilization of the c-spine for any patient in a c-collar. For the patient with a suspected difficult airway, one could do an awake fiberoptic intubation. Awake fiberoptic intubation in this population can be difficult because they may be confused, uncooperative, and sometimes even combative. First, if tolerated, the patient should be preoxygenated for 3 to 5 minutes. Next, ketamine 1 to 2.5 mg per kg might be given followed by succinylcholine 1.5 mg per kg while maintaining cricoid pressure. Ketamine was chosen in this case because of its cardiovascular-stimulating effects and the patient's unstable hemodynamics. Etomidate (0.2 mg per kg) would be another appropriate choice for an induction agent.

If the patient is comatose, in severe shock, or in full arrest on admission to the resuscitation room, no drug other than oxygen and possibly a neuromuscular-blocking drug is required until the patient's blood pressure and heart rate sufficiently rebound so that anesthetics can be titrated. In awake traumatized patients who are thought to be hypovolemic, etomidate is best tolerated.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:2423-2459.

C.3. What technique could you use if single-lung ventilation was indicated?

If the patient does not already have a secure airway, the airway should be secured in the manner described in the previous question. Single-lung ventilation is indicated in this situation if the patient is bleeding from one lung and protection of the other lung is required or to improve the surgical field (lower priority). Once the airway is secured, there are several ways to obtain single-lung ventilation. The easiest and safest technique would be to use an Arndt or Cohen bronchial blocker through the endotracheal tube. If those blockers are not available, one could pass an embolectomy catheter (bronchial blocker) into the trachea and then the endotracheal tube. The bronchial blocker could then be positioned under direct vision using fiberoptic bronchoscopy. Alternatively, the bronchial blocker could be placed through a bronchoscopy adapter and endotracheal tube, and its position can be confirmed by fiberoptic bronchoscopy. The point at which the bronchial blocker enters the bronchoscopy adapter can then be sealed with pliable “bone wax” (a form of sterile bees wax that is soft and kneadable).

Another method of obtaining single-lung ventilation would be to change the endotracheal tube to a double-lumen tube using a Cook exchange catheter. The major risks of this option are losing a previously secured airway and aspiration while attempting to change the tube.

C.4. What agents would you choose to maintain anesthesia?

As the patient stabilizes and the hemodynamics improve, other anesthetic agents can be carefully titrated to prevent hypotension, as follows:

- Sedatives or amnestics should be added to the anesthetic as soon as tolerated. Remember to start with small doses and check the patient's reaction to the drugs between doses.
- Opioids should be titrated to control the hemodynamic response to surgery.
- Nitrous oxide must be carefully considered because it has the capacity to accumulate in closed airspaces or because of the high possibility that this patient has an occult pneumothorax.
- Inhalational anesthetics may be used in low concentrations so the patient's hemodynamics are not compromised.

C.5. What muscle relaxant would you choose?

Vecuronium, rocuronium, and cisatracurium are free of cardiovascular side effects and have an intermediate duration of action. They are acceptable choices. Pancuronium is a longacting muscle relaxant with vagolytic properties that may be deleterious to the patient.

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D-Tubocurarine, metocurine, atracurium, and mivacurium all have the potential to cause hypotension and therefore would not be chosen for this patient.

C.6. What can be done to decrease the incidence of intraoperative awareness?

The incidence of intraoperative awareness is commonly cited as approximately 0.2%. This is probably an overestimation. In other sources, the incidence of traumatic intraoperative recall associated with pain is less that 0.03%. The American Society of Anesthesiologists Closed Claims database states that claims associated to recall during anesthesia constitute 1.5% of claims. An increased relative risk for recall is seen in certain types of surgery, including cardiac surgery, cesarean sections, and trauma surgery. This most likely represents intentional light anesthesia associated with higher levels of stimulation. Bispectral index monitoring may be potentially useful; the application of these monitors during a trauma resuscitation may not be easily accomplished. It has been shown that patients with a bispectral index value of 50 were able to respond to verbal commands less than 10% of the time.

Johansen JW. Update on bispectral index monitoring. *Best Pract Res Clin Anaesthesiol*. 2006;20(1):81-99.

O'Connor MF, Daves SM, Tung A, et al. BIS monitoring to prevent awareness during general anesthesia. *Anesthesiology*. 2001;94:520-522.

Rampil IJ. Monitoring depth of anesthesia. *Curr Opin Anesthesiol*. 2001;14:649-653.

C.7. Five minutes after intubation, the peak airway pressure increased from 20 to 40 cm H_2O. What are the possible causes?

The possible causes of peak airway pressure increase are as follows:

- Tension pneumothorax
- Bronchospasm
- Endobronchial intubation
- Pulmonary edema
- Secretions
- Kink in the anesthesia circuit or endotracheal tube

C.8. How would you make a diagnosis of tension pneumothorax?

A tension pneumothorax can be diagnosed by the absence of breath sounds on the affected side. The chest movement may be asymmetric. Neck veins will be full, and systemic hypotension can occur if the tension pneumothorax is severe. Any patient who deteriorates under anesthesia and has wounds to the upper abdomen, lower neck, or ribs should be assumed to have a tension pneumothorax until proven otherwise.

Marx JA, Hockberger RS, Walls RM, et al, eds. *Rosen's Emergency Medicine-Concepts and Clinical Practice*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2014:431-458.

C.9. What is the treatment of tension pneumothorax?

Immediate decompression of the chest is mandatory for tension pneumothorax because otherwise the patient's hemodynamics will deteriorate. The diagnosis is made clinically and not by a chest radiograph. A 16- or 18-gauge Angiocath is placed into the second intercostal space at the midclavicular plane. After the air escapes confirming your diagnosis and the lung is decompressed, a chest tube should be placed.

Marx JA, Hockberger RS, Walls RM, et al, eds. *Rosen's Emergency Medicine-Concepts and Clinical Practice*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2014:431-458.

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C.10. The patient's blood loss was continuing, and the hematocrit was 18%. What type of blood would you give if the type and crossmatch are not completed?

This patient should have blood transfused as soon as possible. Type O Rh-negative packed red blood cells are the universal donor. This should be started while type-specific blood is being made available. Whenever the type-specific blood is ready, one can switch to it. If the transfusion begins with type O Rh-negative *whole blood* and more than 2 units have been infused, only type O Rh-negative blood should continue to be used. Usually, by the time a patient reaches the operating room from the emergency room, a partial crossmatch can be done. This usually takes 5 to 10 minutes, after which time type-specific blood can be transfused.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1830-1867.

Roberts JR, Hedges JR, Custalow CB, et al, eds. *Roberts and Hedges' Clinical Procedures in Emergency Medicine*. Philadelphia, PA: Elsevier Saunders; 2014:496-517.

C.11. What precautions should be taken if more than 2 units of type O Rh-negative uncrossmatched whole blood is given?

The plasma from type O Rh-negative *whole blood* contains anti-A and anti-B antibodies, which can cause hemolytic reactions with type A and type B blood cells if given in significant quantities. Therefore, only type O Rh-negative blood should continue to be transfused, although this will lead to minor hemolysis of the patient's own red blood cells. The patient should not receive his type-specific blood until the blood bank determines that the transfused anti-A and anti-B antibody levels have fallen sufficiently low to permit safe transfusion of type-specific blood. This usually requires a 2-week waiting period.

Packed red blood cells have smaller volumes of plasma and are virtually free of anti-A and anti-B antibodies. Therefore, whenever type-specific blood is not yet available, type O Rh-negative uncrossmatched packed red blood cells should be used in preference to type O Rh-negative *whole blood*. Once type-specific blood is available, it can be used safely.

Cain JG. Current practices in fluid and blood component therapy in trauma. *Semin Anesth*. 2001;20:28-35.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1830-1867.

C.12. What are the complications associated with any blood transfusion?

Complications associated with blood transfusion are as follows:

Transfusion reactions

- Transfusion-related acute lung injury (TRALI) is a new acute lung injury that happens within 6 hours of transfusion in a patient with no other risk factor for lung injury. It occurs when donor plasma human leukocyte antigen class I and II neutrophil antibodies or possibly monocyte antibodies activate recipient white blood cells to cause an acute lung injury. In 2006, U.S. blood collection agencies instituted a male-only plasma donor policy because multiparous females are more likely to carry the offending antibodies. The TRALI rate decreased to about one-third of its previous level. TRALI is now the leading cause of transfusion-related mortality. The treatment of this noncardiogenic pulmonary edema is supportive.

- Transfusion-associated circulatory overload (TACO) occurs and can cause pulmonary edema secondary to fluid overload; it occurs in 1% to 6% of transfused patient. Large amounts of plasma transfusion that may occur during massive transfusion or coagulopathy correction increase the likelihood of TACO.
- Transfusion-related immunomodulation (TRIM) is a risk with allogenic red blood cell transfusion. Although incompletely

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understood, there is a decrease in immunity with an increased incidence of nosocomial infection, postoperative infection, and cancer recurrence.

- Febrile reactions occur in approximately 1% of all transfusions. In an awake patient, this is usually no more than an annoyance that requires decreasing the infusion rate.
- Allergic nonhemolytic reactions to properly crossmatched blood will manifest as an increase in temperature, pruritus, and urticaria. This may be difficult to diagnose in the anesthetized patient. Treatment consists of administration of antihistamines and discontinuation of the transfusion.
- Hemolytic reactions occur when incompatible blood is administered. Caused by activation of the complement system, they can be life-threatening. In the awake patient, fever, chills, dyspnea, substernal, and lumbar pain are seen in addition to hypotension. Under general anesthesia, the only sign that is not masked is hypotension. Also, if free hemoglobin can be documented in the plasma or urine, this too would be indicative of a transfusion reaction. Substances released by the hemolyzed cells can lead to disseminated intravascular coagulation (DIC) and acute renal failure (ARF). Treatment consists of immediate discontinuation of the transfusion. Hypotension should be treated with hydration, vasopressors, and inotropic agents if needed. Urinary output must be maintained by adequate hydration. Although its value is uncertain, sodium bicarbonate has been used to alkalinize the urine to improve the solubility of the hemoglobin-degradation products. The risk of an ABO-incompatible transfusion is 1:33,500 red blood cell transfusions. Mortality associated with this remains high, at approximately 40%.
- Other reactions include posttransfusion purpura, microchimerism, and graft-versus-host disease.

Transmission of disease

- Transmission of disease can be a serious problem. HIV, hepatitis B virus, hepatitis C virus, and cytomegalovirus can all be transmitted by transfusion. Because the risk of disease transmission increases with each unit of blood or its components given, they must be carefully scrutinized before they are administered. Currently, the incidence of posttransfusion HIV infection is 1:1,476,000 per transfused unit of blood. The risk of hepatitis B transmission is approximately 1 per 350,000 units. The risk of hepatitis C transmission is 1:1,149,000 per unit transfused. Cytomegalovirus is the most common viral agent transmitted by blood transfusion; it produces clinically important infections only in immunodepressed patients. Malaria, syphilis, Lyme disease, Chagas disease, West Nile virus, Creutzfeldt-Jakob, and other diseases may also be transmitted through transfusion of blood and blood products. Bacterial infection occurs in 1:75,000 transfusions. As new nonhemoglobin solutions appear on the market, less blood will be transfused and disease transmission will diminish.

Microembolization

Microembolization can occur from the transfusion of blood or its components. Stored blood forms microaggregates that are too small to be removed by the standard 170-micron blood filters. Smaller filters have been developed to remove these particles. When using blood filters of the 20- to 40-micron range, the rate of transfusion is dramatically decreased because of the increased resistance of the filters. Some early reports suggested that these microaggregates may lead to pulmonary dysfunction, but this has never been proven.

Chestnut DH, Wong CA, Tsen LC, et al. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Saunders Elsevier; 2014:900-901,1235.

Greer JP, Arber DA, Glader B, et al, eds. *Wintrobe's Clinical Hematology*. 13th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2014:547-586.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1830-1867.

C.13. What is considered a massive transfusion?

A massive transfusion is defined as the replacement of the patient's total blood volume in a 24-hour period. This is usually between 8 and 10 units of packed red blood cells. Many trauma cases far exceed this amount and may require other blood components in addition to the red blood cells.

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Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1830-1867.

C.14. What are the complications associated with a massive transfusion?

Complications of a massive transfusion include hypothermia, acidosis, coagulopathy, DIC, fibrinolysis, citrate toxicity, hyperkalemia, hypokalemia, acid-base imbalance, and impaired hemoglobin function.

- Hypothermia is an obvious consequence of infusing cold, banked blood. Therefore, it is recommended that the blood be reconstituted with warm normal saline. In addition, all fluids should pass through a warming device and the operating room should be kept warm in order to help prevent hypothermia.
- The coagulopathy associated with trauma is multifactorial. It is a combination of thrombocytopenia and dilutional and consumptive factors. Furthermore, the systemic inflammatory response syndrome that is associated with trauma produces activated protein C, an anticoagulant. In addition, hypothermia and acidosis are commonly seen during massive transfusions, and this worsens the coagulopathy. Both platelets and coagulation factors are markedly decreased and must be replaced. In trauma, the best approach to transfusion is unknown. In cases requiring massive transfusions when there is insufficient time to obtain laboratory values to guide transfusion, it may be necessary to take the “damage control” approach of transfusing a set ratio of pRBC:FFP:platelets, such as 1:1:1 ratio. In patients who do not require a massive transfusion, component therapy after laboratory documentation of the deficiency is utilized. DIC and fibrinolysis may occur after massive transfusions. An important triggering event of DIC and fibrinolysis is shock, with its accompanying tissue ischemia, acidemia, and waste product accumulation. Therefore, early and prompt treatment of hypoperfusion is mandatory.
- Citrate toxicity is frequently discussed, but it is rarely a problem. However, in the pediatric population, citrate toxicity is much more of a problem and should be considered in any child who does not respond to rapid volume administration of blood products. Citrate is added to stored blood to bind calcium and therefore prevent clotting. Citrate binds calcium and decreases the patient's ionized calcium level. Hypocalcemia may present as a prolongation of the QT interval with little effect of cardiac performance. In some cases, ventricular performance may be compromised. Cardiac performance also may be decreased by acidemia, hyperkalemia, and hypothermia, which all accompany the shock state. Citrate is metabolized to bicarbonate, and it can contribute to posttransfusion metabolic alkalosis.
- Hyperkalemia can be a rare occurrence in the massively transfused patient. Plasma potassium levels of stored whole blood range between 12 and 32 mEq per L. The potassium level increases approximately 1 mEq/L/day in stored blood. A unit of whole blood would contain between 4 and 8 mEq of potassium, which is hardly enough to cause hyperkalemia. A unit of packed red blood cells contains insignificant amounts of potassium because most plasma is removed. However, in the shock state with hypoperfusion and acidemia, hyperkalemia may become evident.
- Hypokalemia is also a possibility after a massive transfusion. Citrate is metabolized to bicarbonate, resulting in a metabolic alkalosis that can cause hypokalemia. In addition, the transfused red blood cells take up potassium, which can also result in hypokalemia.
- Acid-base imbalance is a problem after massive transfusion. Banked blood with a pH level of 6.8 is acidotic and may worsen the acidosis that accompanies shock. This acidosis is easily reversible with the restoration of normal perfusion. No need is seen to give supplemental bicarbonate based on an arbitrary number of units transfused. Nevertheless, if metabolic acidosis persists, sodium bicarbonate is warranted. As stated, citrate from stored blood and lactate from lactated Ringer's solution are metabolized to bicarbonate, and this can cause metabolic alkalosis.

- Impaired hemoglobin function is a theoretic possibility after massive transfusion. The 2,3-diphosphoglycerate level is decreased in banked blood. This will shift the oxygen-hemoglobin dissociation curve to the left, and oxygen will be held more tightly by the hemoglobin molecule. No studies have documented any adverse effects from this.

Drummond JC, Petrovitch CT. The massively bleeding patient. *Anesthesiol Clin North America*. 2001;19:633-649.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1830-1867.

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Shaz BH, Dente CJ, Nicholas J, et al. Increased number of coagulation products in relationship to red blood cell products transfused improves mortality in trauma patients. *Transfusion*. 2010;50(2):493-500.

C.15. Can the shift of the oxygen-hemoglobin dissociation curve be quantitated?

Yes, the shift of the oxygen-hemoglobin dissociation curve is quantified by means of the P_{50} values (i.e., the partial pressure of oxygen at which hemoglobin is 50% saturated with oxygen). A leftward shift of the curve indicates a low P_{50} value. The normal P_{50} value of blood is 27 mm Hg and the normal level of 2,3-diphosphoglycerate is 4.8 mmol per mL of erythrocytes.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2010:179-215.

C.16. How is hypothermia defined?

Hypothermia is defined as a core body temperature of less than 35°C (95°F). A trauma patient brought to the emergency room may already be hypothermic. Prolonged exposure to a cold operating room, evaporative heat loss from the respiratory tract, infusions of cold fluids, and loss of heat production secondary to shock cause decreased core temperatures in most patients.

All skin surfaces not in the surgical field should be covered to reduce convective and radiant heat loss. Humidification of inspired gases reduces evaporative heat loss from the lung. All intravenous fluids should be warmed. Warming the operating room may also lessen heat loss, as will the use of warming blankets.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1622-1646.

Roberts JR, Hedges JR, Custalow CB, et al, eds. *Roberts and Hedges' Clinical Procedures in Emergency Medicine*. Philadelphia, PA: Elsevier Saunders; 2014:496-517.

C.17. What are the adverse effects of hypothermia?

- Shivering-induced increase in oxygen consumption by as much as 400%
- A leftward shift in the oxygen-hemoglobin dissociation curve
- Decreased coagulation of blood (10% reduction in coagulation factor activity for every 1°C drop in body temperature)
- Increased epinephrine and norepinephrine levels, causing vasoconstriction
- As hypothermia becomes severe, possible decreases in both heart rate and blood pressure
- Cardiac arrhythmias that can progress to ventricular fibrillation

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Saunders Elsevier; 2015:1622-1646.

Sihler KC, Napolitano LM. Complications of massive transfusion. *Chest*. 2010;137:209-220.

Tanaka M, Nagasaki G, Nishikawa T. Moderate hypothermia depresses arterial baroreflex control of heart rate during, and delays its recovery after general anesthesia in humans. *Anesthesiology*. 2001;95:51-55.

C.18. What is the treatment of hypothermia?

The normal response to hypothermia is shivering, which is blocked by general anesthesia. Therefore, it is of utmost importance to prevent and treat hypothermia. Recommendations include the following:

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- Increase the temperature of the operating room.
- Use a warming blanket.

- Preheat intravenous fluids.
- Pass all fluids through a warming device.
- Use low-flow anesthesia.
- Use a heat moisture exchanger in the anesthesia circuit.

C.19. What are the effects of blood transfusion on the immune system?

Blood transfusion will result in immunologic changes that can be harmful in some patients and helpful in others. This immunomodulation occurs from immune suppression. The blood components crucial to these changes are thought to be the white blood cells or plasma.

An example of a beneficial effect is the increased survival of the renal allograft in patients who had received a prior transfusion. In patients who have cancer, a possible harmful effect of immunosuppression is the increased cancer recurrence rate seen in patients who have had prior transfusion. Finally, clinical studies have demonstrated that perioperative transfusion is associated with an increased incidence of infection and sepsis.

Greer JP, Arber DA, Glader B, et al, eds. *Wintrobe's Clinical Hematology*. 13th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2014:547-586.

Landers DF, Hill GE, Wong KC, et al. Blood transfusion-induced immunomodulation. *Anesth Analg*. 1996;82:187-204.

C.20. What are the guidelines for transfusion of blood products?

The New York-Presbyterian Hospital Guidelines for blood product usage are as follows:

Red blood cell transfusion criteria

- Hemoglobin level less than 8 g per dL and mean red cell volume within normal limit (81 to 100 fL, 70 to 125 fL for patients aged 14 years)
- Hemoglobin level less than 8 g per dL and high risk/acute bleed[1]
- Hemoglobin level less than 11 g per dL and clinically symptomatic[2]
- Hemoglobin level less than 11 g per dL and bleed more than 1 unit per 24 hours
- Any hemoglobin level and high risk[1] and acute bleed
- Any hemoglobin level and symptomatic[2] and acute bleed
- Any hemoglobin level and bleed more than 2 units per 24 hours, or more than 15% of blood volume per 24 hours

Platelet transfusion criteria

- Platelet count less than 10,000 per μL without thrombotic thrombocytopenic purpura, idiopathic thrombocytopenic purpura, posttransfusion purpura, or hemolytic-uremic syndrome
- Platelet count less than 50,000 per μL with minor bleed, preoperative for a minor procedure or prematurity
- Platelet count less than 100,000 per μL with bleed requiring red blood cell transfusion or preoperative for a major procedure
- Bleeding with loss of 1 blood volume
- Bleeding time longer than 10 minutes

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- Open heart surgery transfusion of more than mean number of red blood cell units (6 units per case)

Fresh frozen plasma transfusion criteria

- Massive transfusion more than 6 units of red blood cells per 24 hours (more than 1 blood volume infants/children)
- Abnormal coagulation test results, with prothrombin time more than 15 seconds or partial thromboplastin time more than 45 seconds during prior 24 hours, or known congenital coagulation factor disorder and bleeding, or prophylaxis for major procedures

- Clinical evidence of abnormal bleeding from venipuncture sites or generalized oozing
- Patients with diagnosis of thrombotic thrombocytopenic purpura
- Open heart surgery transfusion of more than mean number of red blood cell units (6 units per case)

Cryoprecipitate transfusion criteria

- Massive transfusion more than 8 units of red blood cells per 24 hours
- Open heart surgery transfusion of more than mean number of red blood cell units (6 units per case)
- Bleeding or invasive procedure with hypofibrinogenemia or DIC
- Deficient factor VIII or von Willebrand factor or abnormal fibrinogen and presurgical or bleed

Carson JL, Grossman BJ, Kleinman S, et al. Red blood cell transfusion: a clinical practice guideline from the AABB. *Ann Intern Med*. 2012;157(1):49-58.

Kaufman RM, Djulbegovic B, Gernsheimer T, et al. Platelet transfusion: a clinical practice guideline from the AABB. *Ann Intern Med*. 2015;162(3):205-213.

New York-Presbyterian Hospital. *Weill/Cornell Medical Center Protocols*. New York: Weill/Cornell Medical Center; 2011.

Roback JD, Caldwell S, Carson J, et al. Evidence-based practice guidelines for plasma transfusion. *Transfusion*. 2010;50(6):1227-1239.

C.21. What are the guidelines for the ratio of plasma/platelet transfusion to packed red blood cells in a massive transfusion?

Coagulopathy is frequently a problem for the trauma patient requiring massive transfusion. The causes are multifactorial. It is due to dilution of platelets and coagulation factors in addition to acidosis and hypothermia. Most trauma centers have implemented massive transfusion protocols that use the strategy of “hemostatic resuscitation.” These protocols are highly variable, but the strategy involves minimizing aggressive crystalloid use, early resuscitation with blood products, and early administration of FFP and platelets.

At present, there are no specific guidelines to the transfusion ratio of FFP to packed red blood cells in massive transfusion. Although clearly more studies are required, the early results show an association toward increased survival when a ratio of FFP to packed red blood cells is 1:2 or higher during massive transfusion.

For platelets, in civilian clinical practice, the standard is still to use 1 apheresis unit or a pool of 4 to 6 concentrates from individual units of whole blood for every 5 to 7 units of red blood cells administered. Initial data from the trauma literature suggests that increasing the platelet to packed red blood cell ratio may also potentially be beneficial.

Griffee MJ, Deloughery TG, Thorborg PA. Coagulation management in massive bleeding. *Curr Opin Anaesthesiol*. 2010;23:263-268.

Ketchum L, Hess JR, Hiippala S. Indications for early fresh frozen plasma, cryoprecipitate, and platelet transfusion in trauma. *J Trauma*. 2006;60:S51-S58.

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Teixeira PG, Inaba K, Shulman I, et al. Impact of plasma transfusion in massively transfused trauma patients. *J Trauma*. 2009;66:693-697.

C.22. If a patient were a member of the Jehovah's Witness religious sect, would you give a blood transfusion?

Jehovah's Witnesses are best known for refusing the transfusion of blood and blood products. This belief is based on the Bible (Acts 15:28-29). In the awake and otherwise competent adult, courts have ruled that physicians cannot be held liable if they comply with a patient's directive and withhold life-saving blood administration after specific and detailed informed consent of the consequences of such an omission of treatment. The issue becomes clouded when patients are incompetent, unconscious (most Jehovah's Witnesses carry cards informing medical personnel of their religious beliefs), or minors. They believe all hope of eternal life is forfeited if they accept a transfusion. Therefore, a blood transfusion is considered a physical violation. The right of a Jehovah's Witness to refuse a blood transfusion is absolute. The courts have upheld their rights to refuse a blood

transfusion. Most Witnesses take adequate legal steps to relieve the liability of the medical personnel. Most carry a medical alert card that states their wishes and they usually have made arrangements for proxy or surrogate decision makers. In addition, an open and honest avenue of communication must exist between the patient, surgeon, and anesthesiologist.

They will refuse transfusion of whole blood, packed red blood cells, white blood cells, plasma, and platelets, although they will allow the use of cardiopulmonary bypass, dialysis, or similar equipment as well as intraoperative blood salvage in which the extracorporeal circulation is uninterrupted. Their religious understanding does not absolutely prohibit albumin, immune globulins, or hemophiliac preparations; those products must be decided on an individual basis. They accept all nonblood replacements, including nonblood colloids, crystalloids, dextrans, or oxygen-carrying blood substitutes.

An anesthesiologist may refuse to care for any patient when a procedure is elective. In an emergency situation, legal and ethical requirements apply. Conversely, any competent adult also has the right to refuse any therapy, and to treat such a patient against that person's will is to commit battery.

Dasen KR, Niswander DG, Schlenker RE. Autologous and allogenic blood products for unanticipated massive blood loss in a Jehovah's Witness. *Anesth Analg*. 2000;90:553-555.

Roberts JR, Hedges JR, Custalow CB, et al, eds. *Roberts and Hedges' Clinical Procedures in Emergency Medicine*. Philadelphia, PA: Elsevier Saunders; 2014:496-512.

Waters JH, Potter PS, Booke M. Cell salvage in the Jehovah's Witness patient. *Anesth Analg*. 2000;90:229-230.

C.23. If a child is a Jehovah's Witness and suffered from hemorrhagic shock, what would you do?

Care of minors presents the greatest concern and often leads to legal action against the parents under child-neglect status. Such actions are questioned by Jehovah's Witnesses who do seek good medical care for their children while claiming that consideration be given to their families' religious beliefs. Doctors can appeal to the court for permission to transfuse blood to children of this sect who are underage. In an unforeseeable emergency, generally, blood may be given without consulting a court.

C.24. What are the concentrated factors available for bleeding patients?

Recombinant Activated Factor VII (NovoSeven)

NovoSeven is approved in the United States for prophylaxis and treatment of hemorrhage in hemophiliacs with antibodies against factor XIII or IX. Despite its limited approval, it is more commonly used off label in patients with uncontrolled hemorrhage. Although NovoSeven is extremely effective at stopping uncontrolled bleeding, it has been reported to be associated with a significant risk of stroke in patients. A meta-analysis by Zangrillo et al. showed that recombinant activated factor VII was associated with a decrease in surgical revision after cardiac surgery; however, it was also

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associated with an increase in perioperative stroke.

Four-Factor Prothrombin Complex Concentrate

Four-factor prothrombin complex concentrate (PCC) contains II, VII, IX, X, protein C, and protein S. Similar to NovoSeven, it is approved for the treatment of hemophilia A and B with an inhibitor. However, it is also approved for the reversal of warfarin. Four-factor PCC has the advantage of requiring significantly less volume for infusion versus plasma, which could be beneficial in a fluid overloaded patient. A prospective randomized trial by Sarode et al. compared the efficacy of four-factor PCC to plasma for the treatment of major bleeding in patients taking vitamin K antagonists. The efficacy of four-factor PCC was comparable to plasma and found to have a similar safety profile.

Fibrinogen Concentrates

Fibrinogen concentrate is a pasteurized collection from human plasma that is approved for the use in patients with hemophilia A and B with inhibitors as a treatment for or prevention of bleeding. It acts to replenish fibrinogen levels in the blood in place of FFP or cryoprecipitate.

A Cochrane Review by Wikkelsø et al. showed no difference between fibrinogen concentrate versus blood products in regard to adverse event, bleeding, or recovery.

Sarode R, Milling TJ Jr, Refaai MA, et al. Efficacy and safety of a 4-factor prothrombin complex concentrate in patients on vitamin K antagonists presenting with major bleeding. *Circulation*. 2013;128(11):1234-1243.

Wikkelsø A, Lunde J, Johansen M, et al. Fibrinogen concentrate in bleeding patients. *Cochrane Database Syst Rev*. 2013:(8):CD008864.

Zangrillo A, Mizzi A, Biondi-Zoccai G, et al. Recombinant activated factor VII in cardiac surgery: a metaanalysis. *J Cardiothorac Vasc Anesth*. 2009;23(1):34-40.

C.25. What is thromboelastography and thromboelastometry? How can they guide transfusion?

Rotation thromboelastometry (ROTEM®) and thromboelastography (TEG) are two different devices to assess the efficiency of clot formation. Both devices use a suspended pin that sits in a metal cup containing whole blood. As the blood clots, the devices detect the change in viscoelastic force and use this change to assess the strength of the clot formed.

Rotation Thromboelastometry

The ROTEM® uses a rotating pin in a stationary cup to detect increases in viscoelastic force as a clot forms or decreases as a clot lysis. It is a point of care test, which looks at several different parts of the coagulation pathway:

- INTEM—intrinsic pathway of the coagulation cascade
- HEPTEM—intrinsic pathway of the coagulation cascade with the addition of heparinase, which removes the effects of heparin from the results
- EXTEM—extrinsic pathway of coagulation cascade
- FIBTEM—extrinsic pathway of the coagulation cascade after the addition of cytochalasin D, which inhibits the effects of platelets on the formation of the clot
- APTEM—extrinsic pathway with the addition of aprotinin to block fibrinolysis

These tests will generate images based on a patient's coagulation status, which can be used to guide transfusion therapy. (e.g., Figs. 57.1, 57.2, 57.3, 57.4, 57.5 and 57.6). Bolliger et al. developed a chart to guide therapy based on ROTEM® results (Fig. 57.7).

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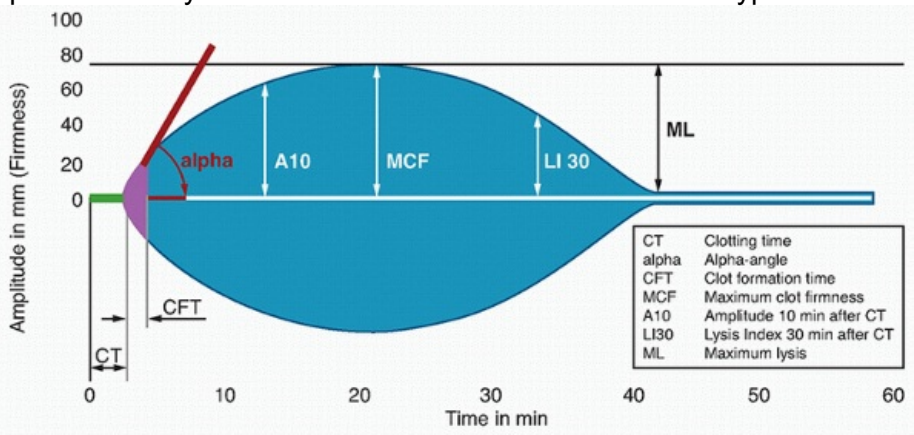


FIGURE 57.1 Basic ROTEM® image. Clot time: the measured time until clot formation starts; affected by clotting factors and anticoagulants. Clot formation time: a measure of initial rate of clot formation, the time from clot formation until the clot forms to an amplitude of 20 mm; depends on platelets and fibrinogen. Alpha angle: a measure of the initial rate of clot formation. Maximum clot firmness: the maximum tensile strength of the clot; describes quality of clot and is dependent on platelets, fibrinogen, factor XIII, and fibrinolysis. Maximum lysis: reduction of clot firmness during measurement; abnormality in the ML at 30 minutes indicated fibrinolysis. Amplitude: A5/10/15 is the amplitude of the clot at 5, 10, and 15 minutes.

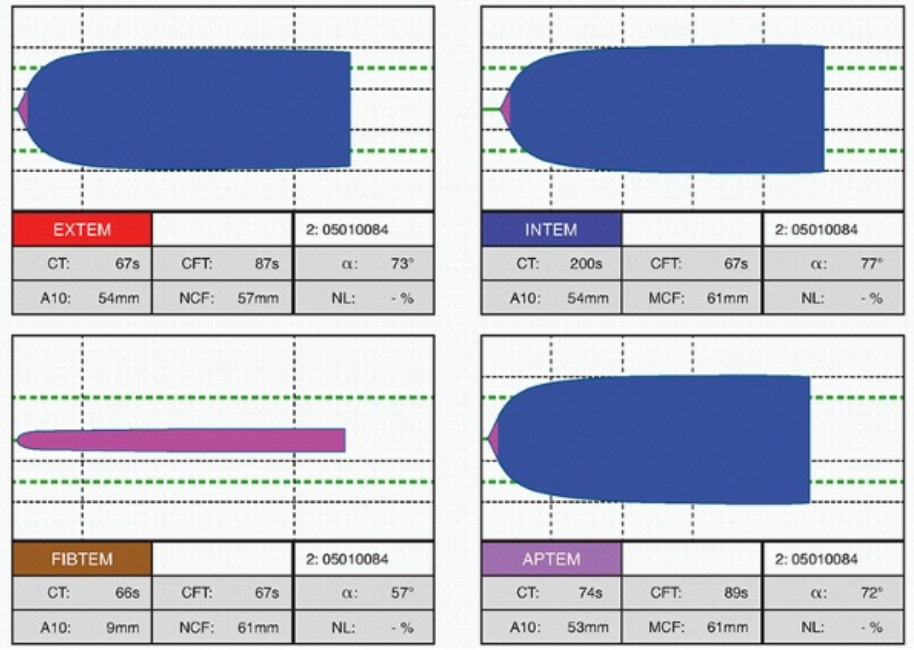


FIGURE 57.2 ROTEM® in a patient with normal coagulation parameters.

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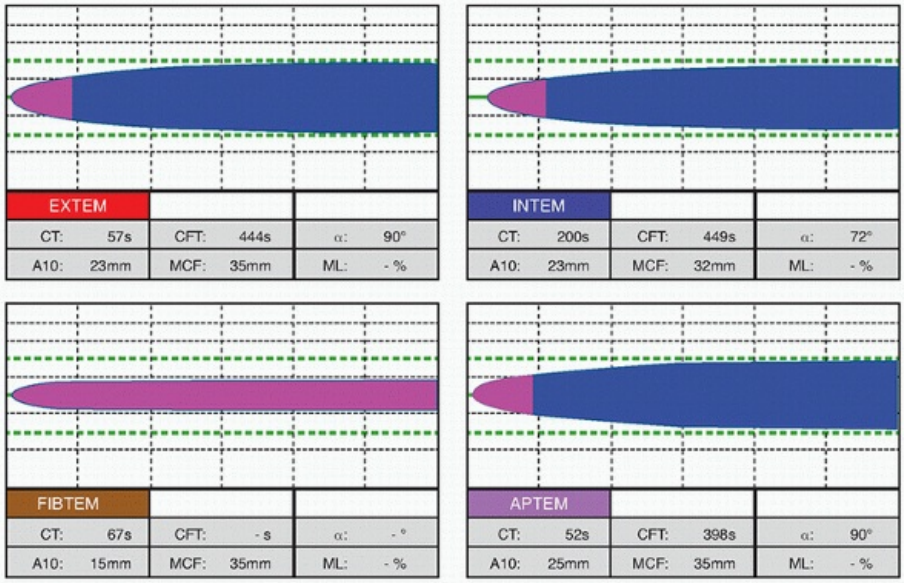


FIGURE 57.3 ROTEM® in a patient with a platelet deficiency.

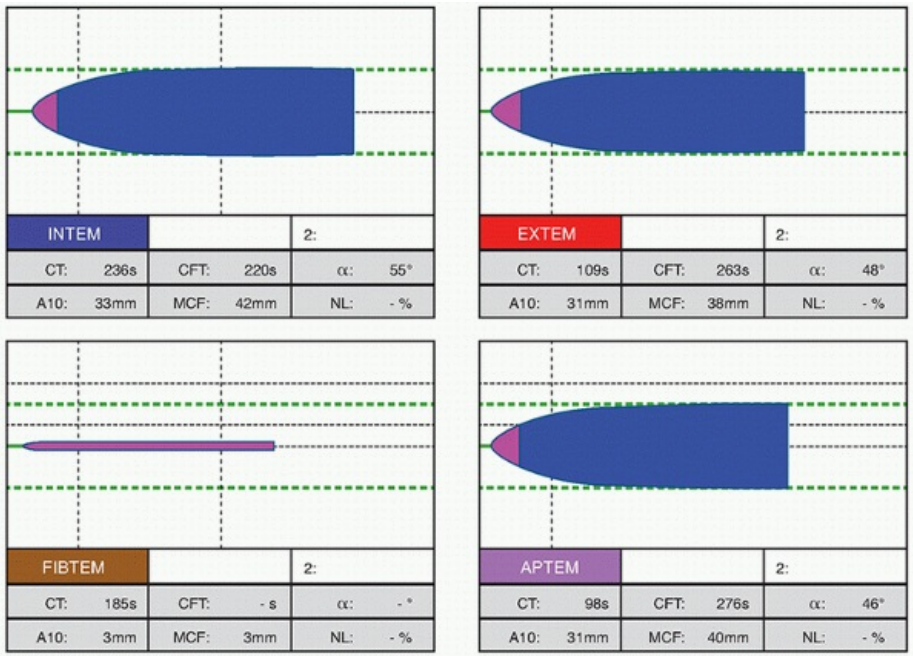


FIGURE 57.4 ROTEM® in a patient with a fibrinogen deficiency.

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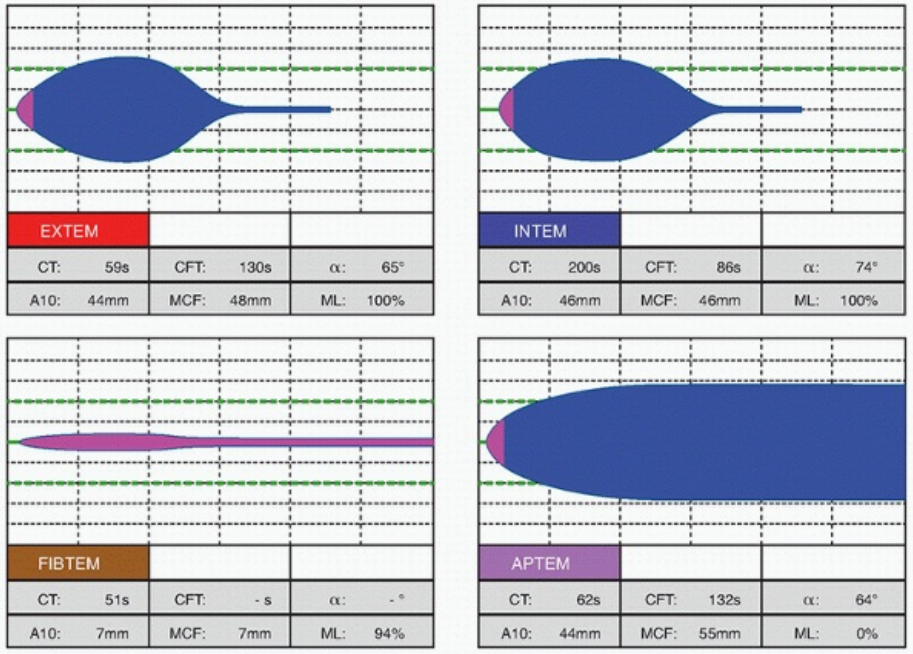


FIGURE 57.5 ROTEM® in a patient with hyperfibrinolysis.

P.1066

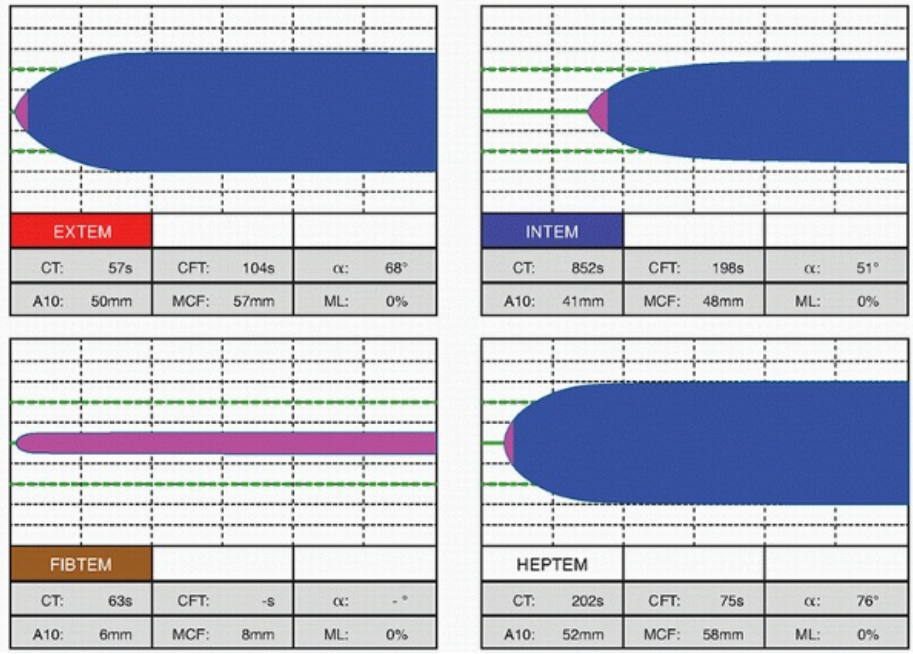


FIGURE 57.6 ROTEM® in a patient with heparin influence.

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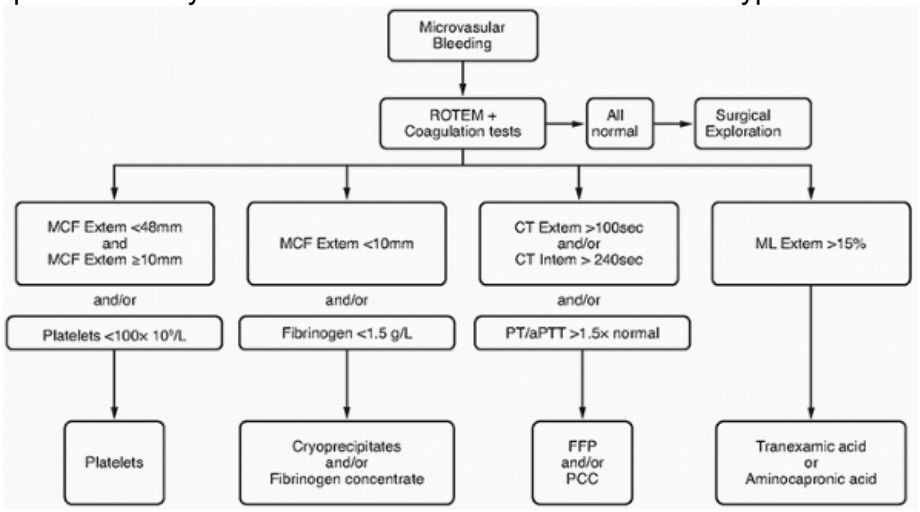


FIGURE 57.7 Guide to therapy based on ROTEM® results. (From Bolliger D, Seeberger MD, Tanaka KA. Principles and practice of thromboelastography in clinical coagulation management and transfusion practice. *Transfus Med Rev*. 2012;26(1):1-13, with permission.)

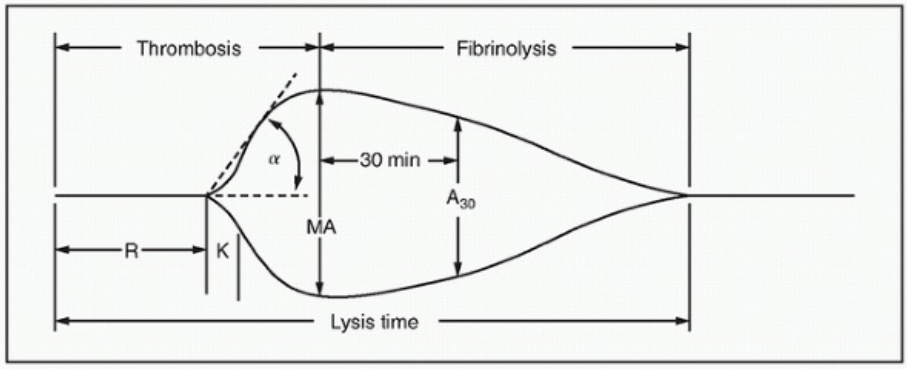


FIGURE 57.8 Basic TEG image.

Thromboelastography

The TEG is based on the same principles as the ROTEM®. The difference is that instead of having a mobile pin in a stationary cup, TEG has a stationary pin in a mobile cup. A sample will generate an image (Fig. 57.8). The TEG values can be compared to ROTEM® values (Table 57.1). Some examples of the effect of different coagulation states on TEG (Fig. 57.9) and a guideline for transfusion therapy (Fig. 57.10) are shown.

Bolliger D, Seeberger MD, Tanaka KA. Principles and practice of thromboelastography in clinical coagulation management and transfusion practice. *Transfus Med Rev*. 2012;26(1):1-13.

Jackson GN, Ashpole KJ, Yentis SM. The TEG vs the ROTEM thromboelastography/thromboelastometry systems. *Anaesthesia*. 2009;64(2):212-215.

Johansson PI, Stissing T, Bochsen L, et al. Thromboelastography and thromboelastometry in assessing coagulation in trauma. *Scand J Trauma Resusc Emerg Med*. 2009;17:45.

Ogawa S, Szlam F, Chen EP, et al. A comparative evaluation of rotation thromboelastometry and standard coagulation tests in hemodilution-induced coagulation changes after cardiac surgery. *Transfusion*. 2012;52(1):14-22.

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TEM Systems, Inc. Result interpretation. http://www.rotem-usa.com/methodology/result-interpretation/. Accessed October 20, 2015.

TABLE 57.1 Thromboelastography (TEG) Values Compared to Their Rotation Thromboelastometry (ROTEM®) Equivalents

TEG	MEASURES	ROTEM® EQUIVALENT
R time	Time to 2 mm amplitude	CT
K time	Time from 2 mm-20 mm	CFT
α Angle	Slope between R and K	*α* Angle
MA	Maximum amplitude of clot	MCF
LY30	Percentage of clot lysis at 30 min after MA	ML
A30	Size of clot at 30 min after MA	A10
G	Clot elasticity	MCE
CI	Coagulation index is value determined by a manufacturer created mathematical formula which takes into account R, K, *α* angle, and MA to give an overall assessment of the state of coagulation.	

CFT, clot formation time; CI, coagulation index; CT, clotting time; K, kinetics; MA, maximum amplitude; MCE, maximum clot elasticity; MCF, maximum clot firmness; ML, maximum lysis.

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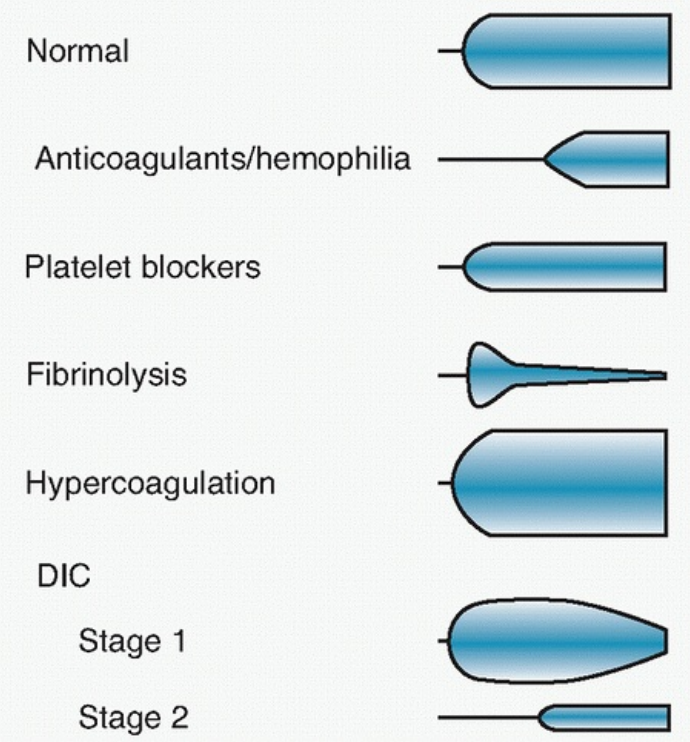


FIGURE 57.9 Effects of different coagulation states on TEG results.

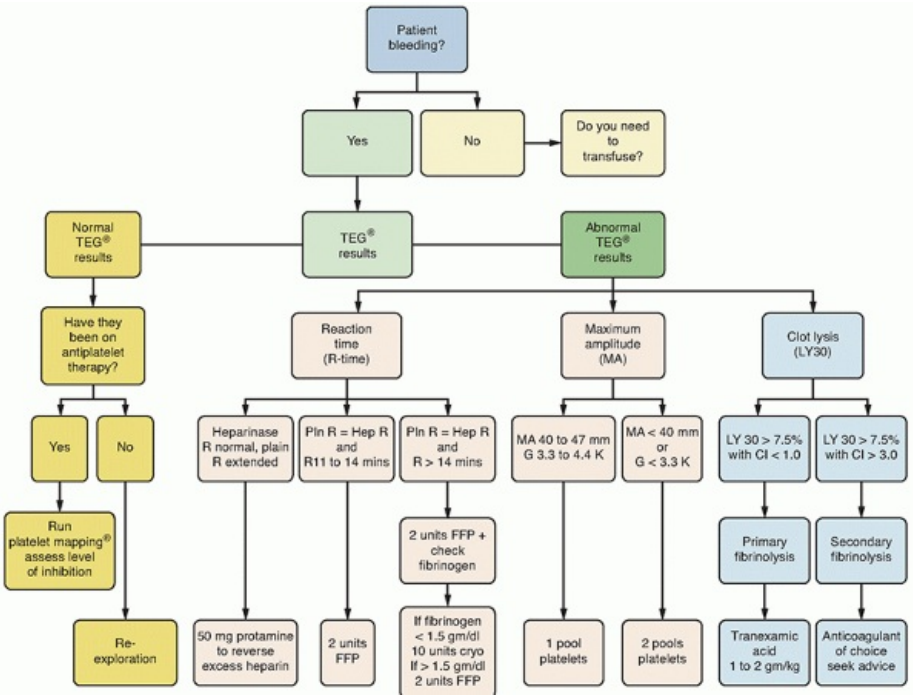


FIGURE 57.10 A guideline for transfusion based on TEG results. CI, coagulation index; FFP, fresh frozen plasma; G, clot elasticity; K, kinetics; Pln, plain.

D. Postoperative Management

D.1. What is acute respiratory distress syndrome (ARDS)? What is acute lung injury?

ARDS is an acute respiratory failure seen in patients with healthy lungs after being exposed to shock, trauma, sepsis,

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aspiration, transfusion, burns, or toxic inhalation. Initially, when this lung injury was thought to be related to the shock state and its resuscitation, names such as “shock lung” and “traumatic wet lung” were applied to the acute respiratory insufficiency following injury. It is now recognized that many types of lung insults will result in damage to the alveolar capillary membrane, resulting in leakage of proteinaceous fluid from the intravascular space into the interstitium and subsequently, into the alveolar spaces. This injury with its resulting interstitial and alveolar edema produces a clinical picture ranging from mild to severe pulmonary dysfunction that can be fatal.

ARDS was formerly defined as:

- The acute onset of respiratory failure
- Bilateral infiltrates on chest x-ray
- PaO_2/FIO_2 ratio of 200 or less
- A pulmonary capillary wedge pressure <18

However, this definition was reevaluated in 2011 secondary to concerns regarding its accuracy. First, the diagnosis of bilateral infiltrates on chest x-ray was found to have wide interobserver variability and thus was inconsistent. Next, the PaO_2/FIO_2 ratio varied greatly based on the patient's ventilator status and needed to be refined. Third, an elevated wedge pressure was not enough to rule out a diagnosis of ARDS. Finally, the definition was found to have low specificity when compared to autopsy results of patients with diffuse alveolar damage.

For these reasons, the Berlin definition was established which characterizes ARDS by the following:

Oxygenation

- Mild—PaO_2/FIO_2 <200 mm Hg or ≤300 mm Hg with positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) ≥5 cm H_2O
- Moderate—PaO_2/FIO_2 ≤100 mm Hg or ≤200 mm Hg with PEEP ≥5 cm H_2O
- Severe—PaO_2/FIO_2 ≤100 mm Hg with PEEP ≥5 cm H2O

Timing—onset within 1 week of a known clinical insult, or the patient has worsening respiratory symptoms

Chest radiograph—demonstrates opacities bilaterally that are not due to pleural effusions, atelectasis, or nodules

Origin of edema—respiratory insufficiency that is not solely caused by cardiogenic causes, that is, left heart failure or volume overload

Acute lung injury—a term for a less severe form of ARDS was removed from the definition and is no longer used

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:408-444.

Bope ET, Kellerman R, eds. *Conn's Current Therapy*. Philadelphia, PA: Saunders Elsevier; 2015:333-406.

Fanelli V, Vlachou A, Ghannadian S, et al. Acute respiratory distress syndrome: new definition, current and future therapeutic options. *J Thorac Dis*. 2013;5(3):326-334.

D.2. How is ARDS treated?

The treatment of ARDS is primarily supportive. Currently, mechanical ventilation is the mainstay of supportive therapy for ARDS. The principal goal of mechanical ventilation is to minimize the deleterious effects on gas exchange. Unfortunately, mechanical ventilation has also been associated with further lung injury. Excessive alveolar volumes (volutrauma), high mean and peak airway pressures (barotrauma), and shearing forces caused by frequent collapse and opening of alveolar units are responsible for this further lung injury. PEEP is used to increase oxygenation at a fixed FIO_2.

Investigators have looked at lung protection in patients with ARDS. Strategies were used to prevent ventilator-associated lung injury. Amato et al. used a strategy to limit peak inspiratory pressures by using low tidal volumes (<6 mL per kg) and

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the institution of PEEP. Their strategy was associated with a lower 28-day mortality (38% vs. 71%), higher weaning rate (66% vs. 29%), and lower barotrauma rate (7% vs. 42%).

The National Heart, Lung, and Blood Institute ARDS Network reported improved survival in patients using a low tidal volume strategy (6 mL per kg vs. 12 mL per kg). These investigators found a decrease in mortality of approximately 25% in the intervention group compared with the control group.

Amato MB, Barbas CS, Medeiros DM, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med*. 1998;338:347-354.

Bope ET, Kellerman R, eds. *Conn's Current Therapy*. Philadelphia, PA: Saunders Elsevier; 2015:333-406.

Brower RG, Ware LB, Berthiaume Y, et al. Treatment of ARDS. *Chest*. 2001;120(4):1347-1367.

Thomson BT, Bernard GR. ARDS Network (NHLBI) studies: successes and challenges in ARDS clinical research. *Crit Care Clin*. 2011;27(3):459-468.

D.3. In the recovery room, you are called to see this patient because of oliguria. How would you evaluate and treat this patient?

Oliguria is a decrease in urinary output to less than 0.5 mL/kg/hr.

ARF is a syndrome characterized by a rapid (hours to weeks) decline in glomerular filtration rate and retention of nitrogenous waste products such as blood urea nitrogen and creatinine. The kidney is remarkable in its ability to recover from almost complete loss of function. Most ARF is reversible. ARF is associated with major in-hospital morbidity and mortality. The diagnosis of ARF usually hinges on serial analysis of blood urea nitrogen and serum creatinine.

Renal failure can be divided into three categories:

Prerenal

Prerenal failure is the most common cause of ARF and is an appropriate physiologic response to renal hypoperfusion. It is usually caused by a low cardiac output resulting from hypovolemia or cardiac failure. It can be evaluated by checking the patient's heart rate, blood pressure, central venous pressure, pulmonary capillary wedge pressure, and cardiac output. If hypovolemia is the cause, then treatment would consist of a fluid bolus. If the patient is in cardiac failure, then inotropic support and diuretics could be administered. Severe renal hypoperfusion may cause ischemic acute tubular necrosis (ATN). Therefore, prerenal azotemia and ischemic ATN are part of a spectrum of manifestations of renal hypoperfusion.

Renal

Intrinsic renal failure is generally due to toxic injury or ischemia. Ischemic injury is caused by a decrease in perfusion pressure that can lead to renal cellular dysfunction. Substances that affect renal tubular function in addition to renal blood flow can cause toxic injury. Ischemic ATN, unlike prerenal azotemia, is associated with injury to renal parenchyma and does not resolve immediately on restoration of renal perfusion. In its more extreme form, renal hypoperfusion may result in bilateral renal cortical necrosis and irreversible renal failure. Urinalysis may show cells or casts that are indicative of ARF. Intrinsic renal failure can be minor and short-lived, or it can progress to chronic renal failure, depending on the severity of the insult. In the absence of congestive heart failure, use of diuretics should generally be avoided because they can exacerbate ATN. In particular, loop diuretics increase oxygen and ATP consumption at the level of the tubules.

Postrenal

Urinary tract obstruction accounts for less than 5% of cases of ARF. Urinary tract obstruction must be sought and corrected to treat possible causes of postrenal oliguria. This usually requires irrigation or changing of the Foley catheter. Consider the possibility of an intraoperative mishap causing postrenal obstruction.

Taal MW, Chertow GM, Marsden PA, et al, eds. *Brenner and Rector's The Kidney*. 9th ed. Philadelphia, PA: Saunders Elsevier; 2012:844-867.

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D.4. If this patient had a crush injury and low urine output, what other concerns might you have? What if the patient has dark or "tea-colored" urine?

Leakage of myoglobin from muscles and damaged muscle cells secondary to a crush injury can result in rhabdomyolysis. Myoglobin at high concentrations precipitates in the nephron, appearing pigmented and causing acute renal injury. The urine may look suspicious for hematuria or have a "tea-colored" appearance. Rhabdomyolysis can be diagnosed by the presence of myoglobinuria or elevated serum creatine kinase levels. Preventing ARF in these patients is essential because the development of ARF is associated with increased mortality. The treatment is hydration with large volumes of crystalloid, resulting in goal urine outputs as high as 100 to 300 mL per hour. In addition, alkalization of the urine, with agents such as bicarbonate, may help by decreasing the rate of precipitation. Mannitol has also been used to induce an osmotic diuresis and flush the myoglobin through the kidney. Other electrolyte abnormalities, including hyperkalemia, hyperphosphatemia, hypocalcemia, and metabolic acidosis, can develop with crush injury and the patient should be monitored.

Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. *N Engl J Med*. 2009;361:62-72.

Gonzalez D. Crush syndrome. *Crit Care Med*. 2005;33:S34-S41.

Taal MW, Chertow GM, Marsden PA, et al, eds. *Brenner and Rector's The Kidney*. 9th ed. Philadelphia, PA: Saunders Elsevier; 2012:844-867.

[1]High risk includes patients with coronary artery disease, chronic pulmonary disease, cerebrovascular disease, or congenital or acquired anemia.

[2]Symptomatic includes patients with signs or symptoms of anemia, such as tachycardia, angina, electrocardiographic changes or of neonatal respiratory distress, known hemoglobinopathy, and so forth.

[1]High risk includes patients with coronary artery disease, chronic pulmonary disease, cerebrovascular disease, or congenital or acquired anemia.

[2]Symptomatic includes patients with signs or symptoms of anemia, such as tachycardia, angina, electrocardiographic changes or of neonatal respiratory distress, known hemoglobinopathy, and so forth.

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Chapter 58
Scoliosis

Kathryn DelPizzo

Victor M. Zayas

A 14-year-old girl with scoliosis is scheduled for posterior spine fusion with segmental instrumentation. She has been told that her scoliosis is idiopathic. Her past medical history is unremarkable, but her mother states that she appears to get short of breath more easily than her friends when she plays basketball.

A. Medical Disease and Differential Diagnosis

1. What is scoliosis?
2. What is the most common type of scoliosis?
3. What are other types of scoliosis?
4. How is the severity of scoliosis assessed, and why is the severity important?
5. What abnormalities in pulmonary function tests are most commonly seen in scoliosis? What is the cause of these abnormalities?
6. What is the most common arterial blood gas abnormality seen in scoliosis? What are possible causes for this abnormality?
7. What abnormalities of ventilatory drive may be associated with scoliosis?
8. How may the cardiovascular system be affected in patients with scoliosis?
9. What is the relationship between scoliosis and malignant hyperthermia?

B. Preoperative Evaluation and Preparation

1. What should the anesthesiologist know about the nature of the spinal curve?
2. What aspects of the history are most important?
3. What aspects of the physical examination are most important?
4. Why is a preoperative neurologic assessment important?
5. What tests would you order preoperatively?
6. What preparation should the patient have preoperatively?
7. How will the surgical procedure influence the anesthetic management?

C. Intraoperative Management

1. What monitoring would you use?
2. What is the incidence of neurologic complications in scoliosis surgery, and which patients are at highest risk?
3. What monitoring techniques are used to minimize neurologic complication?
4. What are somatosensory evoked potentials (SSEPs), and how are they used?
5. How reliable are SSEPs for predicting spinal injury?
6. What are motor evoked potentials (MEPs), and how are they used?
7. How is spinal cord monitoring affected by anesthetic agents? What other factors affect spinal cord monitoring?
8. What is the optimal anesthetic technique for scoliosis surgery?

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9. What should be done if the SSEPs or MEPs become abnormal during surgery?
10. How is the “wake-up” test performed? What complications can occur during this test?
11. Four hours into the surgical procedure, the surgeon reports some bubbling in the thoracic portion of the wound. Shortly thereafter, end-tidal carbon dioxide decreases abruptly from 35 to 18 mm Hg, heart rate increases from 80 to 120 beats per minute, blood pressure begins to fall, and arterial saturation decreases to 90%. On auscultation through esophageal stethoscope, you hear a loud gurgling murmur. What is your diagnosis?
12. How common is significant air embolism during scoliosis surgery?
13. What should be done if an air embolus is suspected?
14. What complications occur related to positioning the patient?
15. What is transfusion-related acute lung injury (TRALI)? How do you distinguish it from transfusion-associated circulatory overload (TACO)?
16. What techniques can be used to minimize transfusion requirements?

D. Postoperative Management

1. When would you extubate the patient?
2. What should be done to optimize pulmonary status?
3. What laboratory tests should be ordered postoperatively?
4. What fluid therapy would you use postoperatively?
5. What complications may occur following scoliosis surgery?
6. How would you manage this patient's pain, nausea, and vomiting postoperatively?

A. Medical Disease and Differential Diagnosis

A.1. What is scoliosis?

The spine normally curves posteriorly in the thoracic region and anteriorly in the lumbar region. These physiologic curves are the thoracic kyphosis and the lumbar lordosis, respectively. The spine is not normally curved when viewed from the front or back. Scoliosis refers to a lateral curvature of the spine. Curves are classified as structural or nonstructural. A nonstructural curve, such as lumbar scoliosis from a leg length discrepancy, will resolve when the patient is supine or uses a shoe lift and does not require surgical correction. In contrast, structural scoliosis lacks normal flexibility and does not correct with bending or lying supine. In addition to the lateral curvature of the spine, the vertebrae are rotated and the rib cage may be markedly deformed (Fig. 58.1). As demonstrated in the computed tomography scan image in Figure 58.2, this thoracic deformity may lead to a significant decrease in total lung volume. Particularly, note the decrease in left lung volume relative to the right.

Canale ST, Beaty JH. *Campbell's Operative Orthopaedics*. 12th ed. Philadelphia, PA: Elsevier Mosby; 2013:1691-1895.

Kusumi K, Dunwoodie SL. *The Genetics and Development of Scoliosis*. New York: Springer; 2010:73-79.

Nnadi C, ed. *Early Onset Scoliosis*. Stuttgart, Germany: Thieme; 2015:23-25.

A.2. What is the most common type of scoliosis?

Idiopathic scoliosis is the most common type of scoliosis (70% of all cases) and occurs in infantile, juvenile, and adolescent forms. As the name implies, the cause is unknown but appears to be multifactorial, including abnormalities of collagen, brainstem function, equilibrium, hormones, and growth. Genetic factors are important in its development, as evidenced by an increased incidence of scoliosis in relatives of affected patients. Evidence suggests that pronounced forms of scoliosis (curve greater than 11 degrees) occur only in the carriers of a mutant allele with incomplete penetrance (30% of men, 50% of women).

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The prevalence of idiopathic scoliosis in large screening studies depends on the definition of scoliosis and the population screened. The prevalence of spinal curves greater than 10 degrees is 1.5% to 3%; greater than 20 degrees, it is 0.3% to 0.5%; and greater than 30 degrees, it is 0.2% to 0.3%. The adolescent form of idiopathic scoliosis is by far the most

common in the United States. The male-to-female prevalence ratio depends in part on the age of the patient, but scoliosis requiring surgical correction is more common in women. The ratio increases with the severity of the curve, with a ratio of girls to boys at 2:1 for curves of 10 degrees, and increasing to 10:1 for curves over 30 degrees.

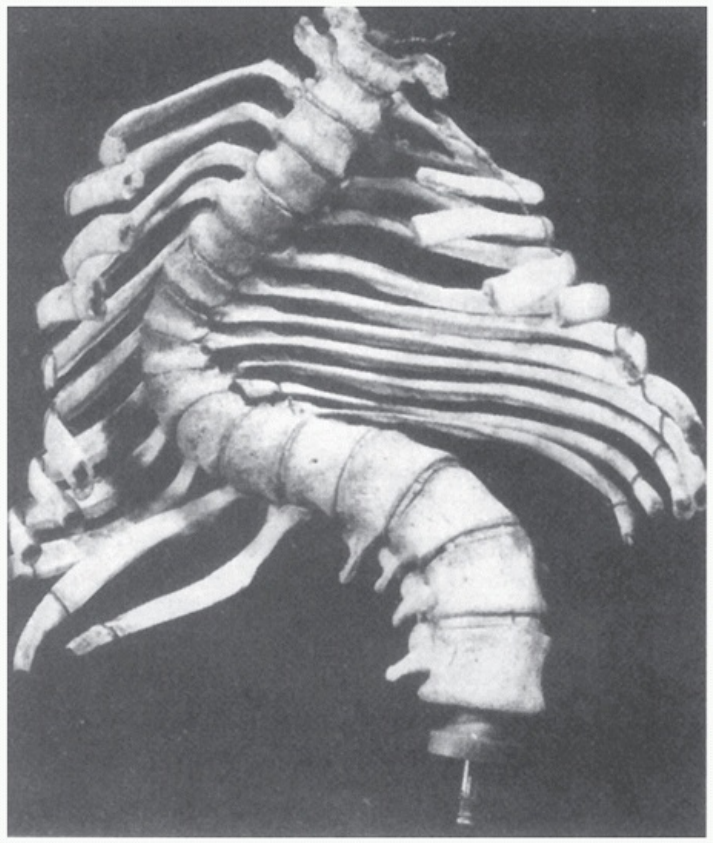


FIGURE 58.1 In addition to producing a lateral deformity of the spine, scoliosis also results in rotation of the vertebral bodies and significant rib cage deformity.

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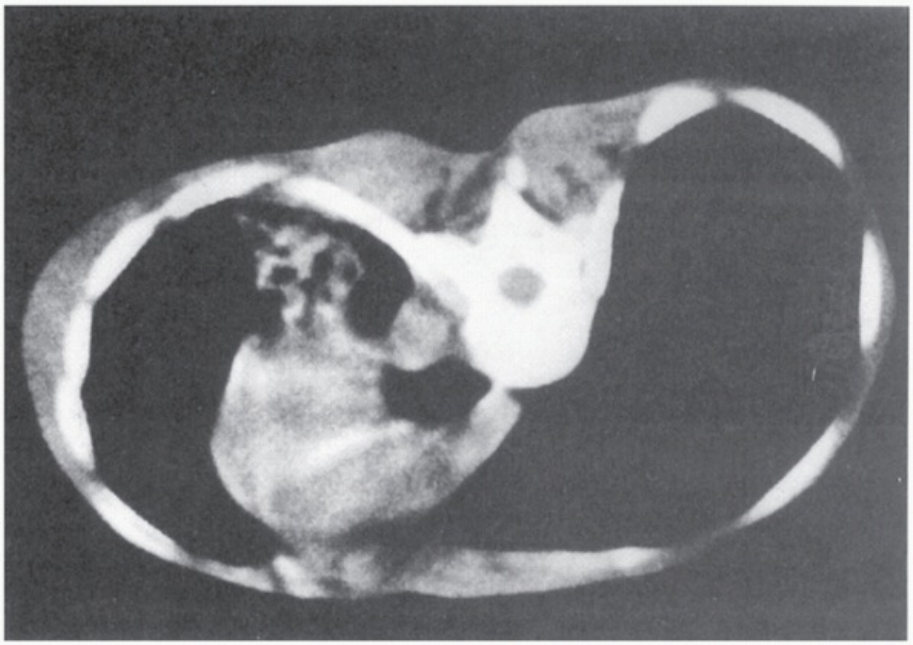


FIGURE 58.2 A computed tomography scan of the thorax demonstrating significant loss of lung volume resulting from the rib cage deformity.

Canale ST, Beaty JH. *Campbell's Operative Orthopaedics*. 12th ed. Philadelphia, PA: Elsevier Mosby; 2013:1691-1895.

Newton PO, O'Brien MF, Shufflebarger HL, et al, eds. *Idiopathic Scoliosis. The Harms Study Group Treatment Guide*. New York: Thieme; 2011:30, 51-53.

Nnadi C, ed. *Early Onset Scoliosis*. Stuttgart, Germany: Thieme; 2015:23-25.

A.3. What are other types of scoliosis?

Many etiologic classifications exist for structural scoliosis. Neuromuscular scoliosis (paralytic scoliosis) may occur as a result of diseases such as cerebral palsy, muscular dystrophy, poliomyelitis, familial dysautonomia, and so on. This type of scoliosis is associated with significantly increased intraoperative blood loss compared with idiopathic scoliosis. Congenital scoliosis is the result of congenital anomalies such as hemivertebrae and fused vertebrae or ribs. Neurofibromatosis and Marfan syndrome are also associated with scoliosis. These underlying conditions may have a major impact on the anesthetic plan. The classification of structural scoliosis is as follows:

Idiopathic

- Infantile
- Juvenile
- Adolescent

Neuromuscular (paralytic)

- Neuropathic
  - Upper motor neuron (e.g., cerebral palsy, spinal cord injury)
  - Lower motor neuron (e.g., poliomyelitis, meningomyelocele)
  - Familial dysautonomia
- Myopathic

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- Muscular dystrophy
- Myotonic dystrophy

Congenital

- Hemivertebrae
- Congenitally fused ribs

Neurofibromatosis

- Marfan syndrome

Mesenchymal disorders

- Ehlers-Danlos syndrome

Trauma

- Vertebral fracture or surgery
- Postthoracoplasty
- Postradiation

Canale ST, Beaty JH. *Campbell's Operative Orthopaedics*. 12th ed. Philadelphia, PA: Elsevier Mosby; 2013:1691-1895.

Nnadi C, ed. *Early Onset Scoliosis*. Stuttgart, Germany: Thieme; 2015:23-25.

A.4. How is the severity of scoliosis assessed, and why is the severity important?

In 1966, the Scoliosis Research Society standardized the method for assessing the severity of scoliosis. The most common measure of severity is Cobb angle. Figure 58.3 illustrates how Cobb angle is measured on a spine radiograph. A perpendicular (*2*) is constructed from the bottom of the lowest vertebrae (*1*) whose bottom tilts toward the concavity of the curve, and another perpendicular (*4*) from the top of the highest vertebrae (*3*) whose top tilts toward the concavity. The angle (*5*) at which these perpendiculars intersect is Cobb angle. Numerous studies have documented that the more severe the thoracic curve (greater Cobb angle), the

more profound the disturbance in pulmonary function. Surgical treatment is usually recommended for curves greater than 45 to 50 degrees. Curves greater than 60 degrees are usually associated with decreases in pulmonary function.

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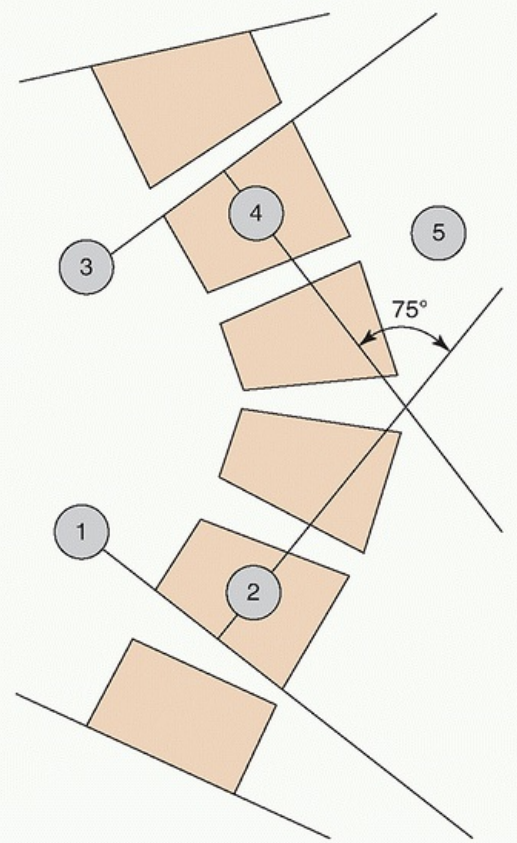


FIGURE 58.3 Measurement of the curve in scoliosis using Cobb angle. (Reprinted with permission from Levine DB. Scoliosis. *Curr Opin Rheumatol*. 1987;2:191.)

In a series of 79 patients with thoracic scoliosis, the mean Cobb angle was 45 degrees and vital capacity was decreased by an average of 22%. Figure 58.4 demonstrates that forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) decrease with increasing thoracic curve severity.

Scoliosis severity and impairment of pulmonary function also increase with greater number of vertebrae involved, more cephalad location of the curve, and loss of the normal thoracic kyphosis. Severe curves have a worse prognosis because they tend to progress and if long-standing can cause permanent damage of the lung parenchyma, respiratory failure, cor pulmonale, and death. It is important to note that patients with neuromuscular types of scoliosis may have a much more profound decrease in pulmonary function for any given curve severity.

Canale ST, Beaty JH. *Campbell's Operative Orthopaedics*. 12th ed. Philadelphia, PA: Elsevier Mosby; 2013:1691-1895.

Nnadi C, ed. *Early Onset Scoliosis*. Stuttgart, Germany: Thieme; 2015:23-25.

A.5. What abnormalities in pulmonary function tests are most commonly seen in scoliosis? What is the cause of these abnormalities?

A decrease in lung volumes, a restrictive pattern, is most commonly seen in thoracic scoliosis. The greatest reduction occurs in vital capacity, which is typically reduced to 60% to 80% of predicted. Total lung capacity, functional residual capacity, inspiratory capacity, and expiratory reserve volume are also decreased. An increase in residual volume has been reported in patients with congenital scoliosis and in patients with idiopathic scoliosis 3 years following corrective spine fusion.

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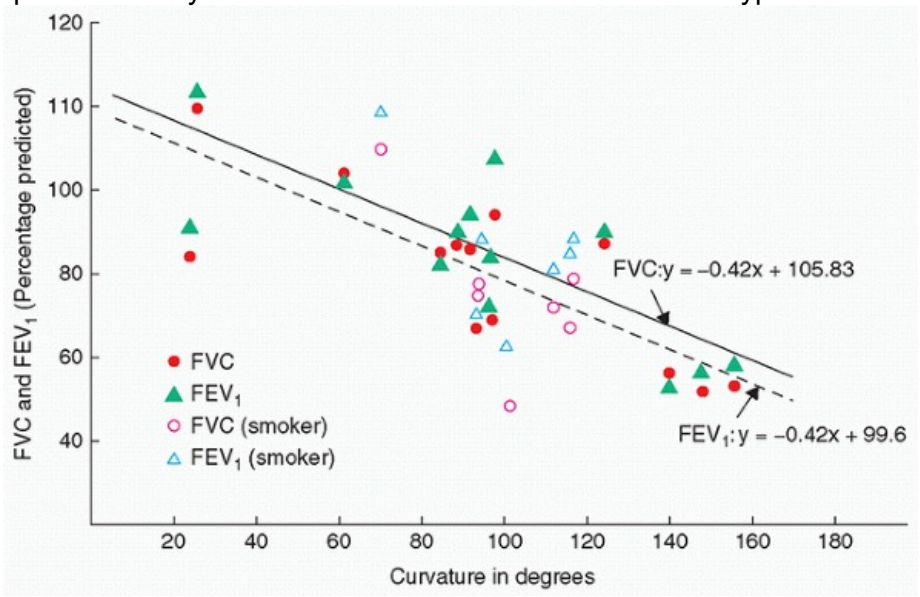


FIGURE 58.4 Relation between forced vital capacity (FVC), and forced expiratory volume in 1 second (FEV_1), and size of the curve in 20 patients with thoracic scoliosis. (Reproduced with permission from Weinstein SL, Zaval DC, Ponseti IV, et al. Idiopathic scoliosis: long-term follow-up and prognosis in untreated patients. *J Bone Joint Surg Am*. 1981;63:702-712.)

During exercise, ventilation is adequate, but tidal volume is reduced and respiratory rate is increased. Maximal work capacity may also be decreased. Unless there is coexisting obstructive airway disease, the ratio of FEV_1/FVC is normal.

Impaired respiratory muscle function also occurs in scoliosis, as evidenced by a decrease in inspiratory force to 70% of normal values. The decrease in inspiratory force is probably due to the inspiratory muscles working at a mechanical disadvantage because of the chest wall deformity.

These abnormalities in pulmonary function are usually the result of abnormal thoracic cage geometry producing a marked decrease in chest wall compliance rather than any abnormality in the lungs or respiratory muscles themselves. In dynamic magnetic resonance imaging, adolescent girls with idiopathic scoliosis and healthy controls showed no difference in diaphragmatic motion. The changes in chest wall compliance can be mimicked in normal volunteers by chest strapping. Exceptions include congenital and infantile scoliosis in which growth of the lungs may be impaired early in development by the thoracic deformity.

Barrios C, Pérez-Encinas C, Maruenda JI, et al. Significant ventilatory functional restriction in adolescents with mild or moderate scoliosis during maximal exercise tolerance test. *Spine (Phila Pa 1976)*. 2005;30:1610-1615.

Canale ST, Beaty JH. *Campbell's Operative Orthopaedics*. 12th ed. Philadelphia, PA: Elsevier Mosby; 2013:1691-1895.

Chu WC, Li AM, Ng BK, et al. Dynamic magnetic resonance imaging in assessing lung volumes, chest wall, and diaphragm motions in adolescent idiopathic scoliosis versus normal controls. *Spine (Phila Pa 1976)*. 2006;31(19):2243-2249.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

Koumbourlis AC. Scoliosis and the respiratory system. *Paediatr Respir Rev*. 2006;7:152-160.

Nnadi C, ed. *Early Onset Scoliosis*. Stuttgart, Germany: Thieme; 2015:23-25.

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A.6. What is the most common arterial blood gas abnormality seen in scoliosis? What are possible causes for this abnormality?

It has been documented that patients with thoracic scoliosis have arterial oxygen desaturation compared to normal controls. Both arterial PCO_2 and pH are usually normal. Several studies

have failed to show a correlation between the severity of the spinal curve and the degree of arterial oxygen desaturation.

Arterial hypoxemia is probably caused by ventilation/perfusion ([V with dot above]/[Q with dot above]) inequalities. Decreased diffusing capacity and alveolar hypoventilation may also play a role. Nevertheless, the diffusing capacity is not decreased sufficiently to be the sole cause of the hypoxemia. Similarly, alveolar ventilation at rest and during exercise is usually normal; therefore, arterial PCO_2 is usually normal. It has been reported that some patients have a closing capacity higher than functional residual capacity, resulting in premature airway closure during normal tidal breathing. Other studies have failed to demonstrate this finding. Some authors have reported an increase in the ratio of dead space to tidal volume (V_D/V_T), whereas other recent series have found V_D/V_T to be normal. This discrepancy may be related to the patient population studied, the severity of the scoliosis, or both. Severe and long-standing scoliosis can produce severe [V with dot above]/[Q with dot above] abnormalities, alveolar hypoventilation, carbon dioxide retention, and more severe hypoxemia. If not surgically treated, severe scoliosis increases the risk of premature death from respiratory failure after 40 years of age. A survey of patients with respiratory failure in Sweden found that a vital capacity less than 50% of predicted and a Cobb angle greater than 100 degrees indicated an increased risk of respiratory failure.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

Koumbourlis AC. Scoliosis and the respiratory system. *Paediatr Respir Rev*. 2006;7:152-160.

McPhail GL, Ehsan Z, Howells SA, et al. Obstructive lung disease in children with idiopathic scoliosis. *J Pediatr*. 2015;166(4):1018-1021.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2402-2404.

A.7. What abnormalities of ventilatory drive may be associated with scoliosis?

The slope of the ventilatory response to carbon dioxide may be decreased in patients with scoliosis. This is probably not specific to scoliosis because this response is known to be reduced in situations in which the work of breathing is increased even in the absence of a chest wall deformity. Patients with mild scoliosis have been reported to exhibit abnormal ventilatory patterns in response to hypoxemia and hypercarbia. This pattern tends to minimize the work of breathing, a higher respiratory rate, and lower tidal volume.

It has also been demonstrated that during maximal exercise, patients with mild-tomoderate scoliosis exhibit a significantly decreased ventilatory capacity, reduced exercise tolerance, and oxygen consumption despite normal pulmonary function testing at rest.

Barrios C, Pérez-Encinas C, Maruenda JI, et al. Significant ventilatory functional restriction in adolescents with mild or moderate scoliosis during maximal exercise tolerance test. *Spine (Phila Pa 1976)*. 2005;30:1610-1615.

Koumbourlis AC. Scoliosis and the respiratory system. *Paediatr Respir Rev*. 2006;7:152-160.

McPhail GL, Ehsan Z, Howells SA, et al. Obstructive lung disease in children with idiopathic scoliosis. *J Pediatr*. 2015;166(4):1018-1021.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2402-2404.

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A.8. How may the cardiovascular system be affected in patients with scoliosis?

Patients with scoliosis may develop elevated pulmonary vascular resistance and pulmonary hypertension. This may result in right ventricular hypertrophy and eventually right ventricular failure. A 50-year study of untreated scoliosis demonstrated that the mortality rate of these patients was twice that of the general population and respiratory failure or right-sided heart failure accounted for 60% of the deaths.

The increase in pulmonary vascular resistance is probably due to several factors. Hypoxemia produces pulmonary vasoconstriction, an increase in pulmonary vascular resistance, and hence an increase in pulmonary arterial pressure. Chronic hypoxemia will produce hypertensive vascular changes, and pulmonary hypertension may become irreversible. It has also been proposed that the chest wall deformity compresses some lung regions, increasing vascular resistance in those regions. Finally, if scoliosis develops in the first 6 years of life, the growth of the pulmonary vascular bed may be impaired by the chest wall deformity.

Supporting this concept are reports of a decrease in the number of vascular units per lung volume in patients with scoliosis.

The most common cardiovascular abnormality in patients with scoliosis is mitral valve prolapse. Some conditions that are associated with scoliosis also affect the cardiovascular system. Patients with Duchenne muscular dystrophy develop a cardiomyopathy in the second decade of life that may not be appreciated on the basis of clinical symptoms because these patients are unable to exercise. The electrocardiogram (ECG) may reveal tachycardia, prolonged PR and QRS intervals, ST abnormalities, bundle branch block, Q waves in the left precordial leads, and tall R waves in the right precordial leads. Ejection fraction may be decreased on echocardiogram.

Patients with Marfan syndrome may have mitral and aortic insufficiency, aneurysm of the proximal ascending aorta, and abnormalities of the conduction system.

The association of scoliosis and congenital heart disease has been well established. Although no specific cardiac lesion has been identified, some series have suggested that scoliosis is more common in patients with cyanotic heart disease.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

Kawakami N, Mimatsu K, Deguchi M, et al. Scoliosis and congenital heart disease. *Spine (Phila Pa 1976)*. 1995;20:1252-1255.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2402-2404.

A.9. What is the relationship between scoliosis and malignant hyperthermia?

In the past 40 years, there has been no supportive evidence of a direct relationship. However, some scoliosis patients may have an associated or underlying muscle disorders such as central core disease or multiminicore disease (also see Chapter 54, section A.3). These muscular dystrophies are associated with an increased risk of malignant hyperthermia.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110:498-507.

Rosenberg H, Davis M, James D, et al. Malignant hyperthermia. *Orphanet J Rare Dis*. 2007;2:21.

B. Preoperative Evaluation and Preparation

B.1. What should the anesthesiologist know about the nature of the spinal curve?

It is important to identify the location of the curve, the age of onset, its severity, the direction of the curve, and the etiology of the scoliosis. The location of the curve is important because thoracic scoliosis is associated with pulmonary function

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abnormalities. Cervical scoliosis may cause difficulties in airway management and may be associated with other congenital anomalies.

The age of onset of scoliosis is of critical importance because the lung continues to grow and develop from birth until 8 years of age. The number of alveoli increases from approximately 20 million at birth to 250 million at 4 years of age. The development of significant thoracic scoliosis during this phase of rapid growth impairs lung development. A significant reduction in alveolar number has been demonstrated in patients with early-onset thoracic scoliosis, predisposing these patients to impaired gas exchange and pulmonary hypertension.

The severity of the curve is important because thoracic curves greater than 60 degrees generally produce significant decreases in pulmonary function. Curves greater than 100 degrees may be associated with significant impairment in gas exchange. Most curves in adolescent idiopathic scoliosis are convex to the right, just as most people are right-handed. A left thoracic convexity should raise the index of suspicion to look for other underlying conditions and congenital anomalies. Finally, an understanding of the etiology of the scoliosis is important because underlying conditions such as muscular dystrophy or cerebral palsy will influence anesthetic management.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. Philadelphia, PA: Elsevier Saunders; 2013:627-652.

B.2. What aspects of the history are most important?

Cardiopulmonary reserve should be assessed by questioning the patient about shortness of breath, dyspnea on exertion, exercise tolerance, and so on. As a general rule, patients who can exercise normally and “keep up with friends” in vigorous activities will have good cardiopulmonary function. Pulmonary symptoms such as episodes of wheezing or cough may indicate parenchymal lung disease and alter perioperative management. Patients with muscular dystrophy, Marfan syndrome, and neurofibromatosis should be questioned about symptoms suggestive of cardiac conduction abnormalities such as palpitations or syncope.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. Philadelphia, PA: Elsevier Saunders; 2013:627-652.

B.3. What aspects of the physical examination are most important?

Particular emphasis in the physical examination should be directed toward the heart and lungs. Auscultation of the lungs may reveal wheezing or rales suggesting obstructive airway disease or parenchymal lung disease. On examination of the heart, in addition to auscultating for murmurs and gallops, signs of pulmonary hypertension and right ventricular hypertrophy should be sought. Pulmonary hypertension causes accentuation of the pulmonic component of the second heart sound, and a right ventricular lift indicates right ventricular enlargement. Signs of right ventricular failure include engorged neck veins, an enlarged liver resulting from passive liver congestion, and lower extremity edema. If neurofibromatosis is suspected, the skin should be examined for the presence of *café au lait spots* or cutaneous neurofibroma. The airway should be evaluated closely for abnormalities such as cervical scoliosis, neurofibroma, or high-arched palate associated with Marfan syndrome that may make endotracheal intubation difficult.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. Philadelphia, PA: Elsevier Saunders; 2013:627-652.

B.4. Why is a preoperative neurologic assessment important?

A preoperative neurologic assessment is important because patients who have preexisting neurologic deficits are at increased risk for developing spinal cord injury during scoliosis surgery. Furthermore, it is important to document preoperative neurologic function in order to avoid confusion about postoperative neurologic complications.

If a patient has a ventriculoperitoneal shunt for hydrocephalus, it should be evaluated preoperatively by the patient's neurosurgeon. Although rare, there have been case reports of life-threatening hydrocephalus following posterior spinal fusion in children with cerebral palsy. The shunt can malfunction during correction of the spinal deformity via disconnection, fracture, kinking, or inadequate length.

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Abu-Sneineh K, Lipton GE, Gabos PG, et al. Dysfunction of a ventriculoperitoneal shunt after posterior spinal fusion in children with cerebral palsy: a report of two cases. *J Bone Joint Surg Am*. 2003;85:1119-1124.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

B.5. What tests would you order preoperatively?

It is best to tailor diagnostic testing based on the severity of the scoliosis and underlying conditions. In the current climate emphasizing medical cost containment, each institution needs to critically reassess preoperative testing. Preoperatively, this healthy 14-year-old may only need a complete blood count. If the history or physical examination suggests that pulmonary reserve is decreased, then standard pulmonary function testing should be considered. If vital capacity is significantly diminished, an arterial blood gas measurement is indicated. If routine pulmonary function testing reveals evidence of obstructive airway disease (a decrease in the ratio of FEV_1/FVC or a decrease in forced expiratory flow [25% to 75%]), a bronchodilator should be administered to determine if the airway obstruction is reversible.

Patients with onset of scoliosis in the first 8 years of life should have pulmonary function testing, arterial blood gas analysis, and an ECG. If the ECG reveals abnormalities such as right ventricular hypertrophy (large R in V_1 and V_2), right atrial enlargement (P_{wave} greater

than 2.5 mm) or evidence of a cardiomyopathy, an echocardiogram, or even cardiac catheterization may be indicated, particularly if pulmonary hypertension is suspected.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

McPhail GL, Ehsan Z, Howells SA, et al. Obstructive lung disease in children with idiopathic scoliosis. *J Pediatr*. 2015;166(4):1018-1021.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:2402-2404.

B.6. What preparation should the patient have preoperatively?

The patient should be prepared both physiologically and psychologically for surgery and the postoperative course. First, preoperative teaching of coughing and incentive spirometry should be emphasized. Patients with evidence of parenchymal lung disease or obstructive airway disease should have aggressive pulmonary toilet or bronchodilator therapy preoperatively. Patients should know that upon awakening, they will be asked to move their extremities and follow basic commands (opening the eyes and mouth, squeezing a hand). Finally, if an intraoperative wake-up test is planned (see subsequent text), the patient should be informed and reassured that he or she will feel no pain or discomfort. It can be helpful to rehearse the wake-up test during the preoperative visit. The patient and family should understand that the wake-up test is often requested by the surgeon.

Some patients may be good candidates for preoperative autologous blood donation, particularly adult-sized patients with a high baseline hemoglobin. There is limited use in many pediatric patients because smaller children do not tolerate the phlebotomy procedure, and it may not be beneficial in patients with smaller blood volumes.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

B.7. How will the surgical procedure influence the anesthetic management?

A variety of surgical procedures are commonly performed for posterior spine fusion. The blood lost during these procedures may be considerable and varies according to the procedure, the operative time, the number of segments

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fused, whether deliberate hypotension is used, and other factors. Even when deliberate hypotension is commonly employed, blood loss in the range of 15 to 25 mL per kg is not uncommon during uncomplicated spine fusion with Harrington rods or Cotrel-Dubousset instrumentation. This represents a blood loss of 1 to 2 L for a 70-kg patient. Postoperative bleeding may equal or exceed this, emphasizing the need for continued monitoring of these patients in the postoperative period. More extensive procedures such as combined anteroposterior spine fusion, instrumentation into the pelvis, or especially osteotomy of the spine to correct rigid deformities may be associated with blood loss exceeding the patient's own blood volume (75 mL per kg). Patients who require these more extensive procedures are frequently those with neuromuscular scoliosis (Duchenne muscular dystrophy, cerebral palsy) who may already have diminished reserves. Before the patient is taken to the operating room, the anesthesiologist should confirm that the blood bank has the anticipated blood products readily available.

Moderate third-space losses of intravascular fluid occur during scoliosis surgery. These should be replaced with balanced salt solution at a rate of 5 to 7 mL/kg/hr. This is in addition to any deficit or maintenance requirements. Procedures that are more extensive may require higher infusion rates.

The anesthesiologist should speak with the surgeon about the surgical approach and technique. The surgical plan could affect the patient's position during the case. For example, patients undergoing an anterior approach or thoracotomy may need to be positioned laterally. Another consideration is whether the surgeon requires single-lung ventilation in which case the patient may need a double-lumen endotracheal tube.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

Guay J, Haig M, Lortie L, et al. Predicting blood loss in surgery for idiopathic scoliosis. *Can J Anaesth*. 1994;41:775-781.

C. Intraoperative Management

C.1. What monitoring would you use?

Basic monitoring for posterior spine fusion should include blood pressure, ECG, pulse oximetry, end-tidal carbon dioxide, esophageal stethoscope, core temperature, and spinal cord monitoring. A radial artery catheter is used for continuous monitoring of blood pressure, particularly if deliberate hypotension is planned to reduce blood loss. This will also facilitate obtaining blood samples for blood gas and hematocrit determination. All patients should have a urinary catheter placed to document urine output during and particularly after the surgical procedure. Monitoring of central filling pressures may be indicated if the expected blood loss is large, or cardiovascular disease is present or suspected. Although rarely placed in routine scoliosis surgery, a pulmonary artery catheter may be useful in patients with cardiomyopathy from Duchenne muscular dystrophy, and patients with pulmonary hypertension or right ventricular failure, in order to optimize volume replacement therapy. When placing pulmonary artery catheters in patients with pulmonary hypertension, it must be considered that the risk of pulmonary artery rupture, a complication with a mortality rate of 50%, is increased in patients with pulmonary hypertension. An alternative technique is the transesophageal echocardiography (TEE), but this requires special expertise, and vigilance must be used when using the TEE probe for a lengthy operation in the prone position.

If neuromuscular block is used throughout the case, be certain to monitor continuously and discuss this with the neuromonitoring team in case there is any confusion interpreting the MEPs.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

C.2. What is the incidence of neurologic complications in scoliosis surgery, and which patients are at highest risk?

In a morbidity report of the Scoliosis Research Society (2006), the rate of complete or partial paraplegia was 0.26%. A study of 6,334 patients undergoing anterior, posterior, or combined anteroposterior spinal fusion reported an overall rate of spinal injury of 0.28%. Of note, combined anteroposterior procedures had a significantly higher rate of spinal cord injuries (1.12%) compared to anterior (0.0%) and posterior (0.21%) procedures.

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It has been proposed that distraction of the cord and straightening of the deformity compresses the spinal cord and disrupts the arterial blood supply of the cord. The spinal cord and nerve roots may also be injured directly by hooks or instrumentation.

Prevention of neurologic complications begins with identification of the high-risk group. Patients are at increased risk for developing paraplegia if they have a severe rigid deformity (greater than 120 degrees), kyphosis, neurofibromatosis, congenital or postinfectious scoliosis, a preexisting neurologic deficit, or more invasive instrumentation. Congenital scoliosis is associated with intraspinal anomalies including lipomas, tethered cord, cysts, and teratomas that also increase the risk of postoperative neurologic complications. A preoperative myelogram or magnetic resonance imaging is indicated in these patients. Preoperative prophylaxis with high-dose corticosteroids should be considered for patients with a preexisting neurologic deficit.

Coe JD, Arlet V, Donaldson W, et al. Complications in spinal fusion for adolescent idiopathic scoliosis in the new millennium. A report of the Scoliosis Research Society Morbidity and Mortality Committee. *Spine (Phila Pa 1976)*. 2006;31:345-349.

Kocher MS, Millis MB, eds. *Operative Techniques: Pediatric Orthopaedic Surgery*. Philadelphia, PA: Elsevier Saunders; 2011:719-730.

C.3. What monitoring techniques are used to minimize neurologic complication?

The two monitoring techniques most commonly used in the United States to monitor spinal cord function during scoliosis surgery are SSEPs and MEPs. Some centers continue to use

the intraoperative wake-up test, although MEP monitoring has replaced the routine use of the wake-up test in many centers. The intraoperative wake-up test may still be required if SSEPs or MEPs become abnormal during the surgical procedure.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

Schwartz D, Auerbach J, Dormans JP, et al. Neurophysiological detection of impending spinal cord injury during scoliosis surgery. *J Bone Joint Surg Am*. 2007;89(11):2440-2449.

C.4. What are somatosensory evoked potentials (SSEPs), and how are they used?

Sensory information from the periphery passes through the posterior columns of the spinal cord on its way to the cerebral cortex. The functional integrity of this pathway can be continually assessed by monitoring SSEPs. This technique involves applying repeated electrical stimuli to a peripheral nerve (e.g., posterior tibial nerve) and measuring the evoked response over the cerebral cortex and subcortical regions using standard electroencephalogram scalp electrodes. These evoked potentials are of very low amplitude, so computer averaging or summation must be used to distinguish these potentials from background noise and the patient's electroencephalogram. A typical evoked potential waveform is shown in Figure 58.5. The time interval between electrical stimulation of peripheral nerve to recording the evoked response over the cortex is defined as the latency. An increase in the latency (slower conduction), a decrease in the amplitude, or a complete loss of the evoked potential should be considered indicative of surgical injury or ischemia until proved otherwise. It is difficult to define standard values for latency and amplitude because of the differences in recording technique among laboratories, and therefore, it is important to be familiar with the normal limits for the system that is in use. In general, an increase in latency of 10% to 15% or more and a decrease in amplitude of greater than 50% should be cause for concern.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

Koht A, Sloan TB, Toleikis JR, eds. *Monitoring the Nervous System for Anesthesiologists and Other Health Care*

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Professionals. New York: Springer; 2012:3-26.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1497-1499.

C.5. How reliable are SSEPs for predicting spinal injury?

Normal intraoperative SSEPs are good predictors of normal postoperative sensory function. Although posterior (sensory) and anterior (motor) spinal injuries tend to occur together during spine surgery or spinal trauma, there have been reports of postoperative paraplegia with normal intraoperative SSEPs. This probably represents selective ischemia in the distribution of the anterior spinal artery. Sensory function and SSEPs are preserved because the posterior columns receive their blood supply from the posterior spinal arteries. For this

reason, it is probably best not to rely exclusively on SSEPs to monitor spinal cord function during scoliosis surgery.

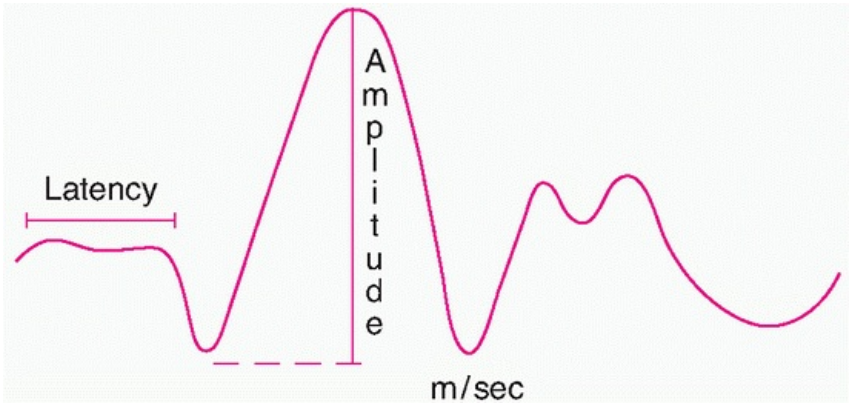


FIGURE 58.5 Typical somatosensory evoked potential trace. (Reprinted with permission from Cunningham JN Jr, Laschinger JC, Merkin HA, et al. Measurement of spinal cord ischemia during operations upon the thoracic aorta: initial clinical experience. *Ann Surg*. 1982;196:285-296.)

In a survey of 173 orthopedic spinal surgeons, it was found that experienced SSEP monitoring teams had fewer neurologic complications per 100 cases than teams with less experience. Neurologic defects with normal SSEPs (false negative) occurred in only 0.063% of cases.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

Kocher MS, Millis MB, eds. *Operative Techniques: Pediatric Orthopaedic Surgery*. Philadelphia, PA: Elsevier Saunders; 2011:719-730.

Koht A, Sloan TB, Toleikis JR, eds. *Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals*. New York: Springer; 2012:3-26.

Nuwer MR, Dawson EG, Carlson LG, et al. Somatosensory evoked potential spinal cord monitoring reduces neurologic deficits after scoliosis surgery: results of a large multicenter survey. *Electroencephalogr Clin Neurophysiol*. 1995;96:6-11.

C.6. What are motor evoked potentials (MEPs), and how are they used?

MEPs assess the integrity of the spinal motor pathways (anterior columns). MEPs are elicited by transosseous electrical stimulation of the motor cortex using scalp electrodes or by stimulation of the anterior columns using epidural electrodes. Conduction of these stimuli through the motor pathways is monitored as peripheral nerve impulses, electromyographic

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signals, or actual limb movements.

In a study of 144 patients undergoing spinal deformity correction surgery, the authors report a sensitivity of 1 and a specificity of 0.97 using transcranial MEPs as the sole modality. No patient had any new neurologic deficits.

Hsu B, Cree AK, Lagopoulos J, et al. Transcranial motor-evoked potentials combined with response recording through compound muscle action potential as the sole modality of spinal cord monitoring in spinal deformity surgery. *Spine (Phila Pa 1976)*. 2008;33:1100-1106.

Koht A, Sloan TB, Toleikis JR, eds. *Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals*. New York: Springer; 2012:27-45.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1499-1500.

C.7. How is spinal cord monitoring affected by anesthetic agents? What other factors affect spinal cord monitoring?

All anesthetic agents may affect spinal monitoring to a varying degree. This has been documented for potent inhalation agents, propofol, nitrous oxide, benzodiazepines, droperidol, etomidate, ketamine, barbiturates, and even opioids. Opioids probably have the least effect on SSEPs of all of these agents. Cortical SSEPs and MEPs are very sensitive to nitrous oxide and potent inhalational agents, whereas subcortical SSEPs are more resistant. The addition of nitrous oxide to isoflurane has been shown to have a profound effect on MEPs. MEPs are also profoundly affected by benzodiazepines and thiopental, whereas ketamine may enhance MEPs.

Nitrous oxide produces a decrease in amplitude in SSEPs without an increase in latency. Isoflurane, sevoflurane, halothane, and so on have similar effects on SSEPs; a dose-dependent increase in latency and decrease in amplitude. The addition of nitrous oxide appears to produce a larger decrease in amplitude than addition of 1% isoflurane or enflurane to a fentanylbased anesthetic.

Muscle relaxants have no effect on SSEPs or MEP impulses monitored from peripheral nerves. They will affect the intensity of the motor response, which may lead to confusion in interpreting MEPs.

Although it is important to realize that anesthetic agents can affect spinal cord monitoring, excellent results can be obtained if anesthetic depth is stable. For example, it is preferable to administer opioids by continuous infusion rather than by intermittent doses. It is most important to maintain a stable anesthetic before and during periods when monitoring is critical, that is, during spine distraction or instrumentation.

A decrease in arterial pressure below levels of cerebral autoregulation, hypothermia, hematocrits below 15%, and hypoxia will affect both SSEPs and MEPs.

Bernard JM, Péréon Y, Fayet G, et al. Effects of isoflurane and desflurane on neurogenic motor- and somatosensory-evoked potential monitoring for scoliosis surgery. *Anesthesiology*. 1996;85:1013-1019.

Koht A, Sloan TB, Toleikis JR, eds. *Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals*. New York: Springer; 2012:337-360.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1511-1521.

C.8. What is the optimal anesthetic technique for scoliosis surgery?

There is no simple answer for the optimal anesthetic technique. Most patients with idiopathic scoliosis are healthy adolescents who tolerate anesthesia and surgery well, and a wide variety of techniques have been used successfully. Many healthy teenagers have a much higher tolerance for opioids and benzodiazepines and will have higher requirements for these agents intraoperatively, compared to adults. The primary concern is the ability to provide an anesthetic that is suitable for spinal cord monitoring while providing analgesia and amnesia. Prior to the use of MEP monitoring, anesthetic techniques were tailored to facilitate the wake-up test. Monitoring of MEPs has now replaced routine use of the wake-up

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test in many centers. Although cortical SSEPs and MEPs may be measurable in most healthy adults receiving 50% to 70% nitrous oxide and 0.5 minimal alveolar concentration isoflurane, this combination is not suitable in small children with immature corticospinal tracts or those with preexisting neurologic deficits. Furthermore, MEPs may be more sensitive to the combination of nitrous oxide and potent inhalational agents than cortical SSEPs.

Therefore, a typical anesthetic is a combination of a low-dose potent agent (e.g., isoflurane 0.4%) in 50% oxygen per air mixture, with a low-dose propofol infusion and primarily opioid-based intravenous anesthetic. Intravenous midazolam should be given before induction for anxiolysis and amnesia. Small doses may be repeated later if necessary. An infusion of ketamine at a low dose (0.1 to 0.2 mg/kg/hr) may improve MEP monitoring. Many centers use total intravenous anesthesia. Dexmedetomidine has been used as an adjunct in total intravenous anesthesia with minimal effect on MEPs and SSEPs. Muscle relaxants, if used, should be administered by continuous infusion and titrated to a constant train-offour because the neuromuscular blockade will affect the intensity of the motor response. A baseline set of SSEPs and MEPs should be performed by the neuromonitoring technician as early as possible, ideally before incision, so that changes to the anesthetic or monitoring technique can be made before the most critical part of the operation (i.e., spine distraction and instrumentation).

Succinylcholine should be avoided in patients with muscle disorders. Its administration in patients with Duchenne muscular dystrophy may produce hyperkalemia, cardiac arrhythmias, myoglobinuria, or precipitate malignant hyperthermia. Patients with myotonic muscular dystrophy may exhibit sustained skeletal muscle contractions in response to succinylcholine. This may produce difficulty in ventilation and intubation.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

Gibson PR. Anaesthesia for correction of scoliosis in children. *Anaesth Intensive Care*. 2004;32:548-559.

Miller RD, ed. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1497-1499.

Tobias JD, Goble TJ, Bates G, et al. Effects of dexmedetomidine on intraoperative motor and somatosensory evoked potential monitoring during spinal surgery in adolescents. *Paediatr Anaesth*. 2008;18:1082-1088.

C.9. What should be done if the SSEPs or MEPs become abnormal during surgery?

If spinal cord monitoring becomes abnormal, the anesthesiologist should ensure that oxygen delivery and spinal cord perfusion are adequate. Hypovolemia and anemia should be corrected. Arterial oxygen tension should be optimized, and arterial PCO_2 should be normalized if the patient is being hyperventilated. It has been reported that normalizing arterial pressure if deliberate hypotension is being used or raising arterial pressure above normal may improve spinal cord perfusion and restore SSEPs to normal. The surgeon should seek a surgical cause such as too much distraction or surgical trespass with instrumentation and correct

the problem as quickly as possible. If the abnormality persists despite corrective action, a wake-up test should be performed to determine if the instrumentation should be adjusted or removed. There is evidence that the shorter the interval between detection of injury and removal of instrumentation, the better is the neurologic outcome.

Grundy BL, Nash CL Jr, Brown RH. Arterial pressure manipulation alters spinal cord function during correction of scoliosis. *Anesthesiology*. 1981;54:249-253.

Koht A, Sloan TB, Toleikis JR, eds. *Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals*. New York: Springer; 2012:337-360.

Lyon R, Lieberman JA, Grabovac MT, et al. Strategies for managing decreased motor evoked potential signals while distracting the spine during correction of scoliosis. *J Neurosurg Anesthesiol*. 2004;16(2):167-170.

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C.10. How is the "wake-up" test performed? What complications can occur during this test?

The wake-up test is used to assess the integrity of the spinal motor pathways and is performed by "lightening" the depth of anesthesia sufficiently to allow the patient to follow commands. This is usually done as soon as all instrumentation is in place or if an abnormality has been detected with spinal cord monitoring. The patient is first instructed to squeeze the anesthesiologist's hand, confirming that he is responsive, and then asked to move his feet and toes. Often the patient wake-up is not a calm event, and the patient wakes up suddenly and moves his or her head and limbs simultaneously. If the patient is able to squeeze his or her hands but unable to move his or her feet, the amount of spine distraction must be reduced until a safe degree of correction is achieved, and in some cases, the hardware is removed. When the patient moves his or her feet, anesthesia is quickly deepened with small doses of propofol (0.5 mg per kg). Additional short-acting benzodiazepines may be given. Recall of intraoperative events is very unusual with this technique.

The anesthesiologist should have one or two assistants available in the event the patient moves excessively during the wake-up test. Although this occurs rarely when an adequate amount of opioid has been administered, it is best to be prepared. The authors do not recommend use of opioid antagonists because of the potential for the patient to experience pain and become agitated in the prone position. If naloxone is deemed necessary to arouse the patient, a small dose (0.3 to 0.5 μg per kg) should be administered and repeated every 2 to 3 minutes until the respiratory depression of the opioid is reversed. It is not typically necessary to reverse neuromuscular blockade if at least three twitches are present on train-of-four stimulation.

Complications of this technique include extubation in the prone position, recall of intraoperative events, myocardial ischemia, self-injury, and dislodgment of instrumentation or intravenous access. Air embolus from open venous sinuses may occur if the patient is breathing spontaneously and inhales vigorously. It is also important to realize that the wake-up test may be performed too late, after a neurologic insult has already occurred and caused irreversible damage.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

Kocher MS, Millis MB, eds. *Operative Techniques: Pediatric Orthopaedic Surgery*. Philadelphia, PA: Elsevier Saunders; 2011:719-730.

C.11. Four hours into the surgical procedure, the surgeon reports some bubbling in the thoracic portion of the wound. Shortly thereafter, end-tidal carbon dioxide decreases abruptly from 35 to 18 mm Hg, heart rate increases from 80 to 120 beats per minute, blood pressure begins to fall, and arterial saturation decreases to 90%. On auscultation through esophageal stethoscope, you hear a loud gurgling murmur. What is your diagnosis?

This constellation of symptoms strongly suggests venous air embolism. There are at least two reports indicating that air bubbling in the wound may be the first clinical sign of an air embolus before cardiovascular collapse. This is thought to occur as a result of retrograde flow of blood containing entrained air through the valveless venous system as a result of an

increase in central venous pressure. Central venous pressure rises as a result of an air lock in the right heart. Positive pressure ventilation and pressure on the spine during placement of hardware may also produce bubbling of entrained air.

McCarthy RE, Lonstein JE, Mertz JD, et al. Air embolism in spinal surgery. *J Spinal Disord*. 1990;3:1-5.

Wills J, Schwend RM, Paterson A, et al. Intraoperative visible bubbling of air may be the first sign of venous air embolism during posterior surgery for scoliosis. *Spine (Phila Pa 1976)*. 2005;30:E629-E635.

C.12. How common is significant air embolism during scoliosis surgery?

Fortunately, clinically significant air embolism is uncommon. Nevertheless, cases of fatal air embolism have been reported during scoliosis surgery in children. Most, but not all, cases involve extensive surgical dissection with excessive bleeding. The mortality rate in the reported cases may be 50%.

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Wills J, Schwend RM, Paterson A, et al. Intraoperative visible bubbling of air may be the first sign of venous air embolism during posterior surgery for scoliosis. *Spine (Phila Pa 1976)*. 2005;30:E629-E635.

C.13. What should be done if an air embolus is suspected?

If an air embolus is suspected, the surgical field should be immediately flooded with saline, ventilation begun with 100% oxygen, and intravascular fluid administered to increase central venous pressure. Air is most likely entrained from open epidural and paravertebral veins and venous sinuses in decorticated bone. Flooding the field with saline prevents air entrainment. Ventilation with 100% oxygen reduces the volume of the air embolus, particularly if nitrous oxide was administered. Hypovolemia and low central venous pressure favor air entrainment by increasing the pressure gradient between open veins and the right atrium.

If the patient requires cardiopulmonary resuscitation, placing the patient in the left lateral decubitus position during external cardiac massage may improve blood flow by breaking the air lock of the pulmonary outflow tract. Removing air through either a central catheter or by direct intracardiac aspiration has also been advocated.

McCarthy RE, Lonstein JE, Mertz JD, et al. Air embolism in spinal surgery. *J Spinal Disord*. 1990;3:1-5.

Sutherland RW, Winter RJ. Two cases of fatal air embolism in children undergoing scoliosis surgery. *Acta Anaesthesiol Scand*. 1997;41:1073-1076.

C.14. What complications occur related to positioning the patient?

If the head is not positioned carefully, pressure on the eyes may cause thrombosis of the central retinal artery producing loss of vision or blindness. The horseshoe-type headrest (Fig. 58.6) has been implicated in a number of reports of unilateral eye blindness and should not be used for long procedures. The head should be positioned without excessive flexion or extension and in such a way that the face and eyes can be inspected easily. The position of the head and neck will move during surgical manipulation of the spine and should be inspected frequently during the procedure. It is extremely helpful to have a mirror under the patient's face that can be viewed throughout the case (Fig. 58.7). Patients with Marfan syndrome and neurofibromatosis may have abnormalities of the cervical spine and must be turned and positioned with great caution.

The upper extremities should be positioned at no more than 90 degrees of abduction to the trunk, as illustrated in Figure 58.8A. Figure 58.8B demonstrates improper arm positioning because the arms are abducted above the head. This stretches the brachial plexus and may result in a brachial plexus palsy. Both axillae should be inspected to ensure that the frame does not compress the axillary sheath. Proper positioning is shown in Figure 58.9A. Note that there is ample space between the thoracic bolster of the frame and the axilla. Figure 58.9B demonstrates improper positioning on the frame resulting in pressure on the axilla. Care should be taken to pad the ulnar nerves at the elbow. Often, the surgeons will compress or unintentionally move the upper extremities, so the arms and shoulders must be continuously monitored. Impairment of ventilation and increased bleeding from increased venous pressure may occur if the abdomen is compressed by the operating frame.

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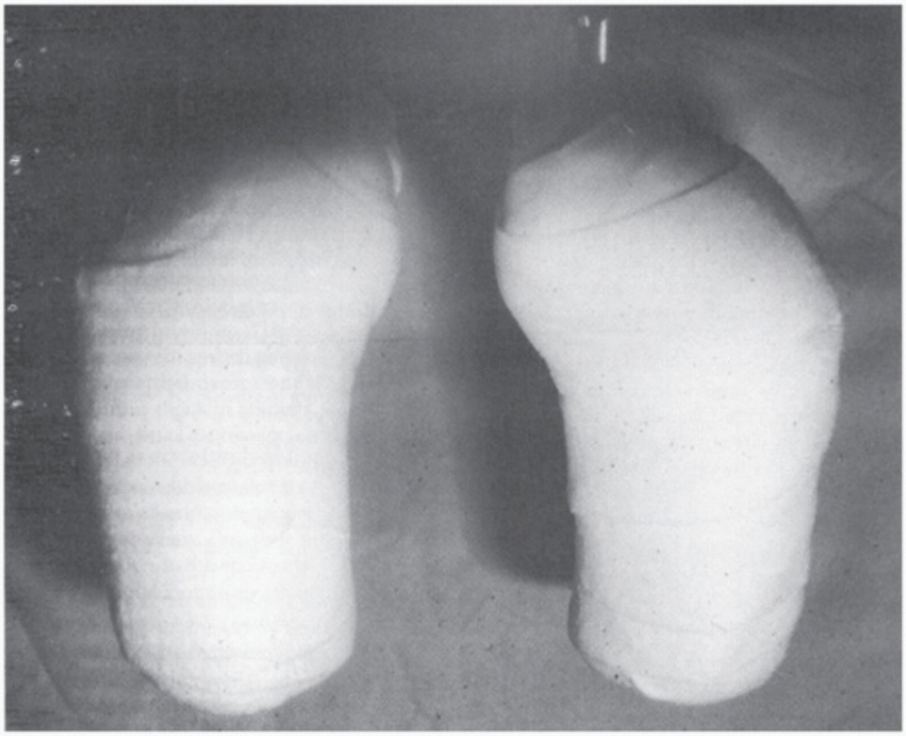


FIGURE 58.6 This horseshoe-type headrest has been associated with unilateral eye blindness resulting from pressure on the eye during surgery. The forehead rests on the upper portion, with the chin free in the wider, open portion.



FIGURE 58.7 Foam face rest with mirror.

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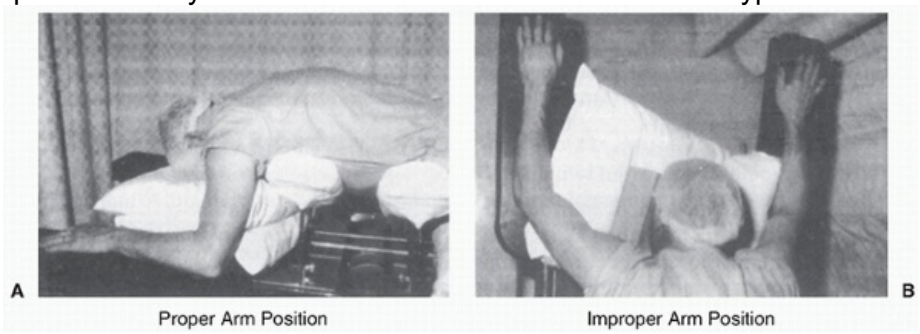


FIGURE 58.8 Proper arm position and improper arm position during scoliosis surgery. **A.** Degrees of abduction (relative to the trunk). **B.** Improper arm positioning with the arms abducted above the head. This results in stretching of the brachial plexus.

Life-threatening cardiovascular events have occurred due to right ventricular outflow tract obstruction, and resultant decreased venous return due to positioning of bolsters.

Neira VM, Gardin L, Ryan G, et al. A transesophageal echocardiography examination clarifies the cause of cardiovascular collapse during scoliosis surgery in a child. *Can J Anaesth*. 2011;58:451-455.

C.15. What is transfusion-related acute lung injury (TRALI)? How do you distinguish it from transfusion-associated circulatory overload (TACO)?

TRALI is noncardiogenic pulmonary edema occurring within 1 to 6 hours of transfusion of a plasma-containing blood product. In intubated patients, it presents as copious, pink, and frothy pulmonary edema fluid in the endotracheal tube. Although clinically indistinguishable from adult acute respiratory distress syndrome, TRALI is associated with a much lower mortality rate (5% to 10%). Typically, the chest radiograph and arterial oxygen saturation return to baseline within 72 hours. The exact mechanism of TRALI is unknown, but evidence points to pathologic leukocyte antibodies in donor plasma causing agglutination of white blood cells on pulmonary endothelial cells, resulting in increased permeability. Platelet transfusions have been most commonly implicated. Therapy is supportive, similar to that for acute respiratory distress syndrome.

TACO, on the other hand, is a result of increased hydrostatic pressure in the capillaries causing pulmonary edema. The clinical features and radiologic findings are similar, and

the two are hard to differentiate from each other. A thorough understanding of patient's fluid status, cardiac status, amounts and types of blood products transfused along with measurement of brain natriuretic peptide (B natriuretic peptide), and testing for leukocyte antibodies is helpful in identifying the cause.

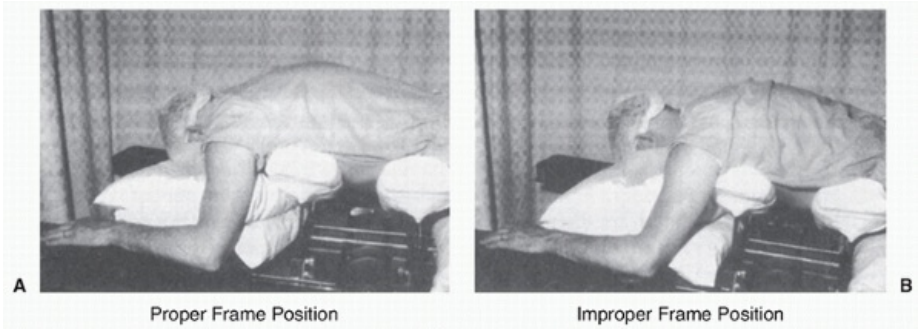


FIGURE 58.9 Proper and improper positioning on the four poster frame during spine surgery. **A.** Proper positioning on the frame with ample space between the axilla and the thoracic bolster of the frame. **B.** Improper positioning on the frame resulting in compression of the axillary sheath by the thoracic bolster of the frame.

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Álvarez P, Carrasco R, Romero-Dapueto C, et al. Transfusion-related acute lung injured (TRALI): current concepts. *Open Respir Med J*. 2015;9:92-96.

Gajic O, Gropper MA, Hubmayr RD. Pulmonary edema after transfusion: how to differentiate transfusionassociated circulatory overload from transfusion-related lung injury. *Crit Care Med*. 2006;34(5 suppl): S109-S113.

Skeate RC, Eastlund T. Distinguishing between transfusion related acute lung injury and transfusion associated circulatory overload. *Curr Opin Hematol*. 2007;14(6):682-687.

C.16. What techniques can be used to minimize transfusion requirements?

Several techniques can be used to minimize homologous blood transfusion requirements and subsequent risks, such as alloimmunization, infections, immunosuppression, and graft-versus-host disease in addition to TRALI and TACO. A simple and important way to minimize bleeding is to minimize intra-abdominal pressure, because any increase in abdominal pressure is transmitted to the vertebral venous plexus, increasing venous bleeding. Careful positioning will avoid external pressure on the abdomen, and muscle relaxants or deeper levels of anesthesia have been used to prevent a rise in abdominal wall tension.

Isovolemic hemodilution may also be used to minimize red blood cell loss during surgery. Before incision, the hematocrit is lowered 20% to 25% by removing blood aseptically and storing it in anticoagulated bags. Intravascular volume is maintained by replacing the blood with three times the volume of a balanced saline solution or an equal volume of colloid. Intraoperatively, the previously collected blood is replaced as needed. Obviously, this technique requires careful monitoring of intravascular volume status and hemoglobin level. Most patients will require a central venous catheter to perform this technique. Some patients who are Jehovah's Witnesses and will not accept blood transfusions may accept this type of blood conservation method if the tubing is kept connected because the blood in the bag and the tubing is in continuity with the circulation.

Salvaging of blood during the surgical procedure can play an important role as an adjunct to an autologous blood program. Using standard salvaging techniques, 50% to 60% of the red blood cells lost can be recovered, concentrated, washed, and returned to the patient using commercially available autotransfusion devices. These red blood cells are obviously lacking in platelets and plasma. Some Jehovah's Witness patients may also accept this technique if the autotransfusion device is kept in continuity with the circulation.

The use of an antifibrinolytic drug such as aminocaproic acid or tranexamic acid has been shown to decrease blood loss in pediatric patients undergoing scoliosis surgery. These drugs may be of particular benefit in patients with neuromuscular scoliosis such as Duchenne muscular dystrophy. These patients have significantly greater intraoperative blood loss compared to patients with idiopathic scoliosis, as much as a twofold to eightfold increased risk. The antifibrinolytic agent is administered as a loading dose followed by a continuous infusion before the activation of the fibrinolytic system, which occurs with surgical incision. It is important to administer the full loading dose before surgical incision for maximum benefit.

Deliberate (controlled) hypotension has been frequently used until recently to decrease blood loss and improve operating conditions during spine fusion surgery. Decrease in blood loss and transfusion requirement has been less significant in spine surgery when compared with oral-maxillofacial surgery employing controlled hypotension techniques. Safety of moderate controlled hypotension (mean arterial pressure [MAP] 50 to 65 mm Hg) with close monitoring of invasive arterial and central venous pressures in conjunction with SSEPs and MEPs has been documented.

However, the major concern of using deliberate hypotension during scoliosis surgery is the potential for spinal cord blood flow to be compromised with resultant spinal cord injury. This is of particular concern when the spine is distracted because levels of hypotension that are considered safe under normal conditions may compromise spinal cord blood

flow after spine distraction. In addition, the use of deliberate hypotension can interfere with neuromonitoring signals, particularly the MEPs. For these reasons of risk versus benefit, the use of controlled hypotension is questioned.

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Florentino-Pineda I, Thompson GH, Poe-Kochert C, et al. The effect of Amicar on perioperative blood loss in idiopathic scoliosis: the results of a prospective, randomized double-blind study. *Spine (Phila Pa 1976)*. 2004;29:233-238.

Kako H, Gable A, Martin D, et al. A prospective, open-label trial of clevidipine for controlled hypotension during posterior spinal fusion. *J Pediatr Pharmacol Ther*. 2015;20(1):54-60.

Paul JE, Ling E, Lalonde C, et al. Deliberate hypotension in orthopedic surgery reduces blood loss and transfusion requirements: a meta-analysis of randomized controlled trials. *Can J Anaesth*. 2007;54:799-810.

Schouten ES, van de Pol AC, Schouten AN, et al. The effect of aprotinin, tranexamic acid, and aminocaproic acid on blood loss and use of blood products in major pediatric surgery: a meta-analysis. *Pediatr Crit Care Med*. 2009;10:182-190.

Sethna NF, Zurakowski D, Brustowicz RM, et al. Tranexamic acid reduces intraoperative blood loss in pediatric patients undergoing scoliosis surgery. *Anesthesiology*. 2005;102:727-732.

Tobias JD, Hoernschemeyer DG. Clevidipine for controlled hypotension during spinal surgery in adolescents. *J Neurosurg Anesthesiol*. 2011;23(4):347-351.

D. Postoperative Management

D.1. When would you extubate the patient?

The decision to continue mechanical ventilation in the postoperative period is often made preoperatively. Most patients with adolescent idiopathic scoliosis have mild to moderate pulmonary function abnormalities and may be extubated in the operating room after they have moved all extremities to the surgeon's satisfaction. Mechanical ventilation should be continued in patients with severe restrictive lung defects (vital capacity less than 30% of predicted) or severe gas exchange abnormalities such as carbon dioxide retention. Postoperative mechanical ventilation should be considered for patients with Duchenne muscular dystrophy, familial dysautonomia, or severe cerebral palsy. Patients who are mechanically ventilated postoperatively should be managed by nurses and physicians in an intensive care setting. Patients should be sedated to tolerate the endotracheal tube, yet arousable enough to be examined every hour for potential neurologic complications. Dexmedetomidine is a good choice for short-term sedation in this population. It offers potent synergy with opioids for analgesia, and it is easily titrated for frequent wake-ups.

The parameters for extubation given below are the same as for other respiratory disorders:

- Vital capacity greater than 10 mL per kg
- Tidal volume greater than 3 to 6 mL per kg
- Spontaneous respiratory rate less than 30 per minute
- Negative inspiratory force greater than 30 cm H_2O

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

Yuen VM. Dexmedetomidine: perioperative applications in children. *Paediatr Anaesth*. 2010;20:256-264.

D.2. What should be done to optimize pulmonary status?

Incentive spirometry should be taught preoperatively and should be used aggressively in the postoperative period. Coughing and deep breathing should be encouraged. Patients with obstructive or reactive airway disease will benefit from bronchodilators. Opioids should be used on a patient-controlled basis with the goal of providing adequate analgesia to allow coughing and incentive spirometry without excessive respiratory depression.

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Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . Philadelphia, PA: Elsevier Saunders; 2013:627-652.

D.3. What laboratory tests should be ordered postoperatively?

Upon the patient's arrival in the postanesthesia care unit, blood should be sent for analysis of arterial blood gases, hematocrit, serum electrolytes, blood urea nitrogen, serum

creatinine, and, if blood loss has been significant, platelet count, prothrombin, and partial thromboplastin time. Determination of arterial blood gases should be repeated if clinically indicated. Hyponatremia with high urinary sodium excretion has been reported following scoliosis surgery and has been attributed to the syndrome of inappropriate antidiuretic hormone secretion (SIADH). These patients produce small amounts of concentrated urine and excrete large amounts of urinary sodium. Efforts to increase urine output by administration of fluid are unsuccessful and worsen the hyponatremia. Therefore, serum electrolyte concentrations should be measured at least every 12 hours for the first 24 hours and then daily for the first 2 days. Rapid decreases in serum sodium concentration or sodium concentrations less than 125 mEq per L may produce swelling of brain cells (intracellular “edema”) and seizures.

Lieh-Lai MW, Stanitski DF, Sarnaik AP, et al. Syndrome of inappropriate antidiuretic hormone secretion in children following spinal fusion. *Crit Care Med*. 1999;27(3):622-627.

Taal MW, Chertow GM, Marsden PA, et al, eds. *Brenner and Rector's the Kidney*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2012:326-352.

D.4. What fluid therapy would you use postoperatively?

Significant losses of intravascular fluid continue to occur in the postoperative period. These should be replaced with balanced salt solution such as lactated Ringer's solution to maintain urine output at a minimum of 0.5 to 1 mL/kg/hr. Hypotonic fluids should be avoided in the first 24 to 36 hours postoperatively. The risk for postoperative hyponatremia is increased if fluid replacement is excessive or if hypotonic fluid is administered. Some authors recommend the use of colloid replacement solutions because serum albumin is often decreased following scoliosis surgery.

Lieh-Lai MW, Stanitski DF, Sarnaik AP, et al. Syndrome of inappropriate antidiuretic hormone secretion in children following spinal fusion. *Crit Care Med*. 1999;27(3):622-627.

Taal MW, Chertow GM, Marsden PA, et al, eds. *Brenner and Rector's the Kidney*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2012:540-594.

D.5. What complications may occur following scoliosis surgery?

Complications that have been reported in the postoperative period include pneumothorax, atelectasis, pleural effusion, hemothorax, thoracic duct injury, and neurologic injury. Pneumothorax may occur as a result of anterior and posterior surgical dissections as well as secondary to central venous line placement. A chest radiograph should be obtained upon arrival in the postanesthesia care unit. Atelectasis may occur because of prolonged supine positioning and the use of opioids. Anterior spine fusion by thoracotomy poses the greatest risk of pulmonary complications. Almost 100% of patients undergoing these procedures will develop some degree of atelectasis. Incentive spirometry and deep breathing should be emphasized and may require specialized nursing care.

In addition to intraoperative neurologic complications during instrumentation or distraction of the spine, delayed paraplegia in the first few days postoperatively has been reported. This emphasizes the need for continued monitoring of neurologic status postoperatively.

In the first few postoperative days, adynamic ileus occurs commonly, and some authors recommend placement of nasogastric tubes in all patients. Less commonly, superior mesenteric artery syndrome has been reported to occur in 0.5% of patients. This presents with nausea, vomiting, and abdominal pain after a mean time of 7.2 days. This is probably due to compression of the distal third of the duodenum by the superior mesenteric artery as a result of anatomic changes

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related to straightening of the spine.

Altiok H, Lubicky JP, DeWald CJ, et al. The superior mesenteric artery syndrome in patients with spinal deformity. *Spine (Phila Pa 1976)*. 2005;30:2164-2170.

Kocher MS, Millis MB, eds. *Operative Techniques: Pediatric Orthopaedic Surgery*. Philadelphia, PA: Elsevier Saunders; 2011:719-730.

Stöckl B, Wimmer C, Innerhofer P, et al. Delayed anterior spinal artery syndrome following posterior scoliosis correction. *Eur Spine J*. 2005;14:906-909.

D.6. How would you manage this patient's pain, nausea, and vomiting postoperatively?

Most patients having scoliosis surgery are developmentally mature enough to use intravenous patient-controlled analgesia (PCA). Hydromorphone and morphine are commonly used opioids, and the PCA is usually used until postoperative day 2. Oral analgesics (e.g., oxycodone or hydrocodone with acetaminophen) should be administered once the patient is awake enough to swallow pills or elixir. Antiemetics should be given prophylactically, starting in the operating room. Serotonin receptor antagonists are the first-line treatment, but small doses of dexamethasone may also be used. Histamine 2-receptor blockers can also be helpful the first few days. A transdermal scopolamine patch may be placed preoperatively for patients with risk factors (female of childbearing age, history of motion sickness or postoperative nausea, nonsmokers).

Recently, ketorolac has become more accepted as a postoperative pain adjunct, even for spine surgery. A meta-analysis in 2011 showed no increased risk of nonunion in spine patients receiving nonsteroidal anti-inflammatory drugs (NSAIDs) postoperatively. Patients at several children's centers receive it for 48 to 72 hours after spine surgery. More children's centers are also encouraging chewing gum postoperatively to speed the return of normal bowel function after spine surgery.

Dodwell ER, Latorre JG, Parisini E, et al. Do non-steroidal anti-inflammatory drugs inhibit bone healing? A meta-analysis of cohort and case control studies. *J Bone Joint Surg Br.* 2011;93(suppl 4):585-586.

Gan TJ. Risk factors for postoperative nausea and vomiting. *Anesth Analg.* 2006;102:1884-1898.

Jennings J, Doyle J, Gilbert S, et al. The use of chewing gum postoperatively in pediatric scoliosis patients facilitates an earlier return to normal bowel function. *Spine Deformity.* 2015;3(3):263-266.

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Chapter 59
Hypoxia and Equipment Failure

James B. Eisenkraft

Andrew B. Leibowitz

A 70-year-old man is to undergo cystoscopy and transurethral resection of a bladder tumor under general anesthesia through a laryngeal mask airway (LMA). He gives a history of mild asthma and uses an albuterol inhaler when necessary. Breathing room air (FIO_2 = 0.21), his pulse oximeter saturation reading (SpO_2) is 94%.

A. Medical Disease and Differential Diagnosis

1. What is hypoxia and what is hypoxemia?
2. Is the partial pressure of oxygen in arterial blood (PaO_2) related to age?
3. Was this patient hypoxemic?
4. What is a pulse oximeter, and what is a hemoximeter?
5. How does a pulse oximeter work?
6. How is a two-wavelength pulse oximeter calibrated by the manufacturer?
7. What may affect the accuracy of a two-wavelength pulse oximeter?
8. How do the dyshemoglobins, methemoglobin (metHb) and carboxyhemoglobin (HbCO) affect SpO_2 readings?
9. What is a capnometer, and what is capnography? Of what value are they in patient monitoring?
10. What is meant by the term *end-tidal carbon dioxide* (*$PETCO_2$*)?
11. What is the appearance of a normal capnogram and what is its significance?
12. What are mainstream and sidestream capnometers?
13. Show some common capnograms and provide a differential diagnosis of each event.
14. What is the arterial-alveolar difference in carbon dioxide (CO_2)?
15. What are some of the important safety features of the contemporary anesthesia workstation?
16. What are common sites for gas leakage?
17. How is the anesthesia machine checked for leaks?

B. Preoperative Evaluation and Preparation

1. What should be included in the equipment checkout in preparation for anesthesia?
2. What emergency equipment should be easily available to the anesthesiologist?
3. How should this patient be premedicated?

C. Intraoperative Management

1. How should this patient be monitored?
2. After uneventful inhalation mask induction, cystoscopy was begun, and the SpO_2 was noted to decrease to 81% with the patient breathing an FIO_2 of 0.4 (oxygen at 2 L per minute and nitrous oxide at 3 L per minute). The patient developed

respiratory distress. The laryngeal mask airway (LMA) was easily maintained, and no gross secretions were noted.

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What acute diagnostic and therapeutic interventions would you perform?

3. The patient was tracheally intubated. Squeezing the reservoir bag in the circle system failed to inflate the lungs, and a leak was noted. What are the common sites for gas leaks?

D. Postoperative Management

1. What criteria would you use for tracheal extubation?
2. What are the causes of postoperative hypoxemia?
3. What is the difference between shunt, ventilation/perfusion mismatch, and dead space?
4. What is the differential diagnosis of pulmonary edema?
5. How should the ventilator be set if mechanical ventilation is required postoperatively?
6. If this patient had acute lung injury (ALI) secondary to aspiration, beside low-tidal volume ventilation, what other changes in routine therapy should be considered?
7. What therapies routinely administered by the anesthesiologist may cause ALI?
8. What methods of oxygen administration may be used postoperatively?

A. Medical Disease and Differential Diagnosis

A.1. What is hypoxia and what is hypoxemia?

Hypoxia is defined as reduction of oxygen supply to tissue below physiologic levels. Hypoxemia is defined as deficient oxygenation of the blood. From the anesthesiologist's perspective, hypoxia is usually considered to be decreased oxygen tension (PO_2) inside the body at the tissue level or outside the body (e.g., hypoxic gas mixture), and hypoxemia is decreased oxygen tension in the arterial blood (PaO_2).

Dorland WAN. *Dorland's Illustrated Medical Dictionary*. 31st ed. Philadelphia, PA: WB Saunders; 2007.

A.2. Is the partial pressure of oxygen in arterial blood (PaO_2) related to age?

Yes. There is an age-dependent decrease in the PaO_2. In 1972, Marshall and Wyche suggested the following relationship in subjects breathing room air:

mean PaO_2 in mm Hg = 102 - 0.33 (age in years) mm Hg

About this regression line, there are 95% confidence limits (two standard deviations [SDs]) of 10 mm Hg.

Cerveri et al. studied PaO_2 in normal nonsmoking subjects ages 40 to 90 years. They found that PaO_2 was related to age in subjects between 40 and 74 years and constructed the following reference equation:

PaO_2 (mm Hg) = 143.6 - (0.39 × age) - (0.56 × BMI) - (0.57 × $PaCO_2$)

For subjects ≥75 years old, there was no correlation with age.

Cerveri I, Zoia MC, Fanfulla F, et al. Reference values of arterial oxygen tension in the middle-aged and elderly. *Am J Respir Crit Care Med*. 1995;152:934-941.

Marshall BE, Wyche MQ Jr. Hypoxemia during and after anesthesia. *Anesthesiology.* 1972;37:178-209.

Shapiro BA, Peruzzi WT, Kozelowski-Templin R. *Clinical Applications of Blood Gases* . 5th ed. St. Louis, MO: Mosby-Year Book; 1994:221.

Sorbini CA, Grassi V, Solinas E, et al. Arterial oxygen tension in relation to age in healthy subjects. *Respiration*. 1968;25:3-13.

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A.3. Was this patient hypoxemic?

No. An SpO_2 reading of 94% does not signify hypoxemia. This patient is five decades older than a 20-year-old subject; therefore, his mean PaO_2 should be 5 × 5 mm Hg per decade, which is 25 mm Hg, less than that (95 mm Hg) expected in a 20-year-old (see section A.2, Sorbini et al.).

95 - 25 = 70 mm Hg

or, using the Marshall and Whyche equation (see section A.2),

102 - 0.33 (70) = 79 mm Hg

Assuming normal adult hemoglobin, temperature, and pH, this PaO_2 corresponds to a hemoglobin oxygen saturation of approximately 94% on the normal hemoglobin oxygen saturation versus PO_2 curve.

Although the definitions of hypoxemia given in sections A.1 and A.2 must take age into consideration, from a practical point of view, hypoxemia (in the absence of anemia) is generally considered to exist when the PaO_2 is less than 60 mm Hg, which is equivalent to a hemoglobin oxygen saturation of 90%.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Elsevier Science; 2010:179-215.

A.4. What is a pulse oximeter, and what is a hemoximeter?

The pulse oximeter is a noninvasive device that provides a real-time estimate (designated the SpO_2%) of the arterial hemoglobin saturation with oxygen. It is a transmissive oximeter in which the patient's fingertip (or other probe site; e.g., earlobe) serves as an in vivo cuvette through which light at two different wavelengths is transmitted.

If one requires an accurate determination of the arterial hemoglobin saturation with oxygen, an arterial blood sample must be drawn and analyzed in a laboratory co-oximeter, sometimes called a *hemoximeter*. The laboratory co-oximeter is a transmissive oximeter that uses six or more wavelengths of light to measure total hemoglobin (HbTOT), oxygenated hemoglobin (HbO_2), deoxygenated ("reduced") hemoglobin (RHb), metHb, HbCO, and other dyshemoglobins, such as sulfhemoglobin. Because each species of hemoglobin has a characteristic absorbance spectrum (i.e., absorbance vs. wavelength), examination of a sample of blood using these six or eight wavelengths permits identification and quantification of each hemoglobin species. Conventional pulse oximeters use only two wavelengths of light; therefore, they are unable to determine all of the different hemoglobin species and assume that only HbO_2 and RHb are present. *Fractional saturation* (*HbO_2%*) is defined as HbO_2 / (HbO_2 + RHb + HbCO + metHb)—that is, HbO_2 per total Hb. Functional saturation (SaO_2) is defined as HbO_2 / (HbO_2 + RHb). Note that dyshemoglobins are absent from the denominator in the definition of SaO_2.

Kurki TS, Eisenkraft JB. Pulse oximetry. In: Reich DL, Kahn R, Mittnacht A, et al, eds. *Monitoring in Anesthesia and Perioperative Care*. New York: Cambridge University Press; 2011:185-198.

A.5. How does a pulse oximeter work?

The pulse oximeter combines the technologies of spectrophotometry and optical plethysmography. In the pulse oximeter probe, light-emitting diodes transmit red light at wavelength 660 nm and infrared light at wavelength 940 nm through the fingertip or other probe site. Light that passes through the probe site is sensed by a single photodetector and expressed as absorbance at each wavelength. It can be shown that the ratio of absorbances, 660/940 nm, is related to the hemoglobin saturation with oxygen. This is spectrophotometry. Detection of pulsatile flow is by optical plethysmography. With each pulse of arterial blood, the probe site (e.g., fingertip) increases in volume, the path length of the transmitted light increases,

and the absorbance of light at 660 nm and 940 nm increases. This *pulse-added* absorbance is considered to be due to the pulsatile flow of arterial blood at the probe site, so that the ratio of pulse-added absorbances, 660/940 nm, can be used to provide an estimate of hemoglobin oxygen saturation in arterial blood.

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Barker SJ. Pulse oximetry. In: Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:256-270.

Kurki TS, Eisenkraft JB. Pulse oximetry. In: Reich DL, Kahn R, Mittnacht A, et al, eds. *Monitoring in Anesthesia and Perioperative Care*. New York: Cambridge University Press; 2011:185-198.

A.6. How is a two-wavelength pulse oximeter calibrated by the manufacturer?

Each pulse oximeter manufacturer creates an empiric calibration algorithm, that is, one based on observations in human volunteers. The algorithm relates the average ratio of pulseadded absorbances, 660/990 nm, to the actual hemoglobin oxygen saturation in arterial blood samples drawn simultaneously and analyzed in a laboratory hemoximeter. Observations are made with the volunteers breathing varying FIO_2 values so that data for saturations as low as 70% are obtained. The calibration algorithm that is created relates the ratio (R) of pulseadded absorbances, 660/940 nm, to the laboratory hemoximeter readings of HbO_2 or SaO_2%, depending on the pulse oximeter manufacturer. The calibration algorithm is then stored in the software of the pulse oximeter as a "lookup" table. Therefore, the pulse oximeter merely measures R, consults its lookup table, and displays the corresponding saturation reading as SpO_2. The pulse oximeter does not actually measure saturation; it infers it from R, and, therefore, it predicts what the laboratory hemoximeter would read if an arterial sample drawn at that moment were analyzed.

A high value for R corresponds to a low SpO_2 reading; R = 1 corresponds to an SpO_2 reading of 85%, and a low value for R corresponds to a high SpO_2 reading. Whenever the SpO_2 reading is approximately 85%, one should consider the possibility of a spurious reading as a result of the "R = 1" phenomenon. This is commonly due to malpositioning of the probe on the fingertip.

The pulse oximeter (SpO_2) reading is usually specified by the manufacturer to have an SD of ±2%. Therefore, assuming a normal distribution, if the SpO_2 reading is 96%, there is a 68% likelihood that the true saturation (as measured by a hemoximeter) is 96 ± 2% (i.e., ±1 SD) and a 95% likelihood that the true saturation is 96 ± 4% (i.e., ±2 SD).

Guan Z, Baker K, Sandberg WS. Misalignment of disposable pulse oximeter probes results in false saturation readings that influence anesthetic management. *Anesth Analg*. 2009;109:1530-1533.

Kelleher JF, Ruff RH. The penumbra effect: vasomotion-dependent pulse oximeter artifact due to probe malposition. *Anesthesiology*. 1989;71:787-791.

A.7. What may affect the accuracy of a two-wavelength pulse oximeter?

The two-wavelength pulse oximeter is most accurate when the conditions of its clinical use most closely resemble those of its calibration. Spurious readings or failure may occur during patient movement (e.g., shivering, peripheral nerve stimulation, "twitching"), presence of intense ambient light (low signal/noise ratio), electrocautery use, administration of intravenous dyes with absorbance peaks at 660 nm (e.g., methylene blue), presence of dyshemoglobins (e.g., metHb, HbCO, and sulfhemoglobin), certain colors of nail polish, poor pulsatile flow at the probe site (e.g., hypotension, vasoconstriction, Raynaud disease), and venous pulsations (e.g., tricuspid regurgitation or earlobe placement of the probe in a patient who is in a headdown position).

Recent improvements in pulse oximetry technology include paradigms to increase the signal/noise ratio, thereby permitting motion artifact reduction and increased sensitivity to pulsatile flow. Such pulse oximeters have significantly lower failure rates during patient movement (such as in the postanesthesia care unit) and during conditions of low flow (e.g., hypothermia).

Barker SJ. "Motion-resistant" pulse oximetry: a comparison of new and old models. *Anesth Analg*. 2002;95:967-972.

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A.8. How do the dyshemoglobins, methemoglobin (metHb) and carboxyhemoglobin (HbCO) affect SpO_2 readings?

In metHb, iron in the heme moiety is oxidized (such as by dapsone, benzocaine, nitric oxide, prilocaine) to the Fe^{3+} state rather than being in the normal Fe^{2+} state. metHb cannot carry oxygen and creates a physiologic anemia. The absorbance spectrum for metHb shows it to have similar absorbances to light at 660 nm and 940 nm. Therefore, the more metHb that is present, the more R tends toward 1 and the SpO_2 reading toward 85%. In the presence of metHb, the SpO_2 reading overestimates the fractional saturation and underestimates the functional saturation.

In carbon monoxide (CO) poisoning, CO combines with hemoglobin to create a physiologic hypoxemia. HbCO has a similar absorbance to HbO_2 at 660 nm but a very low absorbance at 940 nm. In the presence of HbCO, the SpO_2 overestimates fractional saturation and underestimates functional saturation. Although blood that is poisoned with CO appears “cherry red” to the naked eye, and therefore may look like it is fully saturated with oxygen, it is important to recognize that the ratio of absorbances 660/940 nm will suggest that the blood hemoglobin oxygen saturation is in the 90s. In a subject breathing FIO_2 of 1 (when functional saturation is 100%), as the level of HbCO increases, SpO_2 decreases from close to 100% to approximately 91%.

If the presence of dyshemoglobins is suspected, arterial blood must be drawn and analyzed in a laboratory hemoximeter to obtain accurate readings of saturation.

Pulse oximetry technology has evolved rapidly, and multiwavelength pulse oximeters, called pulse co-oximeters, are clinically available. They use more than seven wavelengths of light (Masimo Rainbow SET Pulse CO-Oximetry, Masimo Company, Irvine, CA), similar to the laboratory hemoximeter. This technology makes it possible to measure CO (SpCO), methemoglobin (SpMet), and total hemoglobin (SpHbt), all noninvasively and in real time.

Barker SJ, Badal JJ. The measurement of dyshemoglobins and total hemoglobin by pulse oximetry. *Curr Opin Anaesthesiol*. 2008;21:805-810.

Barker SJ, Curry J, Redford D, et al. Measurement of carboxyhemoglobin and methemoglobin by pulse oximetry: a human volunteer study. *Anesthesiology*. 2006;105:892-897.

Shamir MY, Avramovich A, Smaka T. The current status of continuous noninvasive measurement of total, carboxy, and methemoglobin concentration. *Anesth Analg*. 2012;114:972-978.

A.9. What is a capnometer, and what is capnography? Of what value are they in patient monitoring?

A capnometer is a device that measures the tension (in units of millimeters of mercury [mm Hg] or kilopascals [kPa]) or concentration (volumes %) of CO_2 in the gas near the patient's airway throughout the respiratory cycle. Capnography is the graphic display of the CO_2 concentration on the y-axis against time on the x-axis.

Capnometry may be achieved using different technologies that can monitor CO_2. Most capnometers now use infrared spectroscopy to measure the PCO_2 (i.e., CO_2 partial pressure in millimeters of mercury). A built-in barometer measures barometric pressure (P_B) so that CO_2 can also be displayed as a percentage ($PCO_2 \times 100/P_B = \%CO_2$).

Capnography is one of the American Society of Anesthesiologists' standards for basic anesthetic monitoring (i.e., “Continual monitoring for the presence of expired CO_2 shall be performed unless invalidated by the nature of the patient, procedure or equipment.”). It is the “gold standard” for establishing the presence of ventilation.

American Society of Anesthesiologists. *Standards for Basic Anesthetic Monitoring*. Schaumburg, IL: American Society of Anesthesiologists; 2010.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:245-254.

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A.10. What is meant by the term end-tidal carbon dioxide ($PETCO_2$)?

$PETCO_2$ is the tension of CO_2 in the exhaled gas at the end of an exhalation. Because this gas originates from the alveoli, it is considered to represent the CO_2 tension in the alveolar gas ($PACO_2$). The $PACO_2$ results from the combination of gases coming from ideal alveoli, where ventilation and perfusion are perfectly matched and the CO_2 concentration is the same as

arterial ($PACO_2$), and alveolar dead space (alveoli that are ventilated but not perfused) where CO_2 concentration is the same as inspired ($PICO_2$) and is normally zero.

The presence of a normal capnogram and $PETCO_2$ depends on (1) production of CO_2 by the tissues, (2) cardiac output and pulmonary blood flow to carry CO_2 to the lungs, and (3) ventilation. Monitoring of $PETCO_2$ can be used to adjust the setting of a mechanical ventilator and monitor ventilation as well as to detect ventilator malfunctions and breathing system problems, such as leaks, incompetent unidirectional valves, exhausted CO_2 absorbent, metabolic problems (e.g., malignant hyperthermia), and gas embolism.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:245-254.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Elsevier Science; 2010:159-177.

A.11. What is the appearance of a normal capnogram and what is its significance?

A typical normal capnogram (PCO_2 vs. time) is shown in Figure 59.1. Four phases have been described.

Phase I. This is the expiratory baseline. During exhalation, CO_2-free gas from the mechanical (apparatus) dead space (e.g., flexible or “goose-neck” connector) and anatomic dead space (large conducting airways) flows past the CO_2 sampling port.

Phase II. This is the expiratory upstroke. It is due to CO_2 from alveoli mixed with anatomic dead space gas passing the gas sampling port and is usually a steep upslope.

Phase III. This is the expiratory or alveolar plateau and is due to alveolar CO_2.

In patients with healthy lungs, it is nearly horizontal, but in patients with obstructive airway disease, there is a more pronounced upward slope. The maximum expired CO_2 is usually considered as the $PETCO_2$.

Phase IV. This is the inspiratory downstroke. During the commencement of inspiration, fresh (i.e., CO_2-free) gas is inhaled past the sensor, and the capnogram falls sharply to baseline.

The angle between the upstroke of phase II and the plateau of phase III is referred to as the *α angle*. The angle between phase III and IV is the *β angle*. An increase in the *α* angle and slope of phase III is seen commonly in acute bronchospasm. The angle usually decreases with treatment of the bronchospasm.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:245-254.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Elsevier Science; 2010:174.

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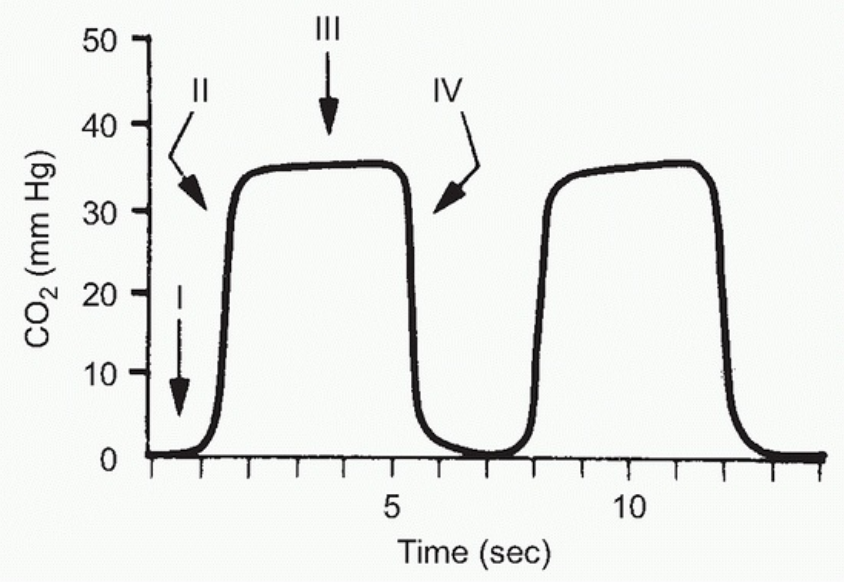


FIGURE 59.1 Phases of the normal capnogram. (*Phase I*) inspiratory baseline. (*Phase II*) expiratory upstroke. (*Phase III*) expiratory plateau. (*Phase IV*) inspiratory downstroke. (From Good ML. Capnography. Uses, interpretation, and pitfalls. In: *ASA Refresher Courses in Anesthesiology* . Park Ridge, IL: American Society of Anesthesiologists; 1990:179, with permission.)

A.12. What are mainstream and sidestream capnometers?

In a mainstream or nondiverting type of analyzer, the gas analyzer sensor is brought to the airway itself, and no gas is removed from the breathing system. A cuvette with a quartz window is placed between the breathing system Y-piece and the tracheal tube connector. As respired gases flow past the window in the cuvette, a beam of infrared radiation (wavelength 4.3 μm) is directed through the window. Absorbance of infrared radiation at 4.3 μm is used to measure PCO_2. Advantages of the nondiverting analyzer are rapid response time, accurate waveform, and no need to scavenge gases. Disadvantages are that this additional device in the airway can be a site for a disconnect and needs sterilization (or replacement of a disposable single-use cuvette) between cases, needs to be heated because water vapor condensing on the window causes error, and can be blocked by secretions or blood on its window. A very lightweight (25 g) mainstream analyzer (IRMA, Masimo, Danderyd, Sweden) capable of measuring CO_2, nitrous oxide, and all five potent inhaled anesthetics is available.

A sidestream or diverting gas analyzer aspirates gas from the breathing circuit through a sampling adapter placed by the airway. The sampled gas passes through a sampling catheter (usually 6 to 10 ft in length) to reach the gas analyzer. Advantages of diverting analyzers are that the breathing circuit adapter is disposable. The analyzer, being remote from the airway, can be more versatile and incorporate several technologies in one “box” to analyze multiple gases (e.g., infrared analysis for CO_2, nitrous oxide, anesthetic agents; paramagnetic sensor or fuel cell for oxygen). Disadvantages of sidestream sampling analysis are slower response times, the possibility of sampling leaks, errors resulting from the length of the gas sampling tube, the need to scavenge gases from the analyzer after analysis, and susceptibility of the sampling tube to becoming clogged by water or secretions. Because of their versatility in regard to gas monitoring, most anesthetizing locations now use sidestream sampling analyzers.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:191-221.

A.13. Show some common capnograms and provide a differential diagnosis of each event.

Elevated baseline equals the amount of CO_2 present in inspired gas (Fig. 59.2A)

- Capnometer not properly calibrated to zero

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- Delivery of CO_2 to breathing system through fresh gas inflow
- Incompetent unidirectional valves
- Failure of CO_2 absorber (channeling, exhaustion, bypass) Prolonged expiratory plateau and expiratory upstroke (Fig. 59.2B)
- Mechanical obstruction to exhalation
- Chronic obstructive pulmonary disease
- Bronchospasm Dips in expiratory plateau (Fig. 59.2C[1])
- Patient making spontaneous inspiratory effort
- “Curare cleft” Cardiogenic oscillations if synchronized with electrocardiogram (Fig. 59.2C[2])
- Ventilator pressure relief valve perturbations

Elevated expiratory plateau (Fig. 59.2D)

- Incorrect calibration
- Increased CO_2 production/delivery versus laparoscopic CO_2 gas insufflation
- Decreased CO_2 removal
- Hypoventilation
- Leak

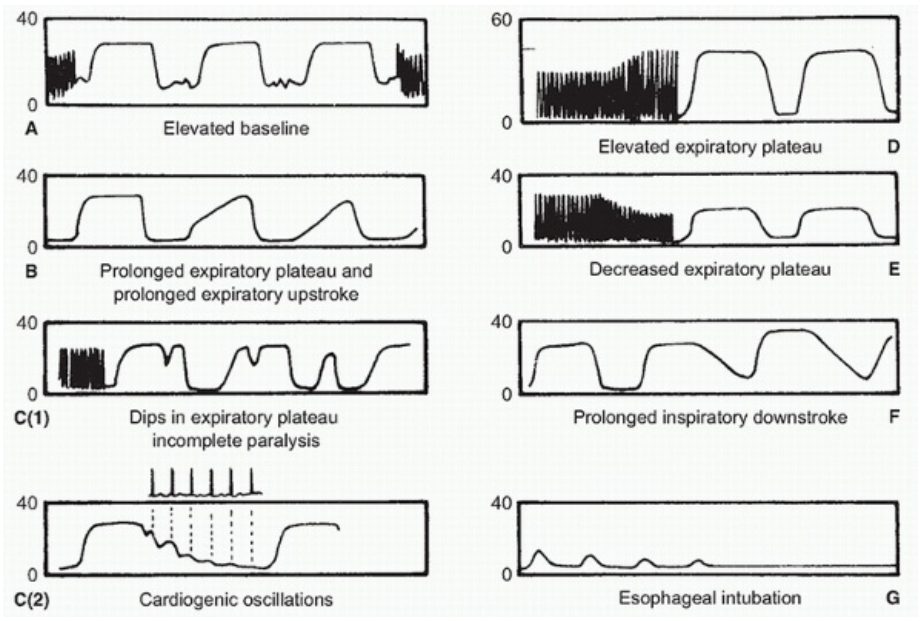


FIGURE 59.2 Abnormal capnograms.

Decreased expiratory plateau (Fig. 59.2E)

- Incorrect calibration
- Air leak into gas sampling system
- Hyperventilation
- Decreased CO_2 production (hypothermia)
- Increased arterial-alveolar CO_2 gradient (ventilation/perfusion mismatch pulmonary embolus)

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Prolonged inspiratory downstroke and raised baseline (Fig. 59.2F)

- Incompetent or missing inspiratory unidirectional valve
- Inspiratory obstruction to gas flow (e.g., kinked tracheal tube) Esophageal intubation (Fig. 59.2G)
- As CO_2 that has been insufflated into the stomach during bag-mask ventilation, or bagmask ventilation produced as a result of ingestion of a carbonated beverage, is washed out during esophageal ventilation, the CO_2 waveform disappears within a few breaths.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:191-221.

A.14. What is the arterial-alveolar difference in carbon dioxide (CO_2)?

The arterial-alveolar difference in CO_2 is usually expressed as the difference between the arterial and $PETCO_2$ tensions. In an ideal alveolus, the $PaCO_2$ equals $PACO_2$ and the "$PaCO_2$-$PACO_2$" difference is zero. Ventilation of unperfused alveoli leads to alveolar dead space or wasted alveolar ventilation. Because the $PETCO_2$ comprises gas from both ideal and dead space alveoli, the $PaCO_2$-$PACO_2$ difference is a measure of alveolar dead space ventilation. For example,

Tidal volume = 500 mL, anatomic dead space = 150 mL

$PaCO_2$ = 40 mm Hg; $PETCO_2$ = 36 mm Hg

Alveolar tidal volume = (500-150) = 350 mL

$$\text{Ratio of } \frac{\text{Alveolar dead space}}{\text{Alveolar tidal volume}} = \frac{\text{Paco}_2 - \text{PETCO}_2}{\text{Paco}_2} = \frac{40 - 36}{40} = 10\%$$

Therefore, 350 mL × 10% = 35 mL wasted ventilation from each alveolar tidal volume.

Ideal alveolar ventilation = (350 - 35) = 315 mL per breath

In this example, physiologic dead space = anatomic + alveolar

= 150 + 35 = 185 mL per breath

$$\frac{\text{Physiologic dead space}}{\text{Tidal volume}} = \frac{185}{500} = 37\%$$

Therefore, $PaCO_2$-$PACO_2$ measures alveolar dead space ventilation as a percentage of total *alveolar* ventilation. The alveolar dead space is increased by ventilation in excess of perfusion or a decrease in perfusion, such as occurs with pulmonary embolism. Shunt has minimal effect on the $PaCO_2$-$PACO_2$ difference.

The $PaCO_2$-$PACO_2$ difference is normally 3 to 5 mm Hg in the patient under general anesthesia, but it is not constant. Therefore, although one commonly uses $PETCO_2$ to noninvasively estimate $PaCO_2$, only analysis of an arterial blood sample in a blood gas analyzer can provide an accurate measure of $PaCO_2$, and this should be measured when critical, such as during neurosurgical anesthesia.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Elsevier Science; 2010:169.

A.15. What are some of the important safety features of the contemporary anesthesia workstation?

Because most problems with anesthesia machines are due to use error, safety design of the contemporary workstation is at four levels.

Features Intended to Prevent Human Error

The medical gas pin index and diameter index safety systems ensure that medical gas connections are made correctly. Therefore, one cannot hang a nitrous oxide cylinder in an oxygen hanger yoke or connect a nitrous oxide hose to the

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oxygen pipeline inlet of the machine.

The “fail-safe” valve is a pressure-sensitive device that interrupts flow of all hypoxic gases on the machine to their flow control valves if the supply pressure of oxygen in the intermediate-pressure system (i.e., components downstream of the first stage oxygen regulator that reduces the high pressure in the tank to 45 pounds per square inch gauge [psig] and upstream of the oxygen flow control needle valve) falls below a threshold (˜20 psig in GE machines; 12 psig in Dräger machines).

When the pressure of oxygen in the intermediate-pressure system falls below 30 psig, an oxygen supply pressure failure alarm is annunciated. The oxygen flow control knob is “touch coded”; that is, it is fluted and larger in diameter than the other gas flow control knobs and is normally located on the right of all other gas flow control valves. In the Dräger Fabius GS workstation, the gas flow controls are arranged vertically, with the oxygen flow control knob as the lowest.

Key-fill systems for anesthesia vaporizers are safety features that also decrease the likelihood of atmospheric contamination during vaporizer filling. The most important of such systems is the Safe-T-Fill system used on desflurane bottles and desflurane vaporizers because filling a vaporizer specific for another agent with desflurane could result in a lethal overdose of desflurane.

A pressure relief valve built into the machine common gas outlet, breathing system, or ventilator provides some protection against positive pressure barotrauma.

Features to Correct for Use Error

Gas flow proportioning systems ensure a minimum oxygen concentration of 25% when nitrous oxide and oxygen are being used. Therefore, if the anesthesiologist were to accidentally attempt to increase the flow of nitrous oxide, either the oxygen flow would be increased automatically or the flow of nitrous oxide would be limited according to the flow of oxygen that was set.

On older machines, during use of the anesthesia ventilator, changes in fresh gas flow, inspiratory-expiratory (I:E) ratio, or respiratory rate cause changes in delivered tidal volume that might result in overventilation, underventilation, or even barotrauma. On modern systems (e.g., GE workstations that incorporate a ventilator with the Smart Vent feature, Dräger

Fabius GS, and Apollo workstations), once the ventilation parameters have been set, they are maintained because the ventilator or circuit automatically compensates for changes in gas flow settings. In the GE workstations with Smart Vent, tidal volume is monitored continually by a computer. If measured tidal volume changes from that set to be delivered, the computer adjusts the volume delivered by the ventilator bellows. Dräger and Datascope Anestar workstations use fresh gas decoupling to maintain a constant tidal volume. In this system, during the inspiratory phase, a decoupling valve closes so that fresh gas entering the breathing system is directed into the reservoir bag and only gas from the ventilator is delivered to the patient. During exhalation, the ventilator chamber refills from the fresh gas flow and the fresh gas that was collected in the reservoir bag during the previous inspiration.

A vaporizer interlock system prevents the unintentional simultaneous use of more than one vaporizer.

Monitoring Systems

A monitor of oxygen in the gas delivered to the patient is mandatorily enabled, and the low oxygen concentration alarm is activated whenever the anesthesia workstation is capable of delivering an anesthetic gas mixture from the common gas outlet.

Other monitors in the anesthesia workstation include pressure, volume, flow, and gas composition. Some also incorporate airway gas flow monitoring. The breathing system lowpressure monitor alarm is automatically enabled when the ventilator is turned on.

Alarm Systems

Contemporary workstations incorporate an integrated prioritized alarm system with visible and audible alerts when set parameter limits are exceeded.

An important safety feature of all modern machines/workstations is the preuse checkout. In 1993, the U.S. Food and Drug Administration (FDA) published anesthesia apparatus checkout recommendations. The machine should be checked by an educated user. Item no. 1 on the FDA checklist is that an alternative means to ventilate the patient's lungs should be present and functioning. Therefore, if a problem arises with the machine, the patient's lungs can be ventilated using a self-inflating resuscitation bag (e.g., Ambu bag). If a machine problem arises and the cause/remedy is not immediately

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obvious, one should instinctively reach for the resuscitation bag and call for help. A recent analysis of the American Society of Anesthesiologists Closed Claims Project data found that 35% of adverse outcomes were likely preventable if a proper preuse checkout had been performed.

Recognizing that not all of the FDA 1993 checkout recommendations can be applied to many of the contemporary workstations, in 2008, the American Society of Anesthesiologists published guidelines applicable to all anesthesia delivery systems so that individual departments can develop their own workstation-specific preuse checkout that can be performed consistently and expeditiously. The 2008 guidelines are intended to provide a template for developing checkout procedures that are appropriate for each individual anesthesia machine design and practice setting. They discuss which systems and components should be checked, the checkout interval (e.g., before first case vs. before every case), and who may be responsible for performing each checkout procedure—the anesthesiologist or technician (Table 59.1). Examples of user-developed workstation-specific checkouts are available on the American Society of Anesthesiologists' website (www.asahq.org).

American Society of Anesthesiologists. *Recommendations for Pre-Anesthesia Checkout Procedures*. Park Ridge, IL: American Society of Anesthesiologists; 2008. http://www.asahq.org/search?q=achine%20checkout%20guidelines. March 13, 2008. Accessed October 12, 2015.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:591-619, 653-680.

Mehta SP, Eisenkraft JB, Posner KL, et al. Patient injuries from anesthesia gas delivery equipment: a closed claims update. *Anesthesiology*. 2013;119:788-795.

U.S. Food and Drug Administration. Anesthesia apparatus checkout recommendations, 1993. http://vam.anest.ufl.edu/FDApreusecheck.pdf. Updated April 20, 2006. Accessed October 12, 2015.

TABLE 59.1 Preanesthesia Equipment Checkout Procedures

TO BE COMPLETED DAILY		RESPONSIBLE PARTY
Item To Be Completed		
Item #1:	Verify auxiliary oxygen cylinder and self-inflating manual ventilation device are available and functioning.	Provider and Tech
Item #2:	Verify patient suction is adequate to clear the airway.	Provider and Tech
Item #3:	Turn on anesthesia delivery system and confirm that AC power is available.	Provider and Tech
Item #4:	Verify availability of required monitors, including alarms.	Provider and Tech
Item #5:	Verify that pressure is adequate on the spare oxygen cylinder mounted on the anesthesia machine.	Provider and Tech
Item	Verify that the piped gas pressures are ≥50 psig.	Provider and Tech

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#6:		
Item #7:	Verify that vaporizers are adequately filled and, if applicable, that the filler ports are tightly closed.	Provider and Tech
Item #8:	Verify that there are no leaks in the gas supply lines between the flowmeters and the common gas outlet.	Provider and Tech
Item #9:	Test scavenging system function.	Provider and Tech
Item #10:	Calibrate, or verify calibration of, the oxygen. Monitor and check the low oxygen alarm.	Provider and Tech
Item #11:	Verify carbon dioxide absorbent is not exhausted.	Provider and Tech
Item #12:	Breathing system pressure and leak testing	Provider and Tech
Item #13:	Verify that gas flows properly through the breathing circuit during both inspiration and exhalation.	Provider and Tech
Item #14:	Document completion of checkout procedures.	Provider and Tech
Item #15:	Confirm ventilator settings and evaluate readiness to deliver anesthesia care. (ANESTHESIA TIME OUT)	Provider

TO BE COMPLETED PRIOR TO EACH PROCEDURE		**RESPONSIBLE PARTY**
Item To Be Completed		
Item #2:	Verify patient suction is adequate to clear the airway.	Provider and Tech
Item #4:	Verify availability of required monitors, including alarms.	Provider or Tech
Item #7:	Verify that vaporizers are adequately filled and, if applicable, that the filler ports are tightly closed.	Provider
Item #11:	Verify carbon dioxide absorbent is not exhausted.	Provider or Tech
Item #12:	Breathing system pressure and leak testing	Provider and Tech
Item #13:	Verify that gas flows properly through the breathing circuit during both inspiration and exhalation.	Provider and Tech

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Item #14:	Document completion of checkout procedures.	Provider and Tech
Item #15:	Confirm ventilator settings and evaluate readiness to deliver anesthesia care. (ANESTHESIA TIME OUT)	Provider

A.16. What are common sites for gas leakage?

Because gas can leak from numerous points in the workstation and breathing system, the anesthesiologist must be able to trace the flow of gases from the supply and storage sources through the system components. Most commonly, leaks occur in the breathing system and low-pressure parts of the machine (i.e., components downstream of the gas flow control valves). For the breathing system, trace the flow of gas from the common gas outlet (if accessible), through the antidisconnect fitting and hose, to the breathing circuit fresh gas inlet. Trace the flow of gas past the inspiratory valve, inspiratory limb, gas sampling connector, elbow adaptor, to the tracheal tube or airway device. Common sites for leaks include a partially deflated tracheal tube cuff or a disconnection of the sidestream sampling gas analyzer sampling line. Check flow back down the expiratory limb, spirometer, expiratory valve, absorber, pressure gauge, pressure sampling lines, and any user-added components such as filters, humidifiers, and positive end-expiratory pressure (PEEP) valves. Check both the bag and the ventilator circuits for leaks.

Leaks in the machine low-pressure system can occur as a result of cracked rotameter flow tubes, incorrectly mounted vaporizers, vaporizer leak around agent filling device, or fracture in the gas piping. Leaks in the high-pressure and intermediate pressure systems usually result from defective valves, connectors, and hanger yokes.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:752-820.

A.17. How is the anesthesia machine checked for leaks?

Leaks in the machine low-pressure system should be tested for according to the manufacturer's specific recommendations for that particular brand and model.

In general, older model Dräger machines are tested using a positive pressure leak check. In principle, the inspiratory and expiratory connections on the absorber are connected by a short length of 22-mm diameter tubing (i.e., the circle breathing system tubing is removed). The reservoir bag (usually 3 L size) is removed, and a test terminal is connected to the bag mount. A short piece of plastic tubing and a sphygmomanometer bulb are connected to the test terminal. With no gases flowing and with the pop-off valve closed, the system is pressurized to 50 cm H_2O by squeezing the sphygmomanometer bulb. Pressure should not decrease by more than 20 cm H_2O in 30 seconds. In this test, the pressure is applied to all of the rigid components of the breathing system and through the fresh gas hose into the machine low-pressure system all the way back to the flow control valves. This test is then repeated with each vaporizer turned on in turn to test for leaks in each vaporizer.

Some anesthesia machines (e.g., GE Excel) have a one-way outlet check valve just upstream of the common gas outlet. Other models have no outlet check valve. The presence of an outlet check valve precludes the application of a positive pressure leak check. If such a valve is present, a negative pressure leak test can be used to check the low-pressure system. In this test, a suction bulb (negative pressure leak-check device) is connected to the common gas outlet. With all gas flows turned off and vaporizers off, the bulb is squeezed empty (to create a negative pressure of -65 mm Hg) and then connected to the common gas outlet of the workstation. Reexpansion of the bulb should not occur in less than 30 seconds. The test is repeated with each vaporizer turned on in turn to check for leaks in the vaporizers.

The FDA 1993 preuse checkout recommendations describe the use of the negative pressure (bulb) leak-check device and state that the bulb should not refill within 10 seconds. The anesthesiologist must understand how to perform a low-pressure system leak check and must have the means (i.e., appropriate leak-check device) to check his or her own particular machine.

The newer electronic anesthesia workstations incorporate an automated checkout to test for leaks. The user of the

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workstation must understand what the automated checkout is designed to check and, more importantly, what it does not check. Even with an automated

preuse checkout, some steps must be performed manually as prompted and directed by the checkout screen.

Eng TS, Durieux MR. Automated machine checkout leaves an internal gas leak undetected: the need for complete checkout procedures. *Anesth Analg*. 2012;114:144-146.

Myers JA, Good ML, Andrews JJ. Comparison of tests for detecting leaks in the low pressure system of anesthesia gas machines. *Anesth Analg*. 1997;84:179-184.

U.S. Food and Drug Administration. Anesthesia apparatus checkout recommendations, 1993. http://vam.anest.ufl.edu/FDApreusecheck.pdf. Updated April 20, 2006. Accessed October 12, 2015.

B. Preoperative Evaluation and Preparation

B.1. What should be included in the equipment checkout in preparation for anesthesia?

In 1993, the FDA published its *14-Step Anesthesia Apparatus Checkout Recommendations*, accessible at http://vam.anest.ufl.edu/fdacheckout.html. It is worthwhile to review in principle the steps in this checkout, recognizing that in contemporary computerized workstations many of the steps have been automated.

The preamble to the FDA 1993 recommendations state that:

This checkout, or a reasonable equivalent, should be conducted before administration of anesthesia. These recommendations are valid only for an anesthesia system that conforms to the then current (1993) and relevant standards and includes an ascending bellows ventilator and at least the following monitors: capnograph, pulse oximeter, oxygen analyzer, respiratory volume monitor (spirometer), and breathing system pressure monitor with high- and lowpressure alarms. This is a guideline that users are encouraged to modify to accommodate differences in equipment design and variations in local clinical practice. Such local modifications should have appropriate peer review. Users should refer to the operator's manual for the manufacturer's specific procedures and precautions, especially the manufacturer's lowpressure leak test (step no. 5).

Emergency ventilation equipment

Step 1. Verify backup ventilation equipment is available and functioning.

High-pressure system

Step 2. Check oxygen cylinder supply.

- Open oxygen cylinder and verify at least half full (approximately 1,000 psi).
- Close cylinder.

Step 3. Check central pipeline supplies.

- Check that hoses are connected and pipeline gauges read approximately 50 psi.

Low-pressure systems

Step 4. Check initial status of low-pressure system.

- Close flow control valves and turn vaporizers off.
- Check fill level and tighten vaporizer filler caps.

Step 5. Perform leak check of machine low-pressure system.

- Verify that the machine master switch and flow control valves are off.
- Attach “suction bulb” to common fresh gas outlet.

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- Squeeze the bulb repeatedly until it is fully collapsed.
- Verify that the bulb stays fully collapsed for at least 10 seconds.
- Open one vaporizer at a time and repeat the tests as discussed earlier.
- Remove suction bulb, and reconnect fresh gas hose.

Step 6. Turn on machine master switch and all other necessary electrical equipment.

Step 7. Test flowmeters.

- Adjust flow of all gases through their full range, checking for smooth operation of floats and undamaged flow tubes.

- Attempt to create a hypoxic oxygen/nitrous oxide mixture and verify correct changes in flow and/or alarm.

Scavenging system

Step 8. Adjust and check scavenging system.

- Ensure proper connections between the scavenging system and both the adjustablepressure limit (APL, or “pop-off”) valve and ventilator relief valve.
- Adjust waste gas vacuum (if possible).
- Fully open APL valve and occlude Y-piece.
- With minimum oxygen flush activated, allow the scavenger reservoir bag to distend fully and then verify that the absorber pressure gauge reads less than 10 cm H_2O.

Breathing system

Step 9. Calibrate oxygen monitor.

- Ensure monitor reads 21% in room air.
- Verify low oxygen alarm is enabled and functioning.
- Reinstall sensor in circuit and flush breathing system with oxygen.
- Verify that monitor now reads more than 90%.

Step 10. Check initial status of breathing system.[1]

- Set selector switch to “bag” mode.
- Check that breathing circuit is complete, undamaged, and unobstructed.
- Verify that CO_2 absorbent is adequate.
- Install breathing circuit accessory equipment (e.g., humidifier, PEEP valve) to be used during the case.

Step 11. Perform leak check of the breathing system.

- Set all gas flows to zero (or minimum).
- Close APL (pop-off) valve and occlude Y-piece.
- Pressurize breathing system to approximately 30 cm H_2O with oxygen flush.
- Ensure that pressure remains fixed for at least 10 seconds.
- Open APL (pop-off) valve and ensure that pressure decreases.

Manual and automatic ventilation systems

Step 12. Test ventilation systems and unidirectional valves.

- Place a second breathing bag on the Y-piece.
- Set appropriate ventilator parameters for the next patient.

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- Switch to automatic ventilation (“ventilator”) mode.
- Fill bellows and breathing bag with oxygen flush and then turn the ventilator on.
- Set oxygen flow to minimum, and other gas flows to zero.
- Verify that during inspiration, bellows deliver appropriate tidal volume and that during expiration, bellows fill completely.
- Set fresh gas flow to approximately 5 L per minute.
- Verify that the ventilator bellows and simulated lungs fill and empty appropriately without sustained pressure at end expiration.
- Check for proper action of unidirectional valves.
- Exercise breathing circuit accessories to ensure proper function.
- Turn ventilator off and switch to manual ventilation (“bag/APL”) mode.
- Ventilate manually and ensure inflation and deflation of artificial lungs and appropriate feel of system resistance and compliance.
- Remove second breathing bag from the Y-piece.

Monitors

Step 13. Check, calibrate, and/or set alarm limits of all monitors.

- Capnometer
- Pulse oximeter
- Oxygen analyzer
- Respiratory volume monitor (spirometer)
- Pressure monitor
- High- and low-airway alarms

Final position

Step 14. Check final status of machine.

- Vaporizers off
- APL valve open
- Selector switch to “bag”
- All flowmeters to zero
- Patient suction level adequate
- Breathing system ready to use

The preanesthesia equipment checkout procedures are shown in Table 59.1.

American Society of Anesthesiologists. *Summary of American Society of Anesthesiologists 2008 Checkout Recommendations by Frequency and Responsible Party. Recommendations for Pre-Anesthesia Checkout Procedures*. Schaumburg, IL: American Society of Anesthesiologists; 2008. http://www.asahq.org/clinical/FINALCheckoutDesignguidelines02-08-2008.pdf. Accessed October 21, 2015.

B.2. What emergency equipment should be easily available to the anesthesiologist?

In checking the anesthesia machine, step no. 1 on the FDA 1993 checklist and the 2008 American Society of Anesthesiologists' guidelines is to verify that backup ventilation equipment is available and functioning. This means a self-inflating resuscitation bag appropriate for patient size (adult vs. pediatric) is present and tested. Emergency airway

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management equipment must be available. The latter may be stored in a “difficult airway cart.”

It is also important to have available means to perform an emergency cricothyrotomy for the “cannot intubate, cannot ventilate” scenario and means to ventilate and oxygenate through the cricothyroid catheter, once placed. A suitable device is the Sanders injector system.

Other emergency equipment include a working flashlight, a backup battery for any electricity-dependent workstation, an oxygen tank and regulator, a malignant hyperthermia cart, a “code” cart and defibrillator, a difficult airway cart, a fire extinguisher, knowledge of appropriate response to a fire, and an evacuation plan.

Apfelbaum JL, Caplan RA, Barker SJ, et al. Practice advisory for the prevention and management of operating room fires: an updated report by the American Society of Anesthesiologists Task Force on Operating Room Fires. *Anesthesiology*. 2013;118:271-290.

ECRI Institute. New clinical guide to surgical fire prevention. Patients can catch fire—here's how to keep them safer. *Health Devices*. 2009;38:314-330.

B.3. How should this patient be premedicated?

The goal of premedication must be established preoperatively. Commonly considered objectives listed in order of most to least common are as follows:

- Anxiolysis
- Minimization of gastric volume and acidity when “full stomach” is of concern
- Antibiotic prophylaxis administered within 1 hour of incision per Surgical Care Improvement Project (SCIP) guideline.
- Antisialagogue effect

This patient may require anxiolysis. Premedication for anxiolysis in an ambulatory patient must consider the patient's need to arrive from home and ambulate as well as the desire for rapid return of clear mental status postoperatively. Most commonly, therefore, no agent is administered preoperatively. Alternatively, for the highly anxious patient, a small dose of a

short-acting agent (e.g., lorazepam, 1 to 2 mg orally) may be administered with a few sips of water 30 to 60 minutes preoperatively.

Longnecker DE, Brown DL, Newman MF, et al. *Anesthesiology*. 2nd ed. New York: McGraw Hill; 2008:1610-1613.

Munday GS, Deveaux P, Roberts H, et al. Impact of implementation of the Surgical Care Improvement Project and future strategies for improving quality in surgery. *Am J Surg*. 2014;208(5):835-840.

C. Intraoperative Management

C.1. How should this patient be monitored?

The “Standards for Basic Anesthetic Monitoring” are established by the American Society of Anesthesiologists and were last amended in October 2010. In summary, they are as follows:

- *Standard I*: Qualified anesthesia personnel shall be present in the room throughout the conduct of all general anesthetics, regional anesthetics, and monitored anesthesia care.
- *Standard II*: During all anesthetics, the patient's oxygenation, ventilation, circulation, and temperature shall be continually evaluated.

Oxygenation

- *Inspired gas*: During every administration of general anesthesia using an anesthesia machine, the concentration of oxygen in the patient breathing system shall be measured by an oxygen analyzer with a low oxygen concentration limit alarm in use.*

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- *Blood oxygenation*: During all anesthetics, a quantitative method of assessing oxygenation such as pulse oximetry shall be employed.* When the pulse oximeter is utilized, the variable pitch pulse tone and the low threshold alarm shall be audible to the anesthesiologist or the anesthesia care team personnel.* Adequate illumination and exposure of the patient are necessary to assess color.*

Ventilation

- Every patient receiving general anesthesia shall have the adequacy of ventilation continually evaluated. Qualitative clinical signs such as chest excursion, observation of the reservoir breathing bag, and auscultation of breath sounds are useful. Continual monitoring for the presence of expired CO_2 shall be performed unless invalidated by the nature of the patient, procedure, or equipment. Quantitative monitoring of the volume of expired gas is strongly encouraged.*
- When an endotracheal tube or laryngeal mask is inserted, its correct positioning must be verified by clinical assessment and by identification of CO_2 in the expired gas. Continual $PETCO_2$ analysis, in use from the time of endotracheal tube/laryngeal mask placement, until extubation/removal or initiating transfer to a postoperative care location, shall be performed using a quantitative method such as capnography, capnometry, or mass spectroscopy.* When capnography or capnometry is utilized, the $PETCO_2$ alarm shall be audible to the anesthesiologist or the anesthesia care team personnel.*
- When ventilation is controlled by a mechanical ventilator, there shall be in continuous use a device that is capable of detecting disconnection of components of the breathing system. The device must give an audible signal when its alarm threshold is exceeded.
- During regional anesthesia and monitored anesthesia care, the adequacy of ventilation shall be evaluated by continual observation of qualitative clinical signs and/or monitoring for the presence of exhaled CO_2.

Circulation

- Every patient receiving anesthesia shall have the electrocardiogram continuously displayed from the beginning of anesthesia until preparing to leave the anesthetizing location.*
- Every patient receiving anesthesia shall have arterial blood pressure and heart rate determined and evaluated at least every 5 minutes.*
- Every patient receiving general anesthesia shall have, in addition to the above, circulatory function continually evaluated by at least one of the following: palpation of a pulse, auscultation of heart sounds, monitoring of a tracing of intra-arterial pressure, ultrasound peripheral pulse monitoring, or pulse plethysmography or oximetry.

Body temperature

- Every patient receiving anesthesia shall have temperature monitored when clinically significant changes in body temperature are intended, anticipated, or suspected.

Under extenuating circumstances, the responsible anesthesiologist may waive the requirements marked with an asterisk (*); it is recommended that when this is done, it should be so stated (including the reasons) in a note in the patient's medical record.

The reader should visit the American Society of Anesthesiologists' website for the most recent version of the standards: http://www.asahq.org/resources/standards-and-guidelines

C.2. After uneventful inhalation mask induction, cystoscopy was begun, and the SpO_2 was noted to decrease to 81% with the patient breathing an FIO_2 of 0.4 (oxygen at 2 L per minute and nitrous oxide at 3 L per minute). The patient developed respiratory distress. The laryngeal mask airway (LMA) was easily maintained, and no gross secretions were noted. What acute diagnostic and therapeutic interventions would you perform?

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Immediately, the patient should be examined for airway obstruction. The presence of bilateral breath sounds and the quality of those breath sounds need to be ascertained. The FIO_2, $PETCO_2$, heart rate, blood pressure, and SpO_2 also need to be checked. The bladder irrigation fluid intake and output, as well as the intravenous fluid intake, should be reviewed.

Therapeutically, the FIO_2 should be increased immediately to 1, and a change to manually assisted ventilation should be considered. If the SpO_2 does not increase rapidly in response to these interventions, tracheal intubation and initiation of positive pressure ventilation should be performed.

Dorotta I, Basali A, Ritchey M, et al. Transurethral resection syndrome after bladder perforation. *Anesth Analg*. 2003;97:1536-1538.

C.3. The patient was tracheally intubated. Squeezing the reservoir bag in the circle system failed to inflate the lungs, and a leak was noted. What are the common sites for gas leaks?

A leak can occur anywhere in the gas circuit. One might logically check for a leak in the circuit starting from the tip of the tracheal tube and working backward toward the gas delivery system, recognizing the following common potential sites:

- Incomplete seal between the tracheal tube cuff and the trachea
- Connection between the tracheal tube and the breathing circuit (e.g., the elbow adapter)
- Spirometric and end-tidal monitoring connections at both the patient end (near the connection between the breathing circuit and tracheal tube) and the monitoring end
- Connection between inspiratory and expiratory gas hoses and the machine
- Within the low-pressure system, including the unidirectional valves, APL valve, reservoir bag or bellows housing, absorber, vaporizers, flowmeters, and scavenging system

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:931-953.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:653-680.

D. Postoperative Management

D.1. What criteria would you use for tracheal extubation?

In the operating room, traditional extubation criteria fall into two categories: global and respiratory. Global criteria include return of consciousness, demonstration of ability to protect the airway, adequate reversal of residual neuromuscular blockade, absence of hypothermia, and presence of a normal metabolic milieu (e.g., no significant anemia, acidosis, and electrolyte abnormality). Commonly applied respiratory criteria are a vital capacity greater than 15 mL per kg, a tidal volume of ≥6 ml per kg, and a predicted SpO_2 >90% while breathing an FIO_2 <0.40.

Patients with a respiratory insult and the need for postoperative mechanical ventilation in the postanesthesia care unit or intensive care unit will be assessed using additional and more stringent criteria. The ratio of respiratory rate to tidal volume is widely used and commonly referred to as the *rapid shallowbreathing index* (RSBI). Slow, deep breathing during minimal respiratory support predicts successful extubation, and rapid, shallow breathing predicts probable failure. To determine this ratio, the patient is observed breathing from a T-bar, or a low level of pressure support (PS) (e.g., usually ˜5 cm H_2O); this is referred to as a spontaneous breathing trial (SBT). The following is then calculated:

RSBI = respiratory rate (breaths per minute) / tidal volume (in liters)

An RSBI greater than 100 is rapid, shallow breathing, and predictably the patient will fail an extubation attempt. When the RSBI is less than 100, it is predicted that the patient will breath at a rate and tidal volume that can be easily maintained

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after extubation and will be able to adequately maintain a normal PaO_2 and $PaCO_2$. It does not, however, rule out the possibility of an upper airway obstruction complicating that effort. If during the period of observation while breathing from a T-bar or on PS, the patient develops signs of distress such as diaphoresis, agitation, tachycardia, bradycardia, hypertension, hypotension, hypoxemia, or hypercarbia, the trial is abandoned and the patient is said to have had a "weaning" or "SBT" failure.

Although more sophisticated measurements might be helpful, including measurement of the maximum negative inspiratory force, vital capacity, elastance index, etc., the routine application of this basic and easy-to-reproduce measurement has stood the test of time and certainly for most patients who are intubated and mechanically ventilated for less than 7 to 10 days should be a daily routine.

Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. *N Engl J Med*. 1991;324:1445-1450.

D.2. What are the causes of postoperative hypoxemia?

The etiology of hypoxemia can be classified physiologically or pathologically.

Physiologically, all instances of hypoxemia have only four potential causes:

- Low FIO_2
- Hypoventilation (which will also be associated with an increased $PaCO_2$)
- Ventilation/perfusion mismatch
- Shunt

Pathologically, common etiologies likely to present postoperatively include airway obstruction, atelectasis (especially with upper abdominal retraction and Trendelenburg positioning), right mainstem intubation, aspiration, pulmonary edema, and pulmonary embolus.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:2924-2946.

D.3. What is the difference between shunt, ventilation/perfusion mismatch, and dead space?

The relative quantity of perfusion and ventilation defines these terms. A normal lung has a small portion in which perfusion and ventilation are perfectly matched. Two extreme conditions may exist at either end of the spectrum of perfectly matched perfusion and ventilation; those extremes are shunt and dead space ventilation.

In a shunt, the alveolus is perfused, but it is not ventilated. The physiologic result is hypoxemia. This is characterized by a failure of the PaO_2 to rise despite an increase in the FIO_2. Hypoxemia caused by small amounts of shunted blood (i.e., less than 20% of cardiac output) is easily overcome by increasing the FIO_2. This is because the blood that is not shunted will contain enough "extra" dissolved oxygen to make up for the deficit that the shunted blood contributes to the combined total blood oxygen content. Once the shunt fraction approaches 0.3 (30%), increasing the FIO_2 even to 1 will not be effective in preventing hypoxemia. The term *venous admixture* is often used synonymously for shunt.

In dead space, the alveolus is ventilated, but it is not perfused; hence, the alveolar space is essentially "dead." The physiologic result is hypercarbia. This is characterized by a failure to maintain a normal $PaCO_2$ despite an increase in minute ventilation (i.e., tidal volume × respiratory rate).

Ventilation/perfusion mismatch is the term applied to any condition that is not a perfect match, completely shunt, or completely dead space. The physiologic result is a variable combination of hypoxemia and hypercarbia. The resultant degree of hypoxemia and hypercarbia depends on the relative contribution of partial shunt and dead space.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Elsevier Science; 2010:119-144.

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D.4. What is the differential diagnosis of pulmonary edema?

Pulmonary edema is categorized into cardiac or noncardiac in etiology. The differential diagnosis of pulmonary edema is shown in Table 59.2.

Conditions that physiologically result from an increase in the pressure within the vessel that cause transudation of fluid from inside the vessel to outside the vessel are traditionally termed congestive heart failure (CHF). CHF will be associated with a diminution of cardiac function (e.g., ejection fraction) and an increase in the left ventricular end-diastolic pressure.

A decrease in the pressure outside of the vessel may also result in the net movement of fluid from inside to outside. A classic example is negative pressure pulmonary edema—a condition seen in young patients who inspire against a closed glottis and generate a large net negative force, which acutely draws fluid into the alveolus, leading to pink frothy sputum and hypoxemia almost instantaneously.

A change in the permeability of the vessel wall is the major cause of pulmonary edema seen in ALI and acute respiratory distress syndrome (ARDS). These conditions require a history of exposure to a risk factor, the development of bilateral infiltrates on chest radiography, and documentation of the absence of heart failure either by echocardiogram or more rarely pulmonary artery catheterization. Risk factors for ALI and ARDS include aspiration, long bone fracture, transfusion-related ALI, pancreatitis, inhalational injury, and sepsis (see Table 59.2).

In this patient, acute fluid overload from absorption of bladder irrigation fluid should be considered. Physiologically, this picture resembles CHF and will respond to treatment with fluid restriction and diuretics.

Bittner EA, Grecu L, George E. Postoperative complications: pulmonary dysfunction. In: Longnecker DE,

Brown DL, Newman MF, et al, eds. *Anesthesiology*. 2nd ed. New York: McGraw Hill; 2012: chap 71.

Dorotta I, Basali A, Ritchey M, et al. Transurethral resection syndrome after bladder perforation. *Anesth Analg*. 2003;97:1536-1538.

D.5. How should the ventilator be set if mechanical ventilation is required postoperatively?

Parameters that must be set include the mode, respiratory rate, tidal volume, PEEP, and FIO_2.

Patients with an acute need for mechanical ventilation should be given full support with the mode set as volume control (sometimes also known as *assist control*) or pressure control, with which all breaths are delivered by the ventilator, even those initiated by the patient. Other modes to be considered as the patient improves include synchronized intermittent

mandatory ventilation, PS, and combinations of synchronized intermittent mandatory ventilation and PS.

TABLE 59.2 Differential Diagnosis of Pulmonary Edema

CONDITION	PATHOPHYSIOLOGY	SAMPLE CAUSE
Congestive heart failure	↑ Filling pressure, ↓ cardiac output	Myocardial infarction
Negative pressure pulmonary edema	↑ Outside-inside pressure gradient	Laryngospasm
Acute lung injury and acute respiratory distress syndrome	↑ Permeability	Sepsis, aspiration, fat embolus, TRALI

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TRALI, transfusion-related acute lung injury.

Tidal volume was traditionally set at 10 mL per kg. Normally, during spontaneous ventilation, the respiratory rate is 12 to 16 breaths per minute, and the tidal volume is 6 mL per kg. However, during spontaneous ventilation, there are yawns and sighs that prevent atelectasis. Yawns and sighs are not administered during routine mechanical ventilation. Therefore, standard mechanical ventilation settings developed more than 50 years ago use a lower respiratory rate and higher tidal volume than spontaneous values, resulting in the same minute ventilation and no need for sigh (150% of tidal volume) breaths.

However, traditional mechanical ventilation utilizing 10 mL per kg has been recognized as a potential cause of morbidity and mortality when applied to injured lungs and more recently has even been suggested to have adverse consequences when applied routinely in the operating room. The excessive tidal volume is associated with alveolar injury and worsened pulmonary function (i.e., volutrauma). This should be distinguished from the more easily recognized concern of pneumothorax, resulting from ventilation of stiff lungs with high inflation pressures, commonly referred to as barotrauma. Hence, the current recommendation in ALI and ARDS is that the tidal volume be set at 6 mL per kg of premorbid weight. Additionally, the peak inspiratory pressure should ideally be less than 35 cm H_2O. This may result in CO_2 retention, but if the pH is more than 7.25, no intervention is necessary. If CO_2 retention is severe and the pH is less than 7.25 after increasing the respiratory rate to as high as 20 breaths per minute, administration of sodium bicarbonate should be considered.

To maximize oxygenation and limit exposure to potentially toxic concentrations of oxygen (i.e., $FIO_2 = 1$), usually an end-expiratory pressure of 10 cm H_2O is set.

In addition to standard monitoring, prolonged mechanical ventilation in ALI and ARDS will require arterial line placement to facilitate frequent arterial blood gas determinations. Further, a daily chest radiograph will be required.

The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342:1301-1308.

D.6. If this patient had acute lung injury (ALI) secondary to aspiration, beside low-tidal volume ventilation, what other changes in routine therapy should be considered?

Other management strategies include efforts at minimizing lung water and usual standard intensive care unit measures aimed at deep venous thrombosis (DVT) prophylaxis, GI prophylaxis, daily sedations breaks, and early mobility. Conservative administration of intravenous fluids originated in a National Institutes of Health-sponsored study that is too lengthy to expound on in this chapter. Suffice it to say, the excessive administration of fluid is harmful, whereas minimizing intravenous fluids appears to be safe and not associated with other organ insufficiency or failure.

Wiedemann HP, Wheeler AP, Bernard GR, et al. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med*. 2006;354:2564-2575.

D.7. What therapies routinely administered by the anesthesiologist may cause ALI?

Transfusion-related ALI has become the leading cause of transfusion-related morbidity and mortality in the United States. This injury is almost always recognized during or shortly after transfusion and is diagnosed by the absence of cardiac failure and fluid overload. Although any blood product can cause this injury, the transfusion of fresh frozen plasma and platelets, especially those donated by women who were previously pregnant, are most often responsible. This injury can be seen even after the transfusion of a single blood product unit and “massive” transfusion is not, as previously thought, a prerequisite.

Alam A, Huang M, Yi QL, et al. Perioperative transfusion-associated lung injury: the Canadian Blood Service experience. *Transfus Apher Sci*. 2014;50:392-398.

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D.8. What methods of oxygen administration may be used postoperatively?

Most postoperative patients who are prone to develop hypoxemia may be managed with a nasal cannula or face mask. Nasal cannulas are cheap and comfortable, but regardless of flow rates, they cannot achieve an FIO_2 of more than 0.30 unless special high-flow devices are used. Face masks have the capability of delivering a wide range of precise FIO_2 levels of up to 1.

Occasionally, a patient may require more aggressive oxygen therapy than can be provided by nasal cannula or face mask but less invasive than tracheal intubation and mechanical ventilation. Noninvasive positive pressure ventilation should be considered. Continuous positive airway pressure and bilevel positive airway pressure may be applied. These modes may be used in patients who either have previously used these devices at home or who are on the verge of requiring tracheal intubation and mechanical ventilation but have conditions thought to be rapidly resolving (e.g., CHF and chronic obstructive pulmonary disease exacerbation). These patients usually do not require an arterial catheter for blood sampling, but do need frequent assessment of their respiratory effort, particularly their respiratory rate and use of accessory muscles, as well as continuous SpO_2 monitoring. Several different types of masks are available. A respiratory therapist should be involved to individually achieve the best mask fit and patient comfort possible. In case noninvasive ventilation fails, preparation to emergently tracheally intubate must always be maintained.

Jaber S, Chanques JS, Jung B. Postoperative noninvasive ventilation. *Anesthesiology*. 2010;112:453-461.

[1]In step no. 10, checking adequacy of the CO_2 absorbent should include changing or hydrating it if there is any possibility that it may have become desiccated. This is because desiccated soda lime can react with desflurane, enflurane, and isoflurane to produce high levels of CO in the breathing system. Baralyme is no longer available for use as an absorbent.

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Chapter 60
Electroconvulsive Therapy

Patricia Fogarty Mack

A 72-year-old man with major depressive disorder is scheduled for electroconvulsive therapy (ECT). His past medical history reveals significant coronary artery disease status after three-vessel coronary bypass surgery 5 years ago. He also has chronic atrial fibrillation. He had a transient ischemic attack (TIA) 2 years previously after which he underwent left carotid endarterectomy. In addition, he has sleep apnea and gastroesophageal reflux disease (GERD). The patient weighs 115 kg and is 5 ft 3 in. tall and had a Mallampati class 2 airway. Medications include warfarin, atenolol, and esomeprazole (Nexium).

A. Medical Disease and Differential Diagnosis

1. What are the indications for ECT?
2. Are there any contraindications to ECT?
3. What is the mechanism of action of ECT?

B. Preoperative Evaluation and Preparation

1. How would you assess the cardiac status of this patient?
2. How should his anticoagulation be managed during ECT?
3. What implications do his history of sleep apnea have on management of ECT?
4. How does his history of TIA and carotid endarterectomy impact your preoperative evaluation?
5. Is ECT contraindicated in a patient with a permanent pacemaker or implantable cardioverter-defibrillator?
6. Are there any psychiatric medications he is taking that would impact your anesthetic care?

C. Intraoperative Management

1. Describe the hemodynamic and cardiac response to ECT in a typical patient.
2. Is an arterial line warranted in this patient?
3. By what means would you attempt to maximize hemodynamic stability?
4. Describe the cerebral hemodynamic effects of ECT.
5. How would you proceed with an anesthetic induction for this procedure?
6. How do you intend to manage his airway during each treatment?

D. Postoperative Management

1. The patient is extremely agitated upon emergence. Discuss the risk factors for postictal agitation (PIA) as well as the therapeutic options?
2. After three consecutive uneventful inpatient treatments, the psychiatrist asks if the patient may undergo ECT as an outpatient. Would you agree to this plan?

A. Medical Disease and Differential Diagnosis

A.1. What are the indications for ECT?

For centuries, it had been noted that psychosis did not tend to occur in those people with epilepsy. Since the 16th century, patients with severe mental illness were treated with various agents, such as camphor, to induce seizures (pharmacoconvulsive therapy). ECT was first instituted in the late 1930s and gained acceptance in providing a better controlled seizure. The addition of curare followed in 1951 by succinylcholine greatly diminished incidence of fracture due to the convulsions. Finally, the advent of methohexital, which ensured unconsciousness without significantly diminishing the seizure, led to the acceptance of ECT as an efficacious and safe treatment.

From the mid-1970s through the 1980s, many new drug treatments for psychiatric illness were developed and found to be efficacious. ECT fell into disfavor as a barbaric treatment when compared to pharmacotherapy.

In the past three decades, the pendulum has again swung back in favor of ECT as a safe and effective treatment for drug-resistant major depressive disorder and bipolar disorder.

Specific indications for ECT include, but are not limited to, major depressive disorder and bipolar disorder, acute schizophrenia (especially with affective or catatonic symptoms), and schizoaffective disorder. Although usually reserved as a second-line therapy for those who are resistant to pharmacologic treatment, ECT has, in some circumstances, been recommended as a first-line therapy, especially if a rapid response is urgently required as in patients with severe suicidal potential, malnutrition/dehydration, and catatonia. Finally, ECT has been recommended in patients who are unable to tolerate pharmacotherapeutic agents for any reason, including during pregnancy.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association.* 2nd ed. Washington, DC: American Psychiatric Association; 2001:5-26.

A.2. Are there any contraindications to ECT?

There is no absolute contraindication to ECT. There is considered to be significantly increased risk in patients with intracranial space occupying lesions, any condition associated with intracranial hypertension, recent myocardial infarction with diminished ventricular function, severe hypertension especially associated with pheochromocytoma, evolving stroke, retinal detachment, and any American Society of Anesthesiologists physical status 4 or 5 patient.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association.* 2nd ed. Washington, DC: American Psychiatric Association; 2001:27-30.

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A.3. What is the mechanism of action of ECT?

The mechanism of ECT is unknown. There are many neurochemical, neuroendocrine, electrophysiologic, and neuropsychological theories regarding the mechanism of ECT (see Table 60.1).

In addition, although it was long assumed that a generalized seizure of adequate duration is sufficient for effective treatment, research has shown that barely suprathreshold stimulation, especially with unilateral ECT is also efficacious. The cognitive impairment associated with ECT may be reduced by utilizing "ultrabrief" stimulus, marked by a shorter pulse width of electrical stimulation, apparently without sacrificing efficacy.

Loo CK, Katalinic K, Smith DJ, et al. A randomized controlled trial of brief and ultrabrief pulse right unilateral electroconvulsive therapy. *Int J Neuropsychopharmacol*. 2014;18(1).

B. Preoperative Evaluation and Preparation

B.1. How would you assess the cardiac status of this patient?

The cardiac status of the patient needs to be assessed as it would for any other general anesthetic. As there can be periods of significant tachycardia and hypertension following seizure induction, it would be useful to ensure that there is no longer significant myocardium at

risk for ischemia and that systolic function is not compromised. If this information cannot be obtained from patient history and assessment of his functional status, it may be useful to obtain a stress test and echocardiogram. Bear in mind that it may be difficult to get an accurate history of functional status from patients who are psychotic or severely depressed.

TABLE 60.1 Mechanism of Action of Electroconvulsive Therapy—Physiologic Theories

NEUROPHYSIOLOGIC
Anticonvulsant (changes in seizure threshold)
Cerebral blood flow and metabolic rate change
Increased slow-wave EEG activity
Antidelirium/sleep theories
NEUROENDOCRINOLOGIC
Prolactin release
Neuropeptide release
Melatonin
NEUROCHEMICAL
Stimulation of β-receptors
Monoamine release
Modulation of serotonin
NEUROPEPTIDE/NEUROTROPHIC
Brain-derived neurotrophic factor
Increased endogenous opioids

EEG, electroencephalography.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:77-80.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:2215-2245.

B.2. How should his anticoagulation be managed during ECT?

The anticoagulation for his atrial fibrillation should be continued throughout his course of therapy, maintaining an international normalized ratio (INR) between 2.0 and 3.0. Although intracerebral hemorrhage is a theoretic concern, a retrospective study from the Mayo Clinic suggests that ECT can be safely performed in patients on warfarin therapy. Although the safety of newer anticoagulants has not been formally investigated in ECT, case series do not report any

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hemorrhagic complication in patients receiving either dabigatran or rivaroxaban. Finally, if a patient has drug-eluting arterial stents, aspirin and clopidogrel or any alternative antiplatelet maintenance medication should be continued.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:40-41.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:2215-2245.

Mehta V, Mueller PS, Gonzalez-Arriaza HL, et al. Safety of electroconvulsive therapy in patients receiving longterm warfarin therapy. *Mayo Clin Proc*. 2004;79:1396-1401.

Schmidt ST, Lapid MI, Sundsted KK, et al. Safety of electroconvulsive therapy in patients receiving dabigatran therapy. *Psychosomatics*. 2014;55:400-403.

Shuman M, Hieber R, Moss L, et al. Rivaroxaban for thromboprophylaxis in a patient receiving electroconvulsive therapy. *J ECT*. 2015;31:e19-e20.

B.3. What implications do his history of sleep apnea have on management of ECT?

His history of sleep apnea is important because suboptimal management of respiratory function may reduce efficacy of treatment and increase complications. Hypocarbia is sometimes required to ensure adequate seizure duration. Additionally, after onset of seizure activity, oxygen consumption is increased dramatically as is CO_2 production.

Hypercarbia can exacerbate the tachycardia and hypertensive responses to seizure. Therefore, adequate mask ventilation is required to ensure optimal respiratory status. The use of a supraglottic airway device may be required to ensure adequate ventilation in this patient.

Finally, if the patient uses continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP) at home, it may be useful to have that machine available to the patient in the postprocedure period when postanesthetic and postictal somnolence may compromise his ability to maintain a patent airway.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142-149.

B.4. How does his history of TIA and carotid endarterectomy impact your preoperative evaluation?

A history of TIA or stroke is an indication for magnetic resonance imaging (MRI) of the head before their first course of ECT. Additionally, this study may be utilized to rule out an organic cause for depression. Although a comprehensive neurologic examination is routinely recommended by the American Psychiatric Association before ECT, it may be that in this patient more sophisticated neuropsychological testing would be useful in documenting subtle deficits and establishing a true baseline. Finally, if the patient has not had follow-up carotid Doppler examination, it may be useful to ensure that there has not been restenosis or that no new plaques have formed. This is particularly important in view of the fact that the rate pressure product may be increased by as much as 400% in the sympathetic phase of the cardiac response.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:77-80.

B.5. Is ECT contraindicated in a patient with a permanent pacemaker or implantable cardioverter-defibrillator?

See Chapter 8, section C.11.

B.6. Are there any psychiatric medications he is taking that would impact your anesthetic care?

Medications for depression can have many serious side effects. In fact, one of the indications for ECT is that the patient cannot tolerate pharmacologic therapy. Furthermore, there are many possible drug interactions between antidepressant medications and anesthetic agents as well as other medications that might be administered in the course of an anesthetic. The most common of these side effects and interactions are shown in Table 60.2.

C. Intraoperative Management

C.1. Describe the hemodynamic and cardiac response to ECT in a typical patient.

First, a parasympathetic discharge occurs within a few seconds of application of the electrical stimulus. This may result in bradycardia, which may be profound and even progress to asystole. Because many patients are volume-depleted due to poor oral intake or mildly hypotensive secondary to their psychotropic medications, they can be susceptible to further hypotension due to anesthetic induction. Within 1 minute, sympathetic activation due to the seizure results in a tachycardia and at times dysrhythmias as well as hypertension to up to 150% of baseline values. This hypertension usually lasts for between 2 and 5 minutes. If the patient is not adequately ventilated, hypercarbia may add to the hypertension. During the first ECT treatment, the electrical stimulus may often be titrated upward in succession until a generalized seizure occurs. When a generalized seizure does not follow the electrical stimulation, the parasympathetic response predominates and the patient may experience a sustained bradycardia.

TABLE 60.2 The Most Common Side Effects and Anesthetic Interactions of Psychiatric Medications

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DRUG GROUP	EXAMPLES OF DRUG	MECHANISM	SIDE EFFECTS/TOXICITIES	PERIOPERATIVE CONCERNS	POTENTIAL INTERACTIONS	ALTERNATIVE MEDICATIONS	PREOPERATIVE CONTINUATION?
SSRIs	Venlafaxine, fluoxetine	Presynaptic inhibition of SER uptake	Nausea, vomiting Sexual dysfunction Headache Agitation SIADH (rare) Cytochrome P450 inhibition	Prolonged/increased action of β-blockers, benzodiazepines, barbiturates, anticholinergics	Serotonin syndrome: MAOIs, meperidine, and highly proteinbound drugs (lidocaine, midazolam, fentanyl, linezolid, methylene blue)	Reduce dose of cytochrome P450 metabolized drugs Avoid serotonin crisis precipitants.	Continue
Lithium	Lithium	Unclear	Sinus node dysfunction AV block Bradycardia Nephrogenic diabetes insipidus	Prolongation of nondepolarizing muscle relaxants Reducing MAC	Toxicity with drugs that decrease renal function: NSAIDs, angiotensin-converting enzyme inhibitors, etc.	Careful dose titration	Discontinue 24 hr before surgery.
TCAs	Amitriptyline, imipramine	Presynaptic inhibition of SER uptake	Conduction deficits (wide QRS, prolonged QT) Postural hypotension Anticholinergic symptoms Sedation	Muscarinic, histaminergic, and α_1-adrenergic blocking effects	MAC increased and increased likelihood of dysrhythmia Hypertensive crisis caused by indirect sympathomimetic drugs Atropine/scopolamine increased emergence delirium, increased muscarinic activity Pancuronium may cause tachyarrhythmia.	Phenylephrine Glycopyrrolate Other nondepolarizing muscle relaxant	Discontinue
MAOIs	Phenelzine, tranylcypromine	Inhibit breakdown of NE and SER by MAO enzyme	Hypertension Nausea Dizziness Headache Sleep disturbance Severe hypertension with tyramine containing foods Thrombocytopenia and anemia	Avoid indirect acting sympathomimetics. Avoid serotonin crisis precipitants.	Indirect sympathomimetic: hypertensive crisis Serotonergic syndrome from meperidine, dextromethorphan, etc. Inhibiting acetylcholinesterase Increasing MAC	Avoid indirect acting sympathomimetics. Avoid serotonin crisis precipitants. Use fentanyl. Use nondepolarizing muscle relaxants. Titration	Irreversible MAOI—discontinue 2 wk before surgery. Reversible MAOI—discontinue on day of procedure.
Antipsychotics	Prochlorperazine, chlorpromazine	Block D2 dopamine receptors Atypical antipsychotics also block some serotonin receptors. Also block histamine and α_1-adrenergic receptors	Hypotension Tachycardia, prolonged QT interval Extrapyramidal symptoms Tremor Tardive dyskinesia Neuroleptic malignant syndrome Muscle rigidity, hyperthermia, autonomic dysfunction		Hypertension with halogenated agents Anticholinergic effects with atropine and scopolamine	Careful titration/TIVA Glycopyrrolate	Continue

Serotonin syndrome: hyperreflexia, agitation, hyperthermia. AV, atrioventricular; MAC, minimal alveolar concentration; MAO, monoamine oxidase; MAOI, monoamine oxidase inhibitor; NE, norepinephrine; NSAIDs, nonsteroidal anti-inflammatory drugs; SER, serotonin; SIADH, syndrome of inappropriate antidiuretic hormone secretion; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants; TIVA, total intravenous anesthesia.

With such a dramatic increase in heart rate and blood pressure, the rate pressure product, an indicator of myocardial oxygen demand, is significantly elevated. This can lead to electrocardiographic ischemia as well as regional wall motion abnormalities on echocardiography.

Messina AG, Paranicas M, Katz B, et al. Effect of electroconvulsive therapy on the electrocardiogram and the echocardiogram. *Anesth Analg*. 1992;75:511-514.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142-149.

C.2. Is an arterial line warranted in this patient?

No, in spite of the potential dramatic perturbations in heart rate and blood pressure, these responses are fairly predictable and can be attenuated by judicious use of anticholinergics and antihypertensives. Atropine (0.4 mg) or glycopyrrolate (0.2 mg) are used to prevent the bradycardia associated with the parasympathetic discharge. The tachycardia and hypertension seen as part of the sympathetic response can be prevented with short-acting β-blockade, nitroglycerin, or even remifentanil, administered just at the beginning of the sympathetic stimulation.

Patients may have transient ECG changes around the time of the procedure. There is also evidence that patients may

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experience a transient decrease in left ventricular function. Rarely, Takotsubo cardiomyopathy occurs. Severe cardiac complications during ECT are very rare, even in patients with underlying coronary disease.

Cristancho MA, Sattherwaite TD, O'Reardon JP. Cardiac complications of ECT: myocardial stunning syndrome and Takotsubo cardiomyopathy after ECT: different names for the same phenomenon. *J ECT*. 2010;26:146-147.

Fuenmayor AJ, el Fakih Y, Moreno J, et al. Effects of electroconvulsive therapy on cardiac function in patients without heart disease. *Cardiology*. 1997;88:254-257.

McCully RB, Karon BL, Rummans TA, et al. Frequency of left ventricular dysfunction after electroconvulsive therapy. *Am J Cardiol*. 2003;91:1147-1150.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142-149.

C.3. By what means would you attempt to maximize hemodynamic stability?

First, one should continue antihypertensive medication on the evening before and the morning of the procedure. Second, a small dose of atropine (0.4 mg) or glycopyrrolate (0.2 mg) may be given several minutes before the electrical stimulation in order to prevent the subsequent bradycardia. At Weill Cornell Medical Center, we are more likely to use glycopyrrolate as it is a quaternary compound, which will not cross an intact blood-brain barrier. In addition, the tachycardic response from the seizure is not as pronounced when glycopyrrolate is used as compared with atropine. Anticholinergic pretreatment is most important during the first treatment when the electrical stimulation is being titrated and it is likely not to progress into a generalized seizure on the first or second stimulus. If the pretreatment with an anticholinergic leaves a fragile patient with an undesirable tachycardia, we may omit it during subsequent treatments as long as the bradycardia is not too severe or prolonged.

Similarly, medications to attenuate the sympathetic response are typically not administered until it is certain that the seizure will generalize. This results in a requirement for very fast-acting drugs to control heart rate and blood pressure. The drug of choice at Weill Cornell Medical Center is esmolol (0.5 to 1.0 mg per kg) or labetalol (5 to 20 mg). If there is a contraindication to β-blockers, diltiazem, nicardipine, or sodium nitroprusside may be substituted. Nitroglycerin may be particularly useful in patients with ischemic cardiac disease. Remifentanil has also been found to be effective in attenuating the sympathetic response.

A study of American Society of Anesthesiologists Physical Status I and II patients assessed echocardiographic and hemodynamic parameters when the sympathetic response was pretreated with intravenous β-blocker, calcium channel blocker, or nitroglycerin prior to the electrical stimulus. No new regional wall motion abnormalities were found, but β-blocker seemed to be the most effective medication at attenuating fractional shortening and the entire sympathetic response.

Kadoi Y, Takahashi K, Saito S, et al. Effects of antihypertensive medication on left ventricular function during electroconvulsive therapy: study with transthoracic echocardiography. *J Clin Anesth*. 2006;18:441-445.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142-149.

van Zijl DH, Gordon PC, James MF. The comparative effects of remifentanil or magnesium sulfate versus placebo on attenuating the hemodynamic responses after electroconvulsive therapy. *Anesth Analg*. 2005;101:1651-1655.

C.4. Describe the cerebral hemodynamic effects of ECT.

Electrically induced seizures lead to cerebral hyperemia (increase in cerebral blood flow) as documented by transcranial Doppler and near-infrared spectroscopy. This response occurs even if the seizure does not generalize, suggesting that they are a result of the electric stimulation itself. The increase in cerebral blood flow has been shown to be related to the degree of systemic hypertension and occurs whether bilateral or unilateral stimulus is applied. Although there is a correlation with systemic hypertension, the systemic antihypertensives do not fully ameliorate the increase in cerebral blood flow. This is due to the fact that these drugs have differing effects on the cerebral and systemic circulations.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142-149.

C.5. How would you proceed with an anesthetic induction for this procedure?

Anesthetic induction may be accomplished with any one of a number of medications. Traditionally, methohexital (0.5 to 1.0 mg per kg) has been the induction agent of choice because it has very little effect on seizure duration and has a rapid onset and recovery profile. Unfortunately, methohexital is no longer available in many areas. At Weill Cornell Medical Center, we now use etomidate (0.2 to 0.3 mg per kg) or propofol (0.5 to 1.0 mg per kg). In research studies, etomidate provides for longer seizure duration when compared to methohexital and propofol; however, postictal hypertension is more severe and myoclonic contractions may be undesirable. In addition, there is a greater incidence of nausea, increased confusion, and prolonged recovery time. Although adrenal suppression has been reported in patients on continuous infusions of etomidate, there are no reports of adrenal suppression in patients receiving multiple bolus doses of etomidate as part of a course of ECT. In patients in whom etomidate is not well tolerated, propofol or thiopental may be used. Studies concur that propofol and thiopental reduce seizure duration; however, there is controversy as to how this reduction in seizure duration impacts the efficacy of therapy.

Ketamine has been noted to have antidepressant effects and potentiate the early reduction of depressive symptoms when given in conjunction with ECT. It appears that ketamine may be useful in some patients in whom a rapid decrease in depressive symptoms is essential, such as those with extreme suicidal ideation or catatonia. A randomized controlled trial of “ketofol,” a combination of ketamine and propofol, determines that ketofol was associated with a longer seizure time than propofol, faster recovery than ketamine, with good hemodynamic stability. Current investigations are focused on the optimal dosing of the optimal anesthetic agent to improve ECT efficacy.

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Muscle relaxation is usually achieved with succinylcholine (0.5 to 1.0 mg per kg) unless there is a contraindication. In that case, a short-acting nondepolarizing muscle relaxant may be substituted.

Ding Z, White PF. Anesthesia for electroconvulsive therapy. *Anesth Analg*. 2002;94:1351-1364.

Okamoto N, Nakai T, Sakamoto K, et al. Rapid antidepressant effect of ketamine anesthesia during electroconvulsive therapy of treatment-resistant depression: comparing ketamine and propofol anesthesia. *J ECT*. 2010;26:223-227.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142-149.

C.6. How do you intend to manage his airway during each treatment?

The diagnosis of sleep apnea and the patient's body habitus raise concerns regarding the ease and effectiveness of mask ventilation. In spite of these concerns, a plan to proceed with mask ventilation as well as a backup plan of supraglottic airway or intubation is reasonable. As ECT is usually administered three times a week, repeated intubations may lead to airway trauma and edema.

GERD may also be of concern; however, patients for ECT are not intubated solely because of GERD. Continuation of medication to reduce stomach acid and promote gastric emptying as well as a dose of preinduction sodium bicitrate may be used to reduce gastric acidity.

Effective mask ventilation is important for several reasons. First, hypocapnia may lower seizure threshold and promote more effective therapy. Second, avoidance of postseizure hypercapnia is necessary as hypercapnia will exacerbate hypertension and tachycardia.

In anticipation of potential difficult ventilation during ECT, the patient is preoxygenated for 3 to 5 minutes prior to induction. As soon as induction is accomplished, both an oral and a well-lubricated nasal airway will be placed. A second person ideally is available in case two-person ventilation is required. Jackson-Rees circuits are advantageous for ventilation during ECT. First, they allow you to adjust the amount of positive pressure administered; second, the weight of an Ambu bag can sometimes make maintenance of ideal mask placement difficult; finally, as the patient regains spontaneous ventilation, he or she may breathe comfortably and effectively through the Jackson-Rees circuit. If mask ventilation were not effective, an appropriately sized supraglottic airway may be placed.

If necessary for adequate ventilation, intubation may be considered. Unfortunately, repeated intubations over several days and weeks may lead to glottic edema and trauma.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142-149.

D. Postoperative Management

D.1. The patient is extremely agitated upon emergence. Discuss the risk factors for postictal agitation (PIA) as well as the therapeutic options?

PIA manifests as disorientation, inability to consistently follow commands, and motor agitation. Risk factors for PIA include prolonged seizure duration, bilateral versus unilateral ECT, and concomitant lithium therapy. In addition, low doses of induction agent as well as very low doses of succinylcholine are considered risk factors. The use of low-dose succinylcholine may be related to excess lactate production in those patients who have greater manifestation of clinical seizure activity. Increased lactate levels were noted in patients who experienced PIA versus those who did not.

It is of critical importance to rule out nonconvulsive status epilepticus as an etiology for the PIA. Nonconvulsive status may present as agitation or conversely as mutism.

Treatment of PIA usually consists of benzodiazepine, such as midazolam 1 to 2 mg. If this is not effective, haloperidol may be added. In some circumstances, propofol as a bolus or an infusion have been effective. Current management of PIA may include the use of dexmedetomidine, either as a pretreatment or postseizure therapy.

Augoustides JG, Greenblatt E, Abbas MA, et al. Clinical approach to agitation after electroconvulsive therapy: a case report and literature review. *J ECT*. 2002;18:213-217.

Cohen MB, Stewart JT. Treatment of post-electroconvulsive therapy agitation with dexmedetomidine. *J ECT*. 2013;29:e23-e24.

D.2. After three consecutive uneventful inpatient treatments, the psychiatrist asks if the patient may undergo ECT as an outpatient. Would you agree to this plan?

Outpatient ECT has become an acceptable therapeutic option for many patients. Primarily, it is used for maintenance therapy. It may also be used to complete an initial course of ECT provided that the first several treatments are uneventful medically (i.e., no respiratory or cardiovascular problems) and that the patient is demonstrating improvement in psychiatric status. In addition, because psychiatric patients may be unreliable in following preoperative instructions, such as nothing by mouth status, they must have another adult who assumes responsibility for ensuring that those instructions are followed. Of course, they must also have an escort to bring them home.

Finally, there needs to be close communication between the treating psychiatrist and the ECT psychiatrist to keep abreast of any change in psychiatric status or in any medical condition.

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Chapter 61
Ambulatory Surgery

Kathryn E. McGoldrick

A 38-year-old woman desiring permanent sterility was scheduled for bilateral laparoscopic tubal ligation in the ambulatory surgical suite. Her preoperative outpatient questionnaire indicated a history of hypertension and glaucoma. Additionally, she had surgery 2 weeks ago under general anesthesia for a detached retina, and her postoperative course was complicated by severe postoperative nausea and vomiting (PONV). She is 5 ft 7 in. tall, weighs 195 lb, and complains of chronic fatigue. Her only medications consist of enalapril and “eye drops.”

A. Pathophysiology and Differential Diagnosis

1. What are the anesthetic implications of glaucoma?
2. What side effects and important anesthetic interactions are associated with eye drops used to treat glaucoma?
3. Should glaucoma medications be discontinued before elective surgery?
4. Is this patient morbidly obese?
5. What medical conditions may be associated with obesity and morbid obesity?

B. Preoperative Evaluation and Preparation

1. What advantages does outpatient surgery offer?
2. What are the goals of the preoperative evaluation of the surgical outpatient?
3. In order to thoroughly screen for disease, should one put all outpatients through a full battery of laboratory testing?
4. What preoperative laboratory testing is necessary for the surgical outpatient?
5. Which outpatients should receive a preoperative chest roentgenogram?
6. In which patients is an electrocardiogram (ECG) necessary before outpatient anesthesia and surgery?
7. Would a patient's age or physical status influence the decision to perform outpatient surgery?
8. What patients would be considered inappropriate for ambulatory surgery?
9. What questions are critically important to ask this patient when obtaining her history?
10. What instructions should the patient be given with regard to continuing or discontinuing enalapril in the perioperative period?
11. How would you premedicate this patient?
12. Should every outpatient receive prophylaxis against acid aspiration pneumonitis?
13. Is an overnight fast justified for all outpatients?

C. Intraoperative Management

1. What are the important considerations in choosing an anesthetic technique for outpatient surgery?
2. What are the anesthetic implications of recent retinal detachment surgery?
3. How would you monitor this patient?
4. What is the bispectral index (BIS) monitor, and what information does it convey?
5. What benefits might be derived from using a BIS monitor?
6. Is BIS monitoring applicable to children?

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7. What are the major limitations of BIS monitoring?
8. What does a BIS reading of 56 mean?
9. What are the anesthetic options for laparoscopy?
10. Under what circumstances might spinal anesthesia be appropriate for outpatient laparoscopy?
11. What anesthetic agents would you use to induce and maintain general anesthesia in this patient?
12. Would you avoid the use of nitrous oxide in this ambulatory patient?
13. Discuss the physiologic changes induced by laparoscopy.
14. In addition to the physiologic changes described in the preceding text, what other intraoperative complications are associated with laparoscopy?
15. Why is carbon dioxide the insufflation agent of choice for laparoscopy?
16. What are some alternatives to carbon dioxide for laparoscopy?

D. Postoperative Management

1. What are the common causes of nausea and vomiting in outpatients?
2. How would you pharmacologically prevent PONV in the susceptible ambulatory patient?
3. How is postoperative pain treated?
4. If the patient complained of eye pain postoperatively, how would you manage the situation?
5. What criteria would you use to establish that a patient can be safely discharged after ambulatory surgery?
6. How would you decide when to discharge a patient after regional anesthesia?
7. What instructions should be given to an ambulatory surgical patient upon discharge?

A. Pathophysiology and Differential Diagnosis

A.1. What are the anesthetic implications of glaucoma?

With open-angle glaucoma, elevated intraocular pressure (IOP) exists in conjunction with an anatomically patent anterior chamber angle. It is thought that sclerosis of trabecular tissue produces impaired aqueous filtration and drainage. Treatment consists of medication to produce miosis and trabecular stretching. Commonly used eye drops include epinephrine, echothiophate iodide, timolol, dipivefrin, and betaxolol. Carbonic anhydrase inhibitors such as acetazolamide can also be administered by various routes to reduce IOP by interfering with the production of aqueous humor. All these drugs are systemically absorbed and can, therefore, have anticipated side effects.

It is important to appreciate that maintenance of IOP is determined primarily by the rate of aqueous formation and the rate of aqueous outflow. The most important influence on formation of aqueous humor is the difference in osmotic pressure between aqueous humor and plasma. This concept is illustrated by the equation:

$IOP = K\,[(OP_{aq} - OP_{pl}) + CP]$

where K = coefficient of outflow, OP_{aq} = osmotic pressure of aqueous humor, OP_{pl} = osmotic pressure of plasma, and CP = capillary pressure. The fact that a small change in solute concentration of plasma can dramatically affect the formation of aqueous humor, and hence, IOP is the rationale for administering hypertonic solutions, such as mannitol, to reduce IOP. Fluctuations in aqueous outflow can also markedly change IOP. The primary factor controlling aqueous humor outflow is the diameter of Fontana's spaces, as illustrated by the equation:

$$A = \frac{r^4 \times (P_{IOP} - P_v)}{8\eta L}$$

where A = volume of aqueous outflow per unit of time, r = radius of Fontana's spaces, P_{IOP} = IOP, P_v = venous pressure, η = viscosity, and L = length of Fontana's spaces. When the pupil dilates, Fontana's spaces narrow, resistance to outflow is increased, and IOP rises. Because mydriasis is undesirable in both closed- and open-angle glaucoma, miotics such as pilocarpine are applied conjunctivally in patients with glaucoma to effect papillary constriction.

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The aforementioned equation describing the volume of aqueous outflow per unit of time clearly underscores that outflow is exquisitely sensitive to fluctuations in venous pressure. Because an elevation in venous pressure results in an increased volume of ocular blood as well as decreased aqueous outflow, it is obvious that a considerable increase in IOP occurs with any maneuver that increases venous pressure. Hence, in addition to preoperative instillation of miotics, other anesthetic objectives for the patient with glaucoma include perioperative avoidance of venous congestion and of overhydration. Furthermore, hypotensive episodes are to be avoided because these patients are purportedly vulnerable to retinal vascular thrombosis.

Although glaucoma usually occurs as an isolated disease, it may also be associated with such conditions as Sturge-Weber syndrome, aniridia, mesodermal dysgenesis syndrome, retinopathy of prematurity, Refsum syndrome, mucopolysaccharidosis, Hurler syndrome, Stickler syndrome, Marfan syndrome, and von Recklinghausen disease (neurofibromatosis). Additionally, ocular trauma, steroid therapy, sarcoidosis, some forms of arthritis associated with uveitis, and pseudoexfoliation syndrome can also be associated with secondary glaucoma.

Primary closed-angle glaucoma is characterized by a shallow anterior chamber and a narrow iridocorneal angle that impedes the egress of aqueous humor from the eye because the trabecular meshwork is covered by the iris. Relative pupillary block is common in many angle-closure episodes in which iris-lens apposition or synechiae impede the flow of aqueous from the posterior chamber. In the United States, the prevalence of angle-closure glaucoma (ACG) is one-tenth as common as open-angle glaucoma. In acute ACG, if the pressure is not reduced promptly, permanent visual loss can ensue as a result of optic nerve damage. It is thought that irreversible optic nerve injury can occur within 24 to 48 hours.

McGoldrick KE. Eye, ear, nose, and throat diseases. In: Fleisher LA, ed. *Anesthesia and Uncommon Diseases*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:1-27.

McGoldrick KE, Gayer SI. Anesthesia for ophthalmologic surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1373-1399.

A.2. What side effects and important anesthetic interactions are associated with eye drops used to treat glaucoma?

Echothiophate is a long-acting anticholinesterase miotic that lowers IOP by decreasing resistance to the outflow of aqueous humor. Useful in the treatment of glaucoma, echothiophate is absorbed into the systemic circulation after instillation in the conjunctival sac. Any of the long-acting anticholinesterases may prolong the action of succinylcholine because after a month or more of therapy, plasma pseudocholinesterase activity may be less than 5% of normal. It is said, moreover, that normal enzyme activity does not return until 4 to 6 weeks after discontinuation of the drug. Hence, the anesthesiologist should anticipate prolonged

apnea if these patients are given a customary dose of succinylcholine. In addition, a delay in metabolism of ester local anesthetics should be expected.

Although topical epinephrine has proved useful in some patients with open-angle glaucoma, the 2% solution has been associated with such systemic effects as nervousness, hypertension, angina pectoris, tachycardia, and other dysrhythmias.

Timolol, a nonselective β-adrenergic blocking drug, has historically been a popular antiglaucoma drug. Because significant conjunctival absorption may occur, timolol should be administered with caution to patients with known obstructive airway disease, severe congestive heart failure, or greater than first-degree heart block. Life-threatening asthmatic crises have been reported after the administration of timolol drops to some patients with chronic, stable asthma. Not unexpectedly, the development of severe sinus bradycardia in a patient with cardiac conduction defects (left anterior hemiblock, first-degree atrioventricular block, and incomplete right bundle branch block) has been reported after timolol. Moreover, timolol has been implicated in the exacerbation of myasthenia gravis and in the production of postoperative apnea in neonates and young infants. Patients may report feelings of fatigue and/or depression in association with the use of timolol drops.

In contrast to timolol, a newer antiglaucoma drug, betaxolol, a β_1-blocker, is said to be more oculospecific and have minimal systemic effects. However, patients receiving an oral β-blocker and betaxolol should be observed for potential additive effects on known systemic effects of β-blockade. Caution should be exercised in patients receiving catecholaminedepleting drugs. Although betaxolol has produced only minimal effects in patients with obstructive airway

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disease, caution should be exercised in the treatment of patients with excessive restriction of pulmonary function. Moreover, betaxolol is contraindicated in patients with sinus bradycardia, greater than first-degree heart block, cardiogenic shock, and overt myocardial failure.

McGoldrick KE, Gayer SI. Anesthesia for ophthalmologic surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1373-1399.

A.3. Should glaucoma medications be discontinued before elective surgery?

For all the aforementioned reasons, it is important to continue glaucoma medications in the perioperative period. Moreover, the anesthesiologist must be aware of which medications the patient is taking and the effects of these drugs on anesthetic management.

McGoldrick KE, Gayer SI. Anesthesia for ophthalmologic surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1373-1399.

A.4. Is this patient morbidly obese?

Morbid obesity is defined by a body mass index greater than 40 kg per m^2. This patient has a body mass index of approximately 30 and would, therefore, be considered obese. See Chapter 63, section A.2.

Bucklin BA, Fernandez-Bustamante A. Anesthesia and obesity. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1274-1293.

A.5. What medical conditions may be associated with obesity and morbid obesity?

A plethora of conditions may be associated with obesity and morbid obesity including diabetes, hyperlipidemia, cholelithiasis, gastroesophageal reflux disease, cirrhosis, degenerative joint and disc disease, venous stasis and thrombotic/embolic disease, sleep disorders including obstructive sleep apnea, several types of cancer, and emotional disorders. Diseases of the cardiopulmonary system are common and concerning. They include, but are not limited to, systemic hypertension, pulmonary hypertension and cor pulmonale, restrictive lung disease, and right and left ventricular hypertrophy.

Bucklin BA, Fernandez-Bustamante A. Anesthesia and obesity. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1274-1293.

Qadir N, Smith I. Day surgery: how far can we go and are there still limits? *Curr Opin Anaesthesiol*. 2007;20:503-507.

B. Preoperative Evaluation and Preparation

B.1. What advantages does outpatient surgery offer?

Outpatient surgery typically offers greater convenience to the patient (less time away from home, family, and work), a more pleasant environment with less stress and emotional disturbance, and a reduced risk of infection, particularly for the immunocompromised or the pediatric patient. Additionally, outpatient surgery is more economical and enables more efficient use of operating rooms with greater flexibility in scheduling surgery. Finally, one is not dependent on the availability of hospital beds.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:844-859.

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B.2. What are the goals of the preoperative evaluation of the surgical outpatient?

The objectives of the preoperative evaluation are as follows:

- To perform medical assessments, obtain data, arrange for laboratory tests and consultations as indicated, and prescreen for relevant conditions in order to optimize perioperative outcome
- To obtain informed consent
- To provide information and instructions to reduce patient anxiety and improve perioperative management

Organization of preoperative screening varies among ambulatory surgical facilities throughout the country. The screening process may be organized with an office or facility visit before the day of surgery, by a telephone interview or review of health questionnaire without a visit, or by preoperative screening and visit on the morning of surgery. Each of these systems has its advantages and disadvantages. Nevertheless, the system for preoperative evaluation of ambulatory surgical patients should ensure that screening is performed far enough in advance so that preexisting disease can be evaluated, treatment optimized, and laboratory data recorded before the patient presents for anesthesia. Written instructions should be supplied to the patient in advance describing the preoperative workup, admission, and recovery periods.

Hata TM, Hata JS. Preoperative patient assessment and management. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:583-611.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:844-859.

B.3. In order to thoroughly screen for disease, should one put all outpatients through a full battery of laboratory testing?

No. The practice of preoperative “shotgun” laboratory screening for outpatient surgery has received much criticism. In addition to unnecessarily adding several billion dollars annually to the cost of health care, laboratory screening tests in asymptomatic patients have been shown to be of dubious value. History and physical examination are a better means of screening for disease and should serve to reduce expensive, potentially harmful, and inappropriate tests.

Bader AM, Hepner DL. Update on preprocedure testing. In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:8-13.

Chung F, Yuan H, Yin L, et al. Elimination of preoperative testing in ambulatory surgery. *Anesth Analg*. 2009;108:467-475.

Hata TM, Hata JS. Preoperative patient assessment and management. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:583-611.

B.4. What preoperative laboratory testing is necessary for the surgical outpatient?

Most outpatient surgical facilities consider the operative procedure and the patient's age, medical condition, medication history, and state and local regulations in determining which preoperative tests are “required.” For the healthy ambulatory patient between the ages of 1 and 40 years having a minor surgical procedure, no laboratory testing may be required.

Pregnancy testing is a highly controversial issue. Many believe that pregnancy testing should be offered to all consenting females of childbearing potential. This approach, however, does not substitute for an appropriate pregnancy history and physical examination. Hemoglobin or hematocrit determination is appropriate for surgical procedures associated with substantial blood loss (unlikely in the ambulatory venue) and for patients at risk for anemia or polycythemia, such as children younger than 1 year or with suspected sickle cell disease, patients with a history of anemia, blood dyscrasia or

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malignancy, patients with congenital heart disease or chronic disease, women with heavy menstrual flow, and patients older than 60 years old. Additional testing depends on an individual's preexisting condition. For example, serum electrolyte testing would be indicated for a patient with a history of hypertension, diabetes mellitus, renal disease, or for those patients taking diuretics, digoxin, steroids, or angiotensin-converting enzyme inhibitors. Likewise, measurement of the partial thromboplastin time (PTT) and the prothrombin time (PT) would be indicated in the presence of a bleeding disorder, anticoagulant use, liver disease, or poor nutritional status. Preoperative urinalysis has not been shown to be useful as a screening test and is no longer required in a routine anesthetic evaluation.

Bader AM, Hepner DL. Update on preprocedure testing. In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:8-13.

Finegan BA, Rashiq S, McAlister FA, et al. Selective ordering of preoperative investigations by anesthesiologists reduces the number and cost of tests. *Can J Anaesth*. 2005;52:575-580.

Mollov JL, Twersky RS. Is routine preoperative pregnancy testing necessary? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:26-30.

B.5. Which outpatients should receive a preoperative chest roentgenogram?

Abnormalities in the chest x-ray in asymptomatic patients are rare, and the risks to the patient probably exceed the benefits. A preoperative chest x-ray is indicated only for patients with a history or clinical findings of active pulmonary disease. Extremes of age, smoking, stable chronic obstructive pulmonary disease, stable cardiac disease, or resolved recent upper respiratory infection should not be considered absolute indications for chest x-ray.

American Society of Anesthesiologists Task Force on Preanesthesia Evaluation. Practice advisory for preanesthesia evaluation: a report by the American Society of Anesthesiologists task force on preanesthesia evaluation. *Anesthesiology* 2002;96:485-496.

Hata TM, Hata JS. Preoperative patient assessment and management. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:583-611.

Joo HS, Wong J, Naik VN, et al. The value of screening preoperative chest x-rays: a systematic review. *Can J Anaesth*. 2005;52:568-574.

B.6. In which patients is an electrocardiogram (ECG) necessary before outpatient anesthesia and surgery?

It has not been established that information obtained from the preoperative ECG affects clinical care. Indeed, the American College of Cardiology/American Heart Association (ACC/AHA) guidelines published in 2007 were silent on the need for a preoperative ECG based on age alone. According to the updated 2014 ACC/AHA guideline, a preoperative ECG is “reasonable for patients with known coronary artery disease, significant arrhythmia, peripheral arterial disease, cerebrovascular disease, or other significant structural heart disease, except for those undergoing low-risk surgery.” The 2014 guideline specifically states that a preoperative ECG is “not useful for asymptomatic patients undergoing low-risk surgical procedures.” The 2007 ACC/AHA guidelines considered ambulatory surgery as one entity, classifying *all* ambulatory procedures as low-risk, with reported cardiac mortality <1%. The 2014 version, however, defines a *low-risk* procedure as one in which the combined surgical and patient characteristics predict a risk of major adverse cardiac event (MACE) of death or myocardial infarction to be <1% and cites as examples cataract and plastic surgery. A further refinement in the 2014 guideline was to eliminate the separate categories of *intermediate risk* and *high risk*, substituting the category of *elevated risk*, reflecting procedures with a risk of MACE of ≥1%. These guidelines reflect the belief that in the absence of active cardiac conditions (defined as unstable coronary syndromes, decompensated heart failure, and significant arrhythmias [e.g., high-degree atrioventricular block, symptomatic ventricular arrhythmias,

and supraventricular tachycardia with uncontrolled ventricular rate]), cardiovascular testing in stable patients would rarely

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result in a change in management and it would be appropriate to proceed with surgery without further testing.

Nonetheless, Correll and colleagues found that age older than 65 years is an independent predictor of preoperative ECG abnormalities. In general, a preoperative ECG should be considered in ambulatory patients in whom there is a reasonably high likelihood of cardiac dysfunction and the results of the ECG would have the potential to influence perioperative management. Clearly, the patient's history, including a thorough exploration of activity level and exercise tolerance, the physical examination, and the proposed surgical procedure are vital elements in the assessment of whether an ECG is indicated.

Correll DJ, Hepner DL, Chang C, et al. Preoperative electrocardiograms: patient risk factors predictive of abnormalities. *Anesthesiology*. 2009;110:1217-1222.

Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. *Circulation*. 2007;116:1971-1996.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary. *J Am Coll Cardiol*. 2014;64:2373-3405.

Valentine EA, Fleisher LA. Who should have a preoperative 12-lead electrocardiogram? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology* . 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:20-25.

B.7. Would a patient's age or physical status influence the decision to perform outpatient surgery?

Even patients at the extremes of age (e.g., younger than 6 months and older than 80 years) have been managed successfully at ambulatory centers throughout the country. With the exception of the former preterm infant and newborns in the first few weeks of life, age alone should not be considered a deterrent in the selection of patients for outpatient surgery. Premature infants (gestational age at birth <37 weeks) who undergo general anesthesia during the first months of life are at increased risk for postoperative apnea for up to 12 hours. This risk is greatest for infants younger than 46 weeks postconceptional age, but some investigators have reported apnea in infants as old as 60 weeks postconceptional age. Unfortunately, the postconceptional age at which the former premature infant no longer represents an increased risk for postoperative apnea and, therefore, would be considered an acceptable candidate for an ambulatory surgical procedure is not absolutely known. Thus, at the present time, it is safest to admit to a hospital or to a 24-hour recovery unit all former premature infants less than 46 weeks postconceptional age so that they can be monitored for apnea. Many anesthesiologists are more conservative and adhere to cut-offs ranging from 52 to 60 weeks postconceptional age. If anemia, bronchopulmonary dysplasia, or other neonatal problems are present, this period may need to be extended. Likewise, postoperative apneic episodes have been described in otherwise healthy full-term infants who are anesthetized in the first few weeks of life. For this reason, many anesthesiologists are reluctant to proceed with outpatient anesthesia and surgery on a healthy full-term infant of younger than 2 to 4 weeks of age.

For the geriatric patient, recent clinical experience has not demonstrated an age-related effect on the duration of recovery or the incidence of postoperative complications after outpatient surgery. However, in determining the acceptability of a geriatric patient for an ambulatory surgical procedure, one must consider the patient's physiologic age and physical status, the surgical procedure, the anesthetic technique, and the quality of care that will be provided at home. Chronologic age per se is not a determinant of suitability for ambulatory surgery.

No longer is outpatient surgery restricted to patients of American Society of Anesthesiologists (ASA) physical status I and II. ASA physical status III and IV patients whose diseases are well controlled preoperatively may be considered acceptable candidates for outpatient surgery.

Everett LL. How young is the youngest infant for outpatient surgery? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:523-528.

Lerman J. Pediatric anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1217-1256.

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McGoldrick KE. Anesthesia considerations for the geriatric outpatient. In: Silverstein JH, Rooke GA, Reeves JC, et al, eds. *Geriatric Anesthesiology*. 2nd ed. New York: Springer; 2008:322-337.

B.8. What patients would be considered inappropriate for ambulatory surgery?

An individual may be classified as an inappropriate ambulatory surgery patient for the following reasons:

- The existence of a condition that places an infant at risk
- History of prematurity in an infant less than 46 to 60 weeks postconceptional age
- Apneic episodes, feeding difficulty, or failure to thrive
- Respiratory distress syndrome (RDS) that has required intubation and ventilatory support (may take up to a year for symptoms to resolve)
- Bronchopulmonary dysplasia (BPD) with any degree of significant decrease in pulmonary function or requirement for supplemental oxygen
- Acute concurrent illness
- ASA physical status III or IV with poorly controlled disease
- Active cardiac conditions, as defined by ACC/AHA guidelines
- Acute substance abuse
- Morbid obesity with other serious systemic diseases, such as severe obstructive sleep apnea and ventricular dysfunction
- Placement of a bare metal stent within 4 to 6 weeks of the proposed surgery
- Placement of a drug-eluting stent less than at least 1 year before the date of proposed surgery
- No available adult at home
- Refusal to have surgical procedure done as an outpatient
- Unwilling to follow instructions

The appropriateness of each patient must be evaluated on an individual basis, taking into account a combination of several factors, such as the patient's circumstances, the nature of the surgical procedure, anesthetic technique, anticipated severity of postoperative pain, and comfort level of the anesthesiologist.

American Society of the Anesthesiologists Committee on Standards and Practice Parameters. Practice alert for the perioperative management of patients with coronary artery stents. A report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology*. 2009;110:22-23.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guidelines on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary. *J Am Coll Cardiol*. 2014;64:2373-3405.

Lerman J. Pediatric anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1217-1256.

Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guidelines for percutaneous coronary intervention: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *Circulation*. 2011;124:2574-2609.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed.

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Philadelphia, PA: Lippincott Williams & Wilkins; 2013:844-859.

McGoldrick KE. Anesthesia considerations for the geriatric outpatient. In: Silverstein JH, Rooke GA, Reeves JC, et al, eds. *Geriatric Anesthesiology*. 2nd ed. New York: Springer; 2008:322-337.

Motovska Z. Management of antiplatelet therapy inpatients at risk for coronary stent thrombosis undergoing non-cardiac surgery. *Drugs*. 2011;71:1797-1806.

B.9. What questions are critically important to ask this patient when obtaining her history?

It is important to acquire as much information as possible about the patient's eye disease. For example, does she have open- or closed-angle glaucoma? What eye drops is she taking? When she had retinal detachment surgery 2 weeks ago, did the ophthalmic surgeon inject an air or gas bubble to tamponade the retina? If so, which substance was injected and has it been fully resorbed? Additionally, it is important to rule out obstructive sleep apnea in view of the patient's obesity, hypertension, and complaints of fatigue. Does she snore, have frequent awakenings during the night, and does she fall asleep commonly during the daytime? Not all patients with obstructive sleep apnea are appropriate candidates for ambulatory surgery. It is, therefore, important to probe this possibility further with an assessment instrument

such as the STOPBang questionnaire. A high score on that questionnaire indicates a high probability of obstructive sleep apnea. Moreover, obese patients with severe sleep apnea and certain associated conditions (pulmonary hypertension, ventricular dysfunction, etc.) having painful surgery under general anesthesia that may require significant amounts of opioids postoperatively for pain control are typically considered poor candidates for planned outpatient surgery.

American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on the management of patients with obstructive sleep apnea. *Anesthesiology*. 2014;120:268-286.

Chung F, Subramanyam R, Liao P, et al. High STOP-Bang score indicates a high probability of obstructive sleep apnoea. *Br J Anaesth*. 2012;108:768-775.

Joshi GP, Ankichetty SP, Gan TJ, et al. Society for Ambulatory Anesthesia consensus statement on preoperative selection of adult patients with obstructive sleep apnea scheduled for ambulatory surgery. *Anesth Analg*. 2012;115:1060-1068.

McGoldrick KE, Gayer SI. Anesthesia for ophthalmologic surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia.* 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1373-1399.

B.10. What instructions should the patient be given with regard to continuing or discontinuing enalapril in the perioperative period?

This is a somewhat controversial issue, perhaps especially for ambulatory surgery patients. Notable hypotension has been reported after induction of general anesthesia in patients continuing to take angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II subtype 1 receptor antagonists (ARBs) on the morning of surgery. A recent study, however, compared two groups of ambulatory and same-day admission patients who were taking either ACEIs or ARBs; one group took the ACEI or ARB on the day before surgery but not on the day of surgery, whereas the other group took the drug on the day of surgery at least 2 hours preoperatively along with other prescribed medications. The investigators found that discontinuing ACEIs and ARBs on the morning of surgery did not place patients at risk for preoperative hypertension, increased cancellations, unplanned admissions, or notable hypertension in the postoperative care unit. Moreover, patients who continued treatment on the day of surgery did not have more stable hemodynamics perioperatively than did those who discontinued these drugs. Although current opinion generally favors continuation of antihypertensive medications, especially β-blockers, up to the time of surgery, it would appear that discontinuing ACEIs and ARBs on the day of surgery is safe and does not increase the incidence of adverse hemodynamic outcomes. Specifically, the 2014 ACC/AHA

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guidelines state that continuation of ACEIs or ARBs perioperatively is “reasonable” and that if these drugs are held before surgery, it is “reasonable to restart as soon as clinically feasible postoperatively.”

Augoustides JGT. Should all antihypertensive agents be continued before surgery? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:48-54.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guidelines on perioperative cardiovascular and management of patients undergoing noncardiac surgery: executive summary. *J Am Coll Cardiol*. 2014;64:2373-3405.

Twersky RS, Goel V, Narayan P, et al. The risk of hypertension after preoperative discontinuation of angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists in ambulatory and same-day admission patients. *Anesth Analg*. 2014;118:938-944.

Wolf A, McGoldrick KE. Cardiovascular pharmacotherapeutic considerations in patients undergoing anesthesia. *Cardiol Rev*. 2011;19(1):12-16.

B.11. How would you premedicate this patient?

Whether the ambulatory surgical patient should receive premedication has been the subject of much interest and debate. Keeping in mind that a prompt recovery is an important consideration in outpatient anesthesia, many authors have recommended that little or no premedication (especially the centrally active depressant premedicants) be given to surgical outpatients so that recovery is not prolonged. Interestingly, most prospective clinical studies have failed to demonstrate a prolonged recovery following premedication with sedative-anxiolytic and analgesic drugs. However, narcotic premedicants have been shown to increase the incidence

of postoperative nausea, which could prolong recovery time, and are not recommended unless the patient is in pain preoperatively.

In view of the goals one might want to achieve with outpatient preoperative medication, including anxiety relief, sedation, amnesia, analgesia, vagolysis, prophylaxis against aspiration pneumonia, and prevention of PONV, premedicant drugs may be safely used if needed by the patient provided the drug and the dosage are carefully chosen. Drugs commonly used as premedicants for outpatients include sedative-hypnotics, opioids, anticholinergics, antacids, gastrokinetics, H_2-receptor antagonists, and antiemetics. Most prospective studies have not found recovery to be prolonged after the use of appropriate doses of sedative premedication (e.g., midazolam 1 to 2 mg intravenous). Indeed, proper use of premedication may actually expedite the discharge process as a result of its ability to reduce postoperative side effects. Clearly, however, lorazepam's very long duration of action makes it unsuitable for use in the ambulatory surgical patient.

Hata TM, Hata JS. Preoperative patient assessment and management. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:583-611.

B.12. Should every outpatient receive prophylaxis against acid aspiration pneumonitis?

Despite early studies demonstrating that a large percentage of outpatients are theoretically at risk for gastric aspiration, the actual incidence of pulmonary aspiration is very low (<1 per 35,000) in surgical patients with no specific risk factors. The possibility that outpatients have a greater potential for acid aspiration than inpatients had prompted several authors in the past to recommend that some form of aspiration prophylaxis be given to all patients scheduled for outpatient surgery. Unfortunately, this is costly and may result in undesired side effects. Although individual ambulatory surgery centers must determine their own policies, pharmacologic prevention of acid aspiration should not be routine but rather reserved for outpatients with predisposing factors (e.g., pregnancy, symptomatic hiatal hernia, diabetes mellitus with autonomic neuropathy). When antacids are used, they should be restricted to nonparticulate antacids.

American Society of Anesthesiologists Committee. Practice guidelines for perioperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective

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procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology*. 2011;114:495-511.

Hata TM, Hata JS. Preoperative patient assessment and management. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:583-611.

B.13. Is an overnight fast justified for all outpatients?

Several investigators have questioned the value of the traditional overnight fast for surgical outpatients, particularly pediatric outpatients. Prolonged fasting does not guarantee an empty stomach at the time of induction. It does, however, cause patient discomfort and may produce significant physiologic disturbances in infants and young children. Studies in children and in adults have shown no increase in volume or decrease in pH of gastric fluid when clear liquids were administered as late as 2 hours before induction of anesthesia. Therefore, arbitrary restrictions on the preoperative fast for surgical outpatients without risk factors for pulmonary aspiration, such as “nothing by mouth (NPO) after midnight,” appear to be unwarranted. Clear fluids in reasonable amounts (3 mL per kg) may be safely ingested until 2 hours before surgery. Although coffee is not transparent, it is devoid of particulate matter and is accepted as a clear liquid. There is some evidence that briefer periods of preoperative fasting (2 hours) are accompanied by less PONV as well as a reduced incidence of dizziness, drowsiness, and thirst. Breast milk should be withheld for at least 4 hours in neonates and infants who are being breastfed. Intake of nonclear liquids, nonhuman milk, and solid food should be discontinued at least 6 hours before the induction of anesthesia.

American Society of Anesthesiologists Committee. Practice guidelines for perioperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology*. 2011;114:495-511.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia.* 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:844-859.

C. Intraoperative Management

C.1. What are the important considerations in choosing an anesthetic technique for outpatient surgery?

- Smooth and rapid onset of action
- Intraoperative amnesia and analgesia
- Hemodynamic stability
- Good operating conditions
- Rapid recovery period without side effects
- Cost-effectiveness

To date, no “ideal” anesthetic drug or technique has been identified for outpatients. No single agent or combination of agents, either inhaled or intravenous, has been clearly demonstrated to reduce recovery time and allow faster discharge of the ambulatory surgical patient. However, with its smooth induction profile and short elimination half-life, propofol may prove to be the induction, if not the maintenance, agent of choice for outpatient anesthesia. The newer halogenated ether compounds, sevoflurane and desflurane, have become increasingly popular in ambulatory anesthesia owing to their rapid onset and quick termination of clinical effects. Currently, desirable anesthetic conditions with an acceptable recovery profile may be produced by a large array of pharmacologically active drugs administered in conjunction with either general, regional, or local anesthesia techniques. It is essential, however, to combine these agents in a rational manner and carefully titrate them to optimal effect.

Gupta A, Fleisher LA. What outcomes are important in ambulatory anesthesia? In: Steele SM, Nielsen KC, Klein

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SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia* . New York: McGraw-Hill; 2005:83-91.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:844-859.

C.2. What are the anesthetic implications of recent retinal detachment surgery?

Patients who have had vitreoretinal surgery often have a gas bubble deliberately left within the eye to help tamponade and keep the retina attached as adhesions develop. Filtered room air, sulfur hexafluoride (SF_6), and perfluoropropane (C_3F_8) are the most commonly used gases. By varying the concentration, volume, and type of gas used, bubbles can be produced that will last up to 70 days before being completely absorbed. If nitrous oxide is administered during this time, the bubble will rapidly expand with the attendant risk of retinal and optic nerve ischemia secondary to central retinal artery occlusion. Primate models indicate that irreversible retinal damage occurs after 100 minutes of retinal artery obstruction, suggesting that perhaps some recovery might be expected after briefer anesthetics. However, a narrower window may exist in humans. Therefore, nitrous oxide should be avoided in any patient who has undergone vitreoretinal surgery within the preceding 3 months, unless records are available to confirm that either intraocular gas was not used or that it has subsequently been completely reabsorbed.

Hart RH, Vote BJ, Borthwick JH, et al. Loss of vision caused by expansion of intraocular perfluoropropane (C3F8) gas during nitrous oxide anesthesia. *Am J Ophthalmol*. 2002;134:761-763.

Hayreh SS, Kolder HE, Weingeist TA. Central retinal artery occlusion and retinal tolerance time. *Ophthalmology*. 1980;87:75-78.

Lee EJ. Use of nitrous oxide causing severe visual loss 37 days after retinal surgery. *Br J Anaesth*. 2004;93:464-466.

McGoldrick KE, Gayer SI. Anesthesia for ophthalmologic surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1373-1399.

C.3. How would you monitor this patient?

The effects of anesthesia during ambulatory procedures should be monitored using the same standards applicable to inpatient procedures. Standard monitoring in this patient would include a blood pressure cuff, ECG, pulse oximeter, precordial or esophageal stethoscope, temperature probe, and measurement of inspired oxygen and end-tidal carbon dioxide.

The potential for hypoxia and hypercarbia during laparoscopy requires careful monitoring of oxygen saturation and expired carbon dioxide tension. In addition, intra-abdominal pressure must be measured during gas insufflation into the peritoneal cavity. Although standard intraoperative monitoring is appropriate for most outpatients having laparoscopic surgery, ASA physical status III or IV patients may benefit from invasive hemodynamic monitoring to carefully and continuously determine the cardiovascular response to pneumoperitoneum and position changes.

Joshi GP, Cunningham AJ. Anesthesia for laparoscopic and robotic surgeries. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1257-1273.

Muir HA, Olufolabi AJ. Ambulatory anesthesia for laparoscopic surgery. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia* . New York: McGraw-Hill; 2005:289-301.

C.4. What is the bispectral index (BIS) monitor, and what information does it convey?

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The BIS monitor is a noninvasive monitoring system that is derived from the electroencephalogram (EEG). Using bispectral analysis of the EEG waveform and other features within the EEG, the BIS monitor is used to detect changes in purported depth of anesthesia or hypnosis. A proprietary algorithm translates the complex data generated from the analysis of the EEG over a 30-second period into a single dimensionless number between 0 (i.e., no brain activity) and 100 (i.e., the patient is fully awake) that is displayed on the BIS monitor. The BIS is one of many brain function monitors that record or process brain electrical activity and convert these signals mathematically into a continuous measure, typically scaled from 0 to 100. It is important to appreciate that intraoperative awareness cannot be measured during the intraoperative phase of general anesthesia because the recall component of awareness can only be determined postoperatively by obtaining information directly from the patient. Moreover, although clinically important, intraoperative awareness under general anesthesia is a rare occurrence, with a reported incidence of 0.1% to 0.2% in adults.

American Society of Anesthesiologists Task Force on Intraoperative Awareness. Practice advisory for intraoperative awareness and brain function monitoring: a report by the American Society of Anesthesiologists Task Force on Intraoperative Awareness. *Anesthesiology*. 2006;104(4):847-864.

Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. *N Engl J Med*. 2008;358:1097-1108.

Kent CD, Domino KB. Depth of anesthesia. *Curr Opin Anaesthesiol*. 2009;22:782-787

Sebel PS, Bowdle TA, Ghoneim MM, et al. The incidence of awareness during anaesthesia: a multicenter United States study. *Anesth Analg*. 2004;99:833-839.

C.5. What benefits might be derived from using a BIS monitor?

Information about the patient's hypnotic state obtained from the BIS, in combination with other monitored parameters and clinical signs, may allow better balancing of hypnotic and analgesic administration. Titration of hypnotic agents based on individual requirements arguably is improved, potentially reducing the incidence of relative under- and overdosing. Furthermore, selection of anesthetic interventions (e.g., administration of hypnotics, analgesics, and vasoactive drugs) may be more rational. Reduced drug usage, earlier awakening, and faster recovery have all been associated with using the BIS monitor to help guide anesthesia maintenance. This translates into a higher potential for bypassing the stage 1 postanesthesia care unit (PACU) and earlier discharge eligibility from the PACU. It is not known yet whether these benefits will ultimately reduce medical costs significantly. Indeed, a recent meta-analysis based on 1,380 subjects from 11 trials disclosed that BIS monitoring reduced anesthetic consumption by 19%, reduced the incidence of nausea/vomiting, and reduced time in the PACU by 4 minutes. However, these benefits did not lead to a significant reduction in time until patient discharge from the ambulatory surgery unit. Additionally, BIS monitoring actually increased the cost per patient by $5.55 owing to the cost of the BIS electrodes.

Recently, there has been considerable discussion about depth of anesthesia and 1-year mortality. The investigators in the B-Aware Trial reported their secondary analysis of longterm mortality and found that the absence of low BIS values (BIS <40 for >5 minutes) was

associated with improved long-term survival and reduced morbidity (myocardial infarction, stroke). However, this putative association does not imply causation. Preoperative comorbidity is an important independent risk factor for postoperative mortality.

It has recently been shown, not surprisingly, that patients with a history of intraoperative awareness are at increased risk to develop the complication again. These patients, and others at high risk of intraoperative awareness (e.g., use of total intravenous anesthesia, patients having trauma surgery or cesarean delivery, patients with refractory hypotension), may well benefit from BIS monitoring. That said, it should be acknowledged that other modalities can be used to monitor purported anesthetic depth. These include, but are not limited to, endtidal anesthetic concentration monitoring, auditory evoked potentials, and entropy.

Aranake A, Gradwohl S, Ben-Abdallah A, et al. Increased risk of intraoperative awareness in patients with a history of awareness. *Anesthesiology*. 2013;119(6):1275-1283.

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Leslie K, Myles PS, Forbes A, et al. The effect of bispectral index monitoring on long-term survival in the B-aware trial. *Anesth Analg*. 2010;110:816-822.

Liu S. Effects of bispectral index monitoring on ambulatory anesthesia: a meta-analysis of randomized controlled trials and a cost analysis. *Anesthesiology*. 2004;101:311-315.

Mashour GA, Kent C, Picton P, et al. Assessment of intraoperative awareness with explicit recall: a comparison of 2 methods. *Anesth Analg*. 2013;116:889-891.

Pavlin JD, Souter KJ, Hong JY. Effects of bispectral index monitoring on recovery from surgical anesthesia in 1,580 inpatients from an academic medical center. *Anesthesiology*. 2005;102:566-573.

C.6. Is BIS monitoring applicable to children?

The BIS was developed and tested on adults. Because the EEG in infants and young children is different from that of an adult and changes as the brain matures, the BIS value may not necessarily apply to the pediatric patient population. Validating the BIS monitor in infants and young children poses significant problems. End points used to confirm BIS in adults, such as assessment of sedation, sleep, or purposeful movement in response to voice commands, cannot be reliably obtained in young children. Furthermore, there are serious ethical problems in recruiting healthy children as volunteers in studies of general anesthesia. Nevertheless, recent data from numerous authors comparing BIS values between adults and children at various clinical end points during general anesthesia, such as before anesthesia, during maintenance, at emergence, and with increasing concentrations of volatile anesthetic, suggest that BIS generally performs similarly in adults and children with respect to dose response to anesthetic agents. However, a recent study disclosed that in children, aged 6 months to 12 years, the BIS increased paradoxically as end-tidal sevoflurane concentration increased from 3% to 4%. BIS values showed a wide variation at the same end-tidal sevoflurane concentration, and the age of the patient was considered to be a factor affecting the BIS values. A consensus seems to be forming that BIS monitoring should be used with caution in infants younger than 1 year of age. Clearly, further work in this area is needed. Definitive studies correlating level of sedation, awareness, and anesthetic outcome with BIS in children have not yet been published. Nonetheless, consensus is emerging that the incidence of intraoperative awareness is greater in children than adults. Children, however, seem to be less disturbed by the experience than adults who appear to be more vulnerable to the development of posttraumatic stress.

Bannister CF, Brosius KF, Sigl JC, et al. The effect of bispectral index monitoring on anesthetic use and recovery in children anesthetized with sevoflurane in nitrous oxide. *Anesth Analg*. 2001;92:877-881.

Blussé van Oud-Alblas HJ, van Dijk M, Liu C, et al. Intraoperative awareness during paediatric anaesthesia. *Br J Anaesth*. 2009;102:104-110.

Davidson AJ, Huang GH, Czarnecki C, et al. Awareness during anesthesia in children: a prospective cohort study. *Anesth Analg*. 2005;100:653-661.

Davidson AJ, Huang GH, Rebmann CS, et al. Performance of entropy and bispectral index as measures of anaesthesia effect in children of different ages. *Br J Anaesth*. 2005;95:674-679.

Davidson AJ, Smith KR, Blussé van Oud-Alblas HJ, et al. Awareness in children: a secondary analysis of five cohort studies. *Anaesthesia*. 2011;66(6):446-454.

Kim HS, Oh AY, Kim CS, et al. Correlation of bispectral index with end-tidal sevoflurane concentration and age in infants and children. *Br J Anaesth*. 2005;95:362-366.

C.7. What are the major limitations of BIS monitoring?

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The BIS monitor is not a measure of global anesthetic depth. It is only a measure of the patient's level of sedation and hypnotic state. As such, it helps the anesthesiologist assess the potential for patient awareness, but it cannot prevent it. In fact, use of the BIS has not been proved definitively to reduce or eliminate the risk of intraoperative awareness. The BIS will not predict patient movement or hemodynamic response to noxious stimulation nor will it predict the exact moment when consciousness will return. Sedation produced by both ketamine and nitrous oxide does not produce the expected decrease in BIS. The utility of BIS in patients with neurologic disease has not been adequately studied to validate its use in these patients. Finally, more work is necessary to establish whether BIS is an accurate measure of hypnosis in pediatric patients.

It is important to appreciate that a specific numerical value may not correlate with a specific depth of anesthesia. Moreover, the measured values do not have uniform sensitivity across different anesthetic drugs or types of patients. Artifacts may be introduced by electrocautery, lasers, warming devices, and other devices and circumstances. The BIS cannot be relied upon in all situations, including hypothermia, circulatory arrest, and brain death. Moreover, one small study recently reported that patient position may affect BIS readings, with the head-down position producing an increase in BIS value, and the head-up position being associated with a reduction in BIS value. Clearly, intraoperative monitoring of depth of anesthesia to minimize the risk of awareness should rely on multiple modalities, including clinical observations of purposeful or reflex movement, ECG tracing, blood pressure, heart rate, end-tidal anesthetic analyzer, and capnography.

The consensus of the ASA Task Force on Intraoperative Awareness is that brain function monitoring is not routinely indicated for patients undergoing general anesthesia and that the decision to use a brain function monitor should be made on a case-by-case basis by the individual practitioner for selected patients at increased risk.

American Society of Anesthesiologists Task Force on Intraoperative Awareness. Practice advisory for intraoperative awareness and brain function monitoring: a report by the American Society of Anesthesiologists Task Force on Intraoperative Awareness. *Anesthesiology*. 2006;104(4):847-864.

Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. *N Engl J Med*. 2008;358:1097-1108.

Barr G, Jakobsson JG, Owall A, et al. Nitrous oxide does not alter bispectral index: study with nitrous oxide as sole agent and as adjunct to i.v. anaesthesia. *Br J Anaesth*. 1999;82:827-830.

Bowdle TA. Can we prevent recall during anesthesia? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:332-337.

Chan MT, Gin T. What does the bispectral EEG index monitor? *Eur J Anaesthesiol*. 2000;17:146-148.

Kaki AM, Almarakbi WA. Does patient position influence the reading of the bispectral index monitor? *Anesth Analg*. 2009;109:1843-1846.

Wennervirta J, Salmi T, Hynynen M, et al. Entropy is more resistant to artifacts than bispectral index in braindead organ donors. *Intensive Care Med*. 2007;33:133-136.

C.8. What does a BIS reading of 56 mean?

The BIS scale is a dimensionless scale from 0 to 100. Typically, BIS values between 40 and 60 correspond with a moderate hypnotic state of general anesthesia and are associated with a low probability of patient consciousness. Deep sedation with a low probability of explicit recall occurs in the 60 to 70 BIS range, with higher values up to 85 associated with light to moderate sedation. A BIS number below 40 indicates a deep hypnotic state, with brain isoelectricity increasing as BIS approaches 0. As mentioned previously, however, there are multiple exceptions to these generalities, and the BIS is perhaps best thought of as a trend monitor rather than an “absolute” monitor of hypnotic depth.

Hemmerling TM, Migneault B. Falsely increased bispectral index during endoscopic shoulder surgery attributed to interferences with the endoscopic shaver device. *Anesth Analg*. 2002;95:1678-1679.

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Johansen JW, Sebel PS. Development and clinical application of electroencephalographic bispectrum monitoring. *Anesthesiology*. 2000;93:1336-1344.

C.9. What are the anesthetic options for laparoscopy?

In recent years, anesthesiologists have successfully employed local, regional, and general anesthesia for laparoscopy. Local and regional anesthesia offer the potential advantages of faster postoperative recovery and reduced postoperative complications. These techniques also avoid the postoperative discomforts of general anesthesia, such as sore throat, muscle pains, and airway trauma. However, steep Trendelenburg position, pneumoperitoneum, and surgical manipulation often make spontaneous ventilation difficult during local or regional anesthesia. In addition, the potential for postspinal headache and urinary retention may detract from the use of regional anesthesia in the outpatient. The vast majority of laparoscopic procedures continue to be performed under general endotracheal anesthesia. General anesthesia offers the advantages of elimination of patient anxiety, complete amnesia and analgesia, the ability to control ventilation, muscle relaxation, and a motionless operative field.

Alley E, Mulroy MF. Is regional anesthesia appropriate for outpatient surgery? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:404-409.

Joshi GP, Cunningham AJ. Anesthesia for laparoscopic and robotic surgeries. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1257-1273.

Muir HA, Olufolabi AJ. Ambulatory anesthesia for laparoscopic surgery. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia* . New York: McGraw-Hill; 2005:289-301.

C.10. Under what circumstances might spinal anesthesia be appropriate for outpatient laparoscopy?

The use of regional anesthesia for laparoscopic surgery is not widely practiced in the United States. However, selective spinal anesthesia has been described in several publications. This method is defined as the practice of using minimal doses of dilute intrathecal agents in order to anesthetize only the nerve roots supplying a specific area and to affect only the modalities that need to be affected. Many of these publications have involved the use of hypobaric solutions of 10 mg lidocaine with the addition of 10 μg fentanyl for gynecologic laparoscopy. This solution purportedly gives good to excellent operating conditions with minimal motor block and a brief recovery period. Typically, dorsal column function, proprioception, and touch remain intact perioperatively. Transient neurologic symptoms (TNS) have not been reported with the use of 10 mg hypobaric lidocaine with fentanyl, but TNS has been reported in conjunction with 20 mg intrathecal lidocaine. Recently, low-dose 3 mg levobupivacaine plus 10 μg fentanyl has been used successfully for selective spinal anesthesia in gynecologic outpatient laparoscopy. Clearly, this approach is best used for brief procedures where the surgeon does not require steep Trendelenburg positioning.

Ben-David B, Maryanovsky M, Gurevitch A, et al. A comparison of minidose lidocaine-fentanyl and conventional-dose lidocaine spinal anesthesia. *Anesth Analg*. 2000;91:865-870.

de Santiago J, Santos-Yglesias J, Giron J, et al. Low-dose 3 mg levobupivacaine plus 10 microg fentanyl selective spinal anesthesia for gynecological outpatient laparoscopy. *Anesth Analg*. 2009;109:1456-1461.

Vaghadia H, Viskari D, Mitchell GW, et al. Selective spinal anesthesia for outpatient laparoscopy. I: characteristics of three hypobaric solutions. *Can J Anaesth*. 2001;48:256-260.

C.11. What anesthetic agents would you use to induce and maintain general anesthesia in this patient?

A number of anesthetic agents in a variety of combinations can be used successfully to provide general anesthesia in this patient. A reasonable approach would be to induce anesthesia with propofol or a short-acting barbiturate, such as sodium

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thiopental, after a preinduction dose of a short-acting benzodiazepine. After intubation, anesthesia is maintained with a volatile anesthetic, such as sevoflurane or desflurane, and an air-oxygen mixture, supplemented with a short-acting narcotic as needed and a muscle relaxant. Alternatively, a total intravenous technique with propofol as the primary agent could be administered.

Joshi GP, Cunningham AJ. Anesthesia for laparoscopic and robotic surgeries. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1257-1273.

Muir HA, Olufolabi AJ. Ambulatory anesthesia for laparoscopic surgery. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia* . New York: McGraw-Hill; 2005:289-301.

C.12. Would you avoid the use of nitrous oxide in this ambulatory patient?

As mentioned in the preceding text, if the patient has an intraocular gas bubble that is not completely resorbed, nitrous oxide is contraindicated for fear of causing devastating visual damage. In the absence of this contraindication, the use of nitrous oxide, albeit somewhat controversial, could be considered. Traditionally, there had been concerns about its ability to diffuse into bowel lumen causing distension and to increase PONV. It has been shown that surgical conditions during laparoscopic procedures lasting 70 to 80 minutes were identical (bowel distension did not increase over time) regardless of whether nitrous oxide was used. In a laboratory study involving porcine subjects, nitrous oxide was shown to diffuse into a carbon dioxide peritoneum and the nitrous oxide fraction exceeded 29%, a level that can support combustion, within 2 hours. Therefore, the clinical risk associated with prolonged laparoscopy remains unclear. In fact, leakage of intraperitoneal gas and replacement with fresh carbon dioxide are likely to wash out nitrous oxide and reduce the risk of explosion. Although it had historically been held that nitrous oxide can contribute to PONV, conclusive evidence is lacking to demonstrate an important effect of nitrous oxide on the incidence of postoperative emesis after laparoscopic cholecystectomy or pelvic laparoscopy. A recent review and meta-regression analysis reported that the increase in PONV sometimes seen with administration of nitrous oxide depends on the duration of exposure and is clinically unimportant up to at least 1 hour of exposure. Therefore, any potential benefit from its elimination for surgical cases of limited duration must be balanced against the potential increased risk of intraoperative awareness.

Diemunsch PA, Torp KD, Van Dorsselaer T, et al. Nitrous oxide fraction in the carbon dioxide pneumoperitoneum during laparoscopy under general inhaled anesthesia in pigs. *Anesth Analg*. 2000;90:951-953.

Joshi GP, Cunningham AJ. Anesthesia for laparoscopic and robotic surgeries. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1257-1273.

Peyton PJ, Wu CY. Nitrous oxide-related postoperative nausea and vomiting depends on the duration of exposure. *Anesthesiology*. 2014;120:1137-1145.

C.13. Discuss the physiologic changes induced by laparoscopy.

Physiologic changes occur as a result of the pneumoperitoneum and the Trendelenburg position that are required during laparoscopy. Carbon dioxide or nitrous oxide can be used to produce the pneumoperitoneum. Insufflation of gas into the peritoneal cavity elevates intra-abdominal pressure and impairs venous return. As intra-abdominal pressure increases above 20 mm Hg, central venous pressure, arterial pressure, pulse pressure, and cardiac output all decrease. Although rare, severe hypotension and cardiac arrest have been reported. The pneumoperitoneum also sequesters blood in the legs, thereby decreasing the circulating blood volume. Vital capacity is significantly reduced as the diaphragm is displaced cephalad by the Trendelenburg position and pneumoperitoneum. Pulmonary compliance is decreased, functional residual capacity is diminished, and aeration of the lower lobes is compromised, predisposing the patient to the development of hypoxia and atelectasis. As the intraperitoneal gas is released and intraabdominal pressure decreases, all cardiovascular and respiratory parameters should return to normal.

Joshi GP, Cunningham AJ. Anesthesia for laparoscopic and robotic surgeries. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1257-1273.

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Muir HA, Olufolabi AJ. Ambulatory anesthesia for laparoscopic surgery. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia* . New York: McGraw-Hill; 2005:289-301.

C.14. In addition to the physiologic changes described in the preceding text, what other intraoperative complications are associated with laparoscopy?

Absorption of carbon dioxide used for peritoneal insufflation may produce hypercarbia, resulting in hypertension, hypotension, catecholamine stimulation, cardiac arrhythmias, and acidosis. Arrhythmias may also be produced by vasovagal reflexes. Hemorrhage accounts for nearly half of the complications from laparoscopy. Bowel injury and ischemia can occur. A cephalad shift of the mediastinum may cause the endotracheal tube to pass into a bronchus after the Trendelenburg position is assumed. Other complications include gas embolization,

tension pneumothorax, pneumomediastinum, perforation and electrical injury of organs, and passive regurgitation and aspiration.

Joshi GP, Cunningham AJ. Anesthesia for laparoscopic and robotic surgeries. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1257-1273.

Kim CS, Kim JY, Kwon JY, et al. Venous air embolism during total laparoscopic hysterectomy: comparison to total abdominal hysterectomy. *Anesthesiology*. 2009;111:50-54.

Muir HA, Olufolabi AJ. Ambulatory anesthesia for laparoscopic surgery. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia* . New York: McGraw-Hill; 2005:289-301.

C.15. Why is carbon dioxide the insufflation agent of choice for laparoscopy?

Carbon dioxide is the most commonly used agent for laparoscopy because it is more soluble in blood than air, oxygen, or nitrous oxide. The carbon dioxide-carrying capacity of blood is high owing to bicarbonate buffering and combination with hemoglobin and plasma proteins. Rapid elimination also increases the margin of safety in the event of intravenous injection of carbon dioxide. All of these properties contribute to the rapid reversal of the clinical signs of carbon dioxide embolism when treated properly. Therefore, the lethal dose of carbon dioxide is approximately five times greater than that of air.

Muir HA, Olufolabi AJ. Ambulatory anesthesia for laparoscopic surgery. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative analgesia* . New York: McGraw-Hill; 2005:289-301.

Wolf JS Jr, Carrier S, Stoller ML. Gas embolism: helium is more lethal than carbon dioxide. *J Laparoendosc Surg*. 1994;4:173-177.

C.16. What are some alternatives to carbon dioxide for laparoscopy?

Insufflation of inert gases, such as helium or argon, instead of carbon dioxide avoids the increase in $PaCO_2$ from absorption, thereby avoiding the need for hyperventilation. The ventilatory consequences of the increased intra-abdominal pressure persist, however. Although the hemodynamic consequences of pneumoperitoneum from inert gases are similar to those seen with carbon dioxide, the inert gases blunt the increase in arterial pressure but exacerbate the decrease in cardiac output. Unfortunately, the low blood solubility of the inert gases is concerning in the event of gas embolism.

Gasless laparoscopy, using abdominal wall lift from a fan retractor, is another alternative to carbon dioxide. This technique may be attractive for patients with severe cardiac or pulmonary disease because it avoids the respiratory and hemodynamic consequences of increased intra-abdominal pressure secondary to insufflation. However, gasless laparoscopy compromises surgical exposure and exacerbates technical difficulty.

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Goldberg JM, Maurer WG. A randomized comparison of gasless laparoscopy and CO_2 pneumoperitoneum. *Obstet Gynecol*. 1997;90:416-420.

Wolf JS Jr, Carrier S, Stoller ML. Gas embolism: helium is more lethal than carbon dioxide. *J Laparoendosc Surg*. 1994;4:173-177.

D. Postoperative Management

D.1. What are the common causes of nausea and vomiting in outpatients?

Nausea and vomiting are significant problems after ambulatory surgery, causing patient discomfort and delayed recovery and discharge from the ambulatory center. Prolonged vomiting is one of the most frequent causes of unexpected hospital admission from the ambulatory surgical facility and is a major cause of patients' dissatisfaction with their anesthesia care. Patients who have a history of motion sickness and a previous experience of PONV are more likely to develop postoperative emetic symptoms, as are patients who are obese or pregnant or have diabetes mellitus. PONV are common in children; the incidence decreases with age. Men and women are equally affected until puberty, when the incidence becomes considerably higher in women. Excessive anxiety and noncompliance with fasting can increase gastric volume and predispose patients to PONV. Interestingly, smoking has been shown to decrease the incidence of PONV.

The use of narcotic analgesics, particularly morphine and meperidine, as premedication, as part of the anesthetic technique, or postoperatively to control pain, increases the incidence of PONV after outpatient anesthesia. Methohexital is less likely than either thiopental or etomidate to cause postoperative nausea. Consistently, propofol was shown to have a low incidence of emetic symptoms postoperatively.

Although Apfel's scoring system to predict the likelihood of PONV emphasizes female gender, nonsmoking status, history of PONV or motion sickness, and narcotic administration as the major risk factors, Sinclair also identifies surgical issues. Surgical procedures such as breast augmentation, varicose vein stripping, laparoscopy, dilatation and curettage, strabismus correction, myringotomy and tympanostomy tube placement, and orchiopexy are associated with more PONV, with the incidence escalating with increasing surgical and anesthesia time. A recent study by Ruiz et al. found that the type of surgery, when categorized anatomically, was related to the incidence of PONV; patients having neurologic, head or neck, and abdominal surgery had the greatest likelihood of experiencing emesis in the postanesthesia care unit. In addition, pain, hypotension, and early ambulation are postoperative factors demonstrated to increase nausea and vomiting. Relief of pain often, but not always, relieves concomitant nausea.

Apfel C, Kranke P, Eberhart LH, et al. Comparison of predictive models for postoperative nausea and vomiting. *Br J Anaesth*. 2002;88:234-240.

Apfel CC, Läärä E, Koivuranta M, et al. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. *Anesthesiology*. 1999;91:693-700.

Gan TJ, Diemunsch P, Habib AS, et al. Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg*. 2014;118:85-113.

Ruiz JR, Kee SS, Frenzel JC, et al. The effect of an anatomically classified procedure on antiemetic administration in the postanesthesia care unit. *Anesth Analg*. 2010;110:403-409.

Sinclair DR, Chung F, Mezei G. Can postoperative nausea and vomiting be predicted? *Anesthesiology*. 1999;91: 109-118.

D.2. How would you pharmacologically prevent PONV in the susceptible

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ambulatory patient?

Because of concerns about medication cost and potential side effects, routine prophylactic administration of an antiemetic is not considered appropriate for all ambulatory surgical patients. Instead, antiemetic prophylaxis should be reserved for patients who are considered to be susceptible to developing PONV (see preceding text). A large number of medications have been used to prevent postanesthetic nausea and vomiting in the outpatient, some with only limited success. Unfortunately, the ideal medication for each patient is not known. Serotonin antagonists, such as ondansetron 4 to 8 mg intravenous in adults and 0.1 mg per kg intravenous in children, are highly effective, but their use as single agents in high-risk patients may not suffice. Droperidol has been shown to be effective, inexpensive, and without an increase in postoperative sedation when used in low doses, such as 0.625 to 1.25 mg in adults (or as low as 10 to 20 μg per kg). However, the U.S. Food and Drug Administration (FDA) issued a so-called black box warning on the use of droperidol for antiemetic prophylaxis owing to purported fears about prolongation of the QTc interval and subsequent potentially dangerous ventricular arrhythmias. Nonetheless, Charbit et al. documented that droperidol and ondansetron induce similar clinically relevant QTc prolongation and concluded that the safety of 5-hydroxytryptamine type 3 (5-HT_3) antagonists may not be superior to that of low-dose droperidol. Although the serotonin antagonists are classically believed to lack efficacy with regard to preventing or treating nausea, the newest 5-HT_3 blocker, palonosetron, appears to reduce its severity, and the extended benefits of palonosetron may last up to 3 days, given its long half-life. In addition, palonosetron purportedly has no QT-interval issues.

Prophylactic administration of dexamethasone, 5 to 10 mg intravenous in adults and 0.5 to 1 mg per kg intravenous in children, is effective in the prevention of PONV and appears to offer no evidence of any clinically relevant toxicity. Combining dexamethasone with a serotonin antagonist further decreases the incidence of nausea and vomiting and may prove to be the best prophylactic regimen, although optimal doses of this combination are not currently known. Transdermal scopolamine effectively reduces PONV if given as a premedicant well in advance of the surgery, but the high incidence of anticholinergic side effects and prolonged

residual effects on cognitive performance, especially in the elderly, detract from its usefulness in the ambulatory patient.

Aprepitant is a highly selective, brain-penetrating neurokinin-1 receptor antagonist that is effective against centrally induced emesis. A recent study showed that aprepitant was superior to ondansetron for prevention of vomiting in the first 24 to 48 hours, but no notable differences were detected between aprepitant and ondansetron for nausea control, use of rescue drugs, or complete response.

Because the etiology of PONV is multifactorial, there is increasing evidence that a multimodal approach may lead to improved outcomes. Double and triple antiemetic combinations, using drugs with different mechanisms of action, are recommended for patients at high risk of PONV. Moreover, liberal hydration and effective analgesia play an important role in reducing the incidence of PONV. General anesthesia with volatile agents should be avoided, if possible, in high-risk patients. If general anesthesia is necessary, a total intravenous approach with propofol may be advantageous. Moreover, if rescue therapy for PONV is needed within 6 hours of surgery, patients should not receive a repeat dose of the drug that was administered prophylactically. Rather, a rescue drug with a different mechanism of action should be selected.

Apfel CC, Kranke P, Katz MH, et al. Volatile anesthetics may be the main cause of early but not delayed postoperative vomiting: a randomized controlled trial of factorial design. *Br J Anaesth*. 2002;88:659-668.

Charbit B, Albaladejo P, Funck-Brentano C, et al. Prolongation of QTc interval after postoperative nausea and vomiting treatment by droperidol or ondansetron. *Anesthesiology*. 2005;102:1094-1100.

Gan TJ, Apfel CC, Kovac AL, et al. A randomized, double-blind comparison of the NK_1 antagonist, aprepitant, versus ondansetron for the prevention of postoperative nausea and vomiting. *Anesth Analg*. 2007;104:1082-1089.

Gan TJ, Diemunsch P, Habib AS, et al. Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg*. 2014;118:85-113.

Habib AS, Gan TJ. What is the best strategy for prevention of postoperative nausea and vomiting? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology* . 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:294-300.

Kovac AL, Eberhart L, Kotarski J, et al. A randomized, double-blind study to evaluate the efficacy and safety of three

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different doses of palonosetron versus placebo in preventing postoperative nausea and vomiting over a 72-hour period. *Anesth Analg*. 2008;107:439-444.

Kranke P, Eberhart LH. Possibilities and limitations in the pharmacological management of postoperative nausea and vomiting. *Eur J Anaesthesiol*. 2011;28:758-765.

D.3. How is postoperative pain treated?

Pain control is one of the most important factors in determining when a surgical outpatient can be discharged. Pain should be treated rapidly and effectively to minimize postoperative symptoms so that ambulation and discharge are not delayed. The optimal strategy is to use a preemptive, multimodal approach. Begin controlling postoperative pain intraoperatively by supplementing the anesthetic technique with a short-acting narcotic analgesic or a regional block. Intravenous fentanyl is usually the drug of choice for postoperative pain relief. It may be given in small doses of 12.5 μg at 5-minute intervals and titrated to relief of pain. Ketorolac, a nonsteroidal anti-inflammatory drug, has become increasingly popular in the management of postoperative pain in the ambulatory patient because of its lack of opioidrelated side effects (e.g., sedation, nausea, vomiting, respiratory depression). It is available for oral and parental administration, and its use may decrease a patient's requirement for opioid analgesics. Controversy still surrounds the perioperative use of ketorolac because of the potential for bleeding complications and renal dysfunction. Local and regional anesthetic techniques can be used to provide effective postoperative analgesia and, when used to supplement general anesthesia, facilitate a pleasant emergence and minimize the need for opioids. Commonly used techniques include local infiltration of the incision site, intra-articular injection, nerve blockade (e.g., dorsal nerve penile block for circumcision, or ilioinguinal and iliohypogastric nerve blocks for inguinal hernia repair), and caudal blocks. A few years ago, bupivacaine liposomal injectable suspension, formulated using the DepoFoam® lipid-based delivery system, was approved for administration into the surgical site after bunionectomy and hemorrhoidectomy, offering long-acting analgesia without opioid-associated side effects. When the patient has resumed intake of oral fluids, oral analgesics (e.g., acetaminophen,

nonsteroidal anti-inflammatory drugs, as well as codeine and other opioid analgesics) may be administered for control of pain after discharge.

Golf M, Daniels SE, Onel E. A phase 3, placebo-controlled trial of DepoFoam® bupivacaine (extended-release bupivacaine local analgesic) in bunionectomy. *Adv Ther*. 2011;28(9):776-788.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:844-859.

D.4. If the patient complained of eye pain postoperatively, how would you manage the situation?

Pain due to corneal abrasion is the most common ocular complication of general anesthesia. Patients with a corneal abrasion usually complain of a foreign-body sensation, pain, tearing, and photophobia. The pain is typically exacerbated by blinking and ocular movement. It is wise to have an ophthalmologic consultation immediately. Treatment typically consists of the prophylactic application of antibiotic ointment and possibly patching the injured eye shut. Although permanent sequelae are possible, healing usually occurs within 24 hours.

If the patient complains of intense pain, he or she should be scrupulously observed for signs of red eye, corneal edema, and a fixed mid-dilated pupil as well as complaints of blurred vision. These are characteristic signs of acute ACG, a serious emergency. Ophthalmologic consultation should be secured immediately to acutely decrease IOP with systemic and topical therapy. Topical pilocarpine 2% is administered to cause miosis and pull the iris taut and away from the trabecular meshwork. A topical β-blocker also should be considered. If a prompt reduction in IOP does not ensue, systemic therapy with an agent such as mannitol should be considered, but its potentially adverse hemodynamic effects should be weighed in a patient with cardiovascular disease. If medical therapy is effective in reducing IOP to a safe level and the angle opens, an iridotomy/iridectomy can be performed immediately, or it can be delayed until the corneal edema resolves and the iris becomes less hyperemic. Failure to act effectively and expeditiously in cases of ACG could result in blindness. The excruciating periorbital pain typically described in these patients is an important aid in differential diagnosis.

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Patients with open-angle glaucoma can also experience an acute glaucoma attack after surgery, but the IOP tends to be lower than that seen with ACG. The eye characteristically appears pale, dry, and firm, and the patient generally complains of a dull, periorbital headache. Treatment includes topical miotics and 5 to 7 mg per kg of acetazolamide intravenously. If the patient does not respond to medical therapy, laser trabeculoplasty may be necessary. Should laser treatment be ineffective, conventional filtration surgery, placement of a Molteno valve, or a coablative procedure may be indicated.

McGoldrick KE, Gayer SI. Anesthesia for ophthalmologic surgery. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1373-1399.

McGoldrick KE, Kosarussavadi B. Increased intraocular pressure. In: Atlee JL, ed. *Complications in Anesthesia.* Philadelphia, PA: WB Saunders; 1999:765-768.

D.5. What criteria would you use to establish that a patient can be safely discharged after ambulatory surgery?

For patients to be discharged from an ambulatory facility, they must satisfy specific criteria that are usually summarized on simplified checklists. Although each ambulatory surgical facility must determine its own set of criteria, generally accepted guidelines for safe discharge home after ambulatory surgery include the following:

- Stable vital signs
- No evidence of respiratory depression
- Oriented to person, place, and time
- Able to walk unassisted
- Able to dress unassisted
- Minimal nausea or vomiting
- No active bleeding or oozing

- Pain controllable with oral analgesics
- Responsible adult to escort patient home and to remain with the patient overnight
- Discharge by both the person who administered anesthesia and the person who performed surgery, or their designees. Written instructions for the postoperative period at home must be supplied to the patient before discharge as well as a phone number to call in the case of emergency

The requirement for patients to drink and void before discharge is no longer considered mandatory, except in the case of certain patients who had central neuraxial blockade (see subsequent text).

Chinnappa V, Chung F. What criteria should be used for discharge after outpatient surgery? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology* . 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:343-351.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:844-859.

D.6. How would you decide when to discharge a patient after regional anesthesia?

Patients recovering from regional anesthesia must satisfy the discharge criteria listed in the preceding text. In addition, if spinal or epidural anesthesia has been used for outpatients, it is important to ensure recovery from the sympathetic and the motor blocks. Hypotension and syncope on standing may be signs that the sympathetic nervous system is still blocked. An indication that the motor block is no longer functioning is the ability to move the legs and feet freely. A simple test is to have the patient run each heel up and down the opposite leg from the big toe to the knee. A patient's ability to walk to the bathroom and void are excellent recovery tests after epidural or spinal anesthesia because these abilities reflect recovery of both the motor and the sympathetic functions.

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Recently, Mulroy et al. have suggested that delaying discharge for voiding after spinal or epidural anesthesia with *short-acting local anesthetics* is unnecessary in *low-risk* patients (e.g., age younger 70 years; no hernia, rectal, or urologic surgery; no history of voiding problems). Nonetheless, appropriate measures must be in place for bladder catheterization if the inability to void persists after discharge home. The use of ultrasonographic monitoring of bladder volume before discharge may reduce the incidence of urinary retention after the patient returns home.

Chinnappa V, Chung F. What criteria should be used for discharge after outpatient surgery? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology* . 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:343-352.

Darrah DM, Griebling TL, Silverstein JH. Postoperative urinary retention. *Anesthesiol Clin*. 2009;27(3):465-484.

Mulroy MF, Salinas FV, Larkin KL, et al. Ambulatory surgery patients may be discharged before voiding after short-acting spinal and epidural anesthesia. *Anesthesiology*. 2002;97:315-319.

Pavlin DJ, Pavlin EG, Gunn HC, et al. Voiding in patients managed with or without ultrasound monitoring of bladder volume after outpatient surgery. *Anesth Analg*. 1999;89:90-97.

D.7. What instructions should be given to an ambulatory surgical patient upon discharge?

Patients should be discharged to the care of a responsible adult. Additionally, they should be instructed that after surgery, they should not ingest an alcoholic beverage or depressant medication unknown to their surgeon or anesthesiologist, drive a car, or operate complex machinery for at least 24 hours. In addition, the discharge instructions should provide a list of problems that require immediate notification of the surgeon (e.g., bleeding that does not stop, inability to void, and persistent PONV).

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:844-859.

Marshall SI, Chung F. Discharge criteria and complications after ambulatory surgery. *Anesth Analg*. 1999;88:508-517.

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Chapter 62
Magnetic Resonance Imaging

Jung Hee Han

A 2-year-old boy weighing 15 kg is scheduled for a preoperative magnetic resonance imaging (MRI) of his brain for ongoing seizures with possible craniotomy with intraoperative MRI (iMRI) the following week. The technician reports that an attempt to obtain a scan last week was unsuccessful because of patient movement despite adequate sedation by the pediatrician. The child's past medical history is remarkable for partial tonic-clonic seizures since age 1 year. The child was born full term with no complications at birth and is otherwise healthy. Medications include carbamazepine and valproic acid, both of which were taken the night prior. Nothing orally (NPO) status has been maintained for at least 6 hours.

A. Medical Disease and Differential Diagnosis

1. What is magnetic resonance imaging (MRI), and how does it work?
2. What are some advantages of MRI?
3. What are some disadvantages associated with MRI? What are some safety concerns?
4. What are the contraindications to MRI?
5. What are the biologic effects of clinical MRI?
6. What are the anesthetic considerations for this procedure?
7. What is intraoperative MRI (iMRI)? What is real-time MRI, and in what setting can this be used?

B. Preoperative Evaluation and Preparation

1. What type of patients may require sedation or general anesthesia for a magnetic resonance (MR) examination?
2. What preoperative laboratory testing would you require for this patient?
3. How would you premedicate this patient?

C. Intraoperative Management

1. What are some of the anesthetic options for this patient?
2. How is an MRI conducted?
3. How would you monitor this patient?
4. What special considerations apply to the monitoring equipment used during MRI?
5. How would you induce and maintain general anesthesia in this patient?
6. How would you maintain the airway during the scan?
7. What are the advantages of the supraglottic airway (SGA) compared with the face mask?
8. What are the advantages of the SGA compared with the endotracheal tube (ETT)?
9. What complications are associated with the use of the SGA?
10. What are the contraindications to the use of the SGA?

11. What are the indications for the use of the SGA?
12. Examination of the patient before the table is fed into the MRI scanner reveals wheezing. What most likely is happening, and what do you do?

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D. Postoperative Management

1. When is the SGA removed?
2. How will you have the patient recover from anesthesia?
3. What is emergence delirium (ED) and how do you evaluate it? What has been shown to help decrease ED?

A. Medical Disease and Differential Diagnosis

A.1. What is magnetic resonance imaging (MRI), and how does it work?

MRI is primarily a noninvasive diagnostic technique that uses the magnetic properties of atomic nuclei to produce high-resolution, multiplanar cross-sectional images of the body. In certain fields of medicine though, MRI is being utilized as an interventional aid in diagnosis or in disease therapy, in lieu of conventional approaches. Atoms having an odd number of protons and/or neutrons in their nuclei, for example, hydrogen, have an associated electrical charge, and the net rotation of protons or neutrons produces a local magnetic field similar to the electromagnetic field produced by the flow of electrons in a wire loop. Normally, the magnetic fields surrounding these nuclei are randomly oriented. When placed in the setting of a powerful static magnetic field of the MRI scanner, the nuclei align themselves longitudinally so they lie parallel or antiparallel to the magnetic field.

Within the MRI, a specific radiofrequency (RF) pulse of energy (a second magnetic field) is directed toward the patient at right angles to the static magnetic field, thereby displacing the orientation of the aligned nuclei from the longitudinal magnetic field. As the RF pulse is removed, the nuclei return to their original magnetic alignment positions. This is termed *relaxation*. The energy released from the tissue as the nuclei relax is termed an RF signal. It can be detected by the receiver coil of the scanner and used to produce the MR image. There are two ways to measure relaxation time. T1 relaxation represents the time to revert to the resting magnetic state, and T2 relaxation represents the time to revert to the resting axial spin. These values vary for specific body tissues, especially water and fat. This allows for differentiation of body structures as well as between normal and pathologic tissue. Different atoms respond to different RFs, with the response being proportional to the strength of the static magnetic field. Hydrogen is present in high concentrations in biologic tissues and is the atom most often used for imaging. Resolution of the image requires a strong magnetic field. The magnetic field strength used to quantify the scanners is in tesla units. One tesla is equivalent to 10,000 gauss. Most MRI scanners used now have a magnetic field of 0.5 to 3.0 T (the magnetic field of the earth is 5×10^{-5} T). Weaker field scanners have the advantage of having an open construction, whereas the stronger closed ones generate better image quality. Some research scanners vary in strength from 4 T to 9.4 T. The magnetic field of an MRI takes several days to establish. Therefore, it is constantly applied even in the absence of a patient, and it is deactivated only in an absolute emergency.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:883.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:2660.

Patteson SK, Chesney JT. Anesthetic management for magnetic resonance imaging: problems and solutions. *Anesth Analg*. 1992;74:121-128.

A.2. What are some advantages of MRI?

The advantages of MRI include the lack of ionizing radiation, the capability of using noniodinated intravenous contrast agent, and the production of multiplanar, temperature sensitive, contrast amplified images. MRI also provides excellent resolution of normal tissues (e.g., gray and white matter and soft tissues) without image artifact from bone, and it can differentiate

between normal and pathologic tissue. MRI may be used to evaluate blood and cerebrospinal fluid flow, to assess contraction and relaxation of organs such as the heart, and to provide images of tissues in proximity to bone because calcium does not interfere with MRI.

MRI-guided intervention is another major potential advantage in cases where conventional computed tomography (CT)

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imaging is lacking. These images of the soft tissues and tumors are exceptionally delineated, thus facilitating interventions for biopsies of these areas. In addition, tumor ablation via cryoablation modalities has been performed safely in some centers in the MRI suite. MRI offers better capture of the temperature-related changes that occur during cryoablation and has been effectively used in safely treating liver, kidney, breast, and prostate tumors as well as in uterine fibroids.

MRI has also proven advantageous during interventional electrophysiology studies and catheter ablation procedures. The MRI offers structural real-time three-dimensional (3D) images of the anatomy, presence of scar tissues in the heart and the nearby structures, and exact localization of the ablation catheter. It can also delineate any potential gaps in ablation for a successful therapy. Delayed enhancement (DE) MRI is currently the gold standard for outlining the scar/fibrosis in the heart that potentially may serve as an arrhythmogenic source for patients with ventricular tachycardia (VT). Based on the staging of atrial fibrosis, DE MRI can also provide vital preprocedural information in extrapolating those patients who might be at risk for relapse of atrial fibrillation. In experienced hands and centers, this real-time MRI provides vital information that traditional fluoroscopy could not supply in a radiation-free environment.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:883.

Eitel C, Hindricks G, Grothoff M, et al. Catheter ablation guided by real-time MRI. *Curr Cardiol Rep*. 2014;16(8):511.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:2660.

A.3. What are some disadvantages associated with MRI? What are some safety concerns?

There are many hazards associated with an MRI suite. The constant static magnetic field, the pulsed (time-varied) gradient magnetic fields, and the high-frequency RF waves all interact and when combined with a ferromagnetic object can pose significant risk to the patient or operator. Not only can the attraction of these external objects become fatal but also implantable objects can dislodge and malfunction or burn the patient. Depending on the distance from the core of the magnet, the magnetic field strength diminishes. Distances less than five gauss line can make pacemakers malfunction. Distances less than 50 gauss line can make ferromagnetic gas cylinders become lethal projectile missiles.

Owing to the potential for catastrophic events, recommendations for MRI safety have been proposed by the American College of Radiology. Briefly, the MRI suite should be separated into four zones: zone I is the public zone immediately outside the MRI suite, zone II is the reception area monitored by MRI personnel, zone III encompasses the control room with access to this area being restricted from the public, and zone IV is the physical MRI scanner room. To ensure everyone's safety, entry into zones III and IV should be screened by MRI personnel. Ferromagnetic objects should not be brought into zone III, but if necessary, they should be brought in with extreme caution. Items such as credit cards, pens, keys, laryngoscopes, scissors, stethoscopes, paper clips, and ferromagnetic gas cylinders should be excluded from zone IV. At Weill Cornell Medical Center, all oxygen E-gas cylinders have been replaced by aluminum cylinders to further ensure patient and personnel safety. Adherence to these zones must be maintained especially during emergent situations.

Safety terminology for devices and implants were devised by the U.S. Food and Drug Administration (FDA), Center for Devices and Radiologic Health in 1997 to distinguish the safety of the device (MRI safe) and the compatibility of the device (i.e., the lack of artifacts on the exam) in a particular MR environment (MRI compatible). Over the years though, these labels were potentially being misused, and due to safety concerns, a set of new terminologies were developed by the American Society for Testing and Materials (ASTM) International.

MR safe refers to items with no known hazards in any MR environment. *MR conditional* refers to items that pose no known hazards in a specified MR environment (i.e., strength of the magnetic field). *MR unsafe* refers to items that pose definite hazards in all MR environments (i.e., ferromagnetic scissors). Concerns about a specific device and its potential hazards should be addressed by the staff members, on-site radiologist, and/or manufacturer to determine whether the exam can be conducted in a safe manner.

Obviously, with the growing use of implantable medical devices (e.g., pacemakers, vascular clips, implantable cardioverter-defibrillators [ICDs], mechanical heart valves, and implanted infusion pumps), a potential exists for injury to the patients. Most anesthesiologists agree that MR should not be conducted on patients with an implanted device, but that

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is not an absolute. In 2011, MR conditional pacemakers and leads became available and are available in the United States. They are approved in certain settings and up to 1.5 T MRI examinations. Nevertheless, the majority of cardiac implantable devices are not MR safe, so caution must be used. Currently, there are no ICDs that are MR conditional. Clips used in vascular surgery and neurosurgery must be verified and the model, and type of clip needs to be documented. All intracranial aneurysm clips manufactured after 1995 that the company identifies it as MR conditional need no further testing. Clips manufactured before 1995 require some pretesting and may need the approval of an MR attending radiologist. Despite a prior MR history of a patient, variations can occur in different magnetic fields under the influence of different pulsed frequencies; so, verification may still be needed.

In addition to these devices, many patients have stents, filters, and grafts. Coronary artery stents, especially after 2007, are proven safe for patients having an MRI procedure at ≤3 T with an average whole-body specific absorption rate (SAR) of 2.0 to 4.0 W per kg for 15 minutes of scanning time. Most aortic stent grafts are MR safe, but the Zenith AAA and the TAA endovascular graft (Cook Medical, Bloomington, IN) are MR conditional, and their timing for scanning needs to be individualized. Coil embolization materials, such as platinum, iridium, and nitinol, have been shown to be safe for MR examinations. Most heart valves and annuloplasty rings can be safe under certain conditions, that is, ≤3 T, but if possible, delay the scan for up to 6 weeks after implantation.

Recently, the ASTM has deemed certain cochlear implants as MR conditional and may be safe if the patient is older than 8 years of age and ≤1.5 T is utilized. Care must be taken with patients containing shrapnel and bullets; there may be potential risks if it is ferromagnetic due to movement and heating near vital organs. Patients with implanted stimulators need to be investigated, and some may be MR unsafe or conditional. MRI may be performed on a limited basis for patients with certain deep brain stimulators and vagal nerve stimulators. In each case, care must be individualized and decisions made with the on-site level 2 MR attending radiologist.

Other disadvantages of the MRI include the potential for malfunction of electronic equipment (e.g., monitors and infusion pumps) as well as limited access to the patient. MR safe/conditional monitors and machines should be used in the scanner. Thermal injuries have been reported from electrocardiogram (ECG) electrodes and pulse oximeter probes. All cables and monitoring equipment should be placed in a straight manner without coiling to ensure no such injuries. MR safe/conditional infusion pumps can be used in zone IV, but otherwise, pumps can be left in zone III and the tubing passed through a wave guide. The relatively long scan time necessary to obtain images (as much as 15 minutes per image, with a total scanning period of 1 to 3 hours) and image degradation from any motion including cardiac contractions, respirations, cerebrospinal fluid flow, and bowel peristalsis are additional disadvantages.

Another potential hazard to both the patients and the operators is the high decibels levels of sound emanating from the scanner due to the RF pulses (>90 dB). Hearing protection for both is mandatory even if the patient is under anesthesia. Due to the small bore of most MR scanners (i.e., 50 to 60 cm in diameter), scanning obese patients may be impossible and a sense of claustrophobia and anxiety can be experienced.

Baikoussis NG, Apostolakis E, Papakonstantinou NA, et al. Safety of magnetic resonance imaging in patients with implanted cardiac prostheses and metallic cardiovascular electronic devices. *Ann Thorac Surg*. 2011;91:2006-2011.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:883.

Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document on MR safe practices: 2013. *J Magn Reson Imaging*. 2013;37:501-530.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:2660-2661.

Ocazionez D, Dicks DL, Favinger JL, et al. Magnetic resonance imaging safety in cardiothoracic imaging. *J Thorac Imaging*. 2014;29:262-269.

Practice advisory on anesthetic care for magnetic resonance imaging: a report by the American Society of Anesthesiologists task force on anesthetic care for magnetic resonance imaging. *Anesthesiology*. 2009;110:459-479.

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A.4. What are the contraindications to MRI?

Patients with certain implanted biologic devices, such as pacemakers, ICDs, and certain pumps, should be excluded from MRI studies because of the possibility of device malfunction, inactivation, or damage in the magnetic field. In an MR environment, the device may be moved, rotated, dislodged, or accelerated toward the magnetic core. In the case of certain metallic devices (i.e., leads), they can act as an “antenna” and concentrate the RF energy, which can lead to thermal injuries. Fractured leads are absolutely contraindicated due to the high risk of thermal injuries. The safety of various cardiovascular devices for MR examination was reviewed based on ex vivo, animal, and in vivo studies and reported by the American Heart Association (AHA). Although many coronary stents, peripheral stents, sternal wires, inferior vena cava filters, prosthetic heart valves, and annuloplasty rings have been deemed MR safe or conditional, it is important to review each type carefully and decide whether the proposed MR exam is in line with the specified milieu for the particular device. Currently, the AHA and the American Society of Anesthesiologists (ASA) practice advisory task force on the anesthetic care for MRI regard the presence of a pacemaker or an ICD as a strong relative contraindication to routine MR examination. Although some MR conditional pacemakers and leads are available, the majority are still MR contraindicated. MR is currently contraindicated in patients with an artificial heart or ventricular assist device.

If the benefits far outweigh the risks of the exam, then the scanning should be performed in an experienced center with expertise in MR imaging and electrophysiology. The care of the patient should be performed in collaboration with the cardiologist, radiologist, device manufacturer, and the technician. Written consent must detail all risks to the patient including death. Full resuscitation equipment must be readily accessible in the MRI suite in case of an arrhythmia or equipment malfunction. For a more thorough evaluation of these devices, please refer to the recommendations in the reference article or online at www.MRIsafety.com. Orthodontic braces and dentures and tattoos or cosmetics that contain metallic dyes, although safe, can degrade the image quality significantly.

Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document on MR safe practices: 2013. *J Magn Reson Imaging*. 2013;37:501-530.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:2660-2661.

Ocazionez D, Dicks DL, Favinger JL, et al. Magnetic resonance imaging safety in cardiothoracic imaging. *J Thorac Imaging*. 2014;29:262-269.

Practice advisory on anesthetic care for magnetic resonance imaging: a report by the American Society of Anesthesiologists task force on anesthetic care for magnetic resonance imaging. *Anesthesiology*. 2009;110:459-479.

A.5. What are the biologic effects of clinical MRI?

Although an area of controversy and ongoing investigation, most human data to date suggest that there are no significant deleterious effects to patients or health care professionals from exposure to the static magnetic field of an MRI. However, MRI capabilities were developed relatively recently (the 1960s), and epidemiologic evidence of harmful exposure may not yet be apparent. It seems prudent, therefore, to limit repetitive and readily avoidable exposure to the magnetic field.

Also controversial is the use of MRI during pregnancy because the effects of magnetic fields on the human fetus cannot be easily determined. However, current evidence does not

support the suggestion that routine clinical exposure of the pregnant patient to MRI can cause developmental abnormalities in the fetus. Pregnant patients have undergone MRI safely during all stages of pregnancy. Nevertheless, caution is advised. Studies have shown that gadolinium-based contrast agents enter the fetal circulation and are filtered in the fetal kidneys into the amniotic fluid. It is unclear the duration of the substance in the fluid, but it can potentially form free gadolinium ions that can theoretically pose risks to the developing fetus. The appropriateness of MRI examination and the acuteness of the diagnostic need must be considered. Ultrasonography use is preferred if it can provide equivalent diagnostic information, and consideration should be given to postponing the MRI until late in the pregnancy or until after delivery.

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MR contrast agents have fewer side effects when compared to iodinated contrast agents. However, there are some potential reactions with gadolinium-based contrast agents among patients with moderate to severe chronic renal disease. Patients with severe chronic renal disease, hepatorenal syndrome, and/or patients with perioperative liver transplant have developed “nephrogenic systemic fibrosis (NSF),” which can be fatal. NSF primarily involves the skin, but other organs such as the liver, heart, lungs, diaphragm, and skeletal muscle can be affected. Care must be taken when considering the use of MR contrast agents in these patients. If a pediatric patient with advanced renal disease requires gadolinium, the FDA suggests prompt hemodialysis be considered.

Chernoff D, Stark P. Principles of magnetic resonance imaging. http://www.uptodate.com/contents/principles-of-magnetic-resonance-imaging. Accessed August 11, 2015.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:973.

Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document on MR safe practices: 2013. *J Magn Reson Imaging*. 2013;37:501-530.

Perazella MA. Nephrogenic systemic fibrosis, kidney disease, and gadolinium: is there a link? *Clin J Am Soc Nephrol*. 2007;2:200-202.

A.6. What are the anesthetic considerations for this procedure?

The problems that complicate the anesthetic management of any patient outside the operating room environment exist for patients requiring sedation or general anesthesia for MRI. The MRI suite is often located some distance from the operating room and the anesthesia department, thus limiting the availability of backup assistance and supplies. As with any remote anesthetizing location, the personnel may not be familiar with the requirements of anesthetized patients, thereby decreasing their ability to provide assistance. Frequently, the MRI suites have been designed without the consideration for anesthetic needs, such as pipeline gases, suction, or an anesthetic exhaust system. Access to a recovery suite for postanesthesia care may not be readily available, thereby necessitating a trip to the main recovery room.

In addition, there are anesthetic challenges unique to the MRI suite. Because of the bulkiness of the unit, the patient is often far removed from the anesthesiologist and access to the airway is limited. Intravenous lines, anesthesia circuits, oxygen tubings, and monitoring cables must be of sufficient length to reach the patient deep within the scanner. The strong magnetic field necessitates the exclusion of all ferromagnetic objects and equipment. The displays of standard monitoring devices can be distorted or displaced by the magnetic field and the monitors themselves can degrade the MR image by disturbing the signal/noise ratio. The ASA Task Force understands that the interpretation of the ECG may be limited due to the superimposed voltages from blood flow in a high magnetic field (i.e., ST-segment interpretation unreliable even with filters). Safe monitoring conditions must be maintained with MR safe/conditional monitors and remote monitoring and must be in compliance with ASA standards.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:884.

Practice advisory on anesthetic care for magnetic resonance imaging: a report by the American Society of Anesthesiologists task force on anesthetic care for magnetic resonance imaging. *Anesthesiology*. 2009;110: 459-479.

A.7. What is intraoperative MRI (iMRI)? What is real-time MRI, and in what setting can this be used?

Since 1993, image-guided surgery systems have been introduced that combine the resources of an operating room with MRI technology and high-performance computing. Several low-, mid-, and high-field strength interventional MR systems have been developed that permit access to the patient by surgeons and provide near real-time imaging during surgical

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procedures. iMRI furnishes the surgeon with the simultaneous combination of direct vision and beyond-the-surface MRI, allowing for more accurate localization and targeting during surgery. In addition, iMRI allows the surgeon to detect the full extent of lesions, to devise a surgical approach that is safe with less potential operative morbidity, and to monitor for unseen hemorrhage. In some cases, iMRI may obviate the need for postoperative imaging that may necessitate additional sedation for pediatric patients. In addition to tumor resections, iMRI can be utilized in the surgical revascularization of moyamoya arteriopathy and during the management of arteriovenous malformations (AVMs), placement of deep brain stimulator for Parkinson disease and other movement disorders, evaluation of hematomas, and resection of epileptogenic foci. Other fields of medicine that incorporate iMRI include surgeries of the liver, pancreas, and kidneys as well as radiation therapy guidance when tumors shift. Not surprisingly, iMRI systems are expensive and require the need for MRIcompatible surgical instruments and monitoring equipment. One of the largest challenges anesthesiologists face in this setting is dealing with the high-energy iMRI-generated electrical noise that can interfere with the ECG signal on the monitor. Unlike in an MRI suite, there are multiple people and objects to account for when the iMRI unit is brought out and engaged around the patient. All personnel working in an iMRI environment must take MRI safety courses to ensure the patient's safety as well as their own personal safety. During the duration of the scan, the anesthesiologist has limited or no access to the patient, and visualization of the patient may be limited when enclosed in an electrical noise shield. All ferromagnetic objects, such as laryngoscopes, stylets, and beepers, must be left outside the operating room or placed in a secure area. Lastly, as opposed to an MR exam in a dedicated suite, the anesthetic considerations for iMRI must also include the needs of the ongoing complex surgical procedure.

As opposed to iMRI, real-time MRI integrates exceptional soft tissue visualization in a 3D anatomic and functional manner with delineation of suspected lesions without the exposure to radiation. In the electrophysiology suite, the use of real-time MRI has allowed for a number of catheter ablation procedures for the treatment of and the risk stratification of various arrhythmias, with the reduction in fluoroscopy usage. In addition, DE MRI is the gold standard for scar and fibrosis mapping, which serves as an arrhythmogenic source for VT. This preprocedural MRI may be difficult to obtain, as these patients often have ICDs, which are considered contraindicated for MRI. DE MRI can also be used to predict potential atrial fibrillation ablation failure based on the amount of left atrial fibrosis that is present. After an intervention, MRI can help identify complications, such as pulmonary vein stenosis and esophageal injury. MRI thermography is another useful tool used to show tissue heating during RF ablation.

There are still a lot of hazards with real-time MRI and iMRI. Special MRI conditional and safe monitors, devices, and catheters need to be utilized to avoid catastrophe in the patient. Currently, no acute defibrillation or cardioversion can be performed in the MRI scanner.

Dzwonczyk R, Fujii JT, Simonetti O, et al. Electrical noise in the intraoperative magnetic resonance imaging setting. *Anesth Analg*. 2009;108:181-186.

Eitel C, Hindricks G, Grothoff M, et al. Catheter ablation guided by real-time MRI. *Curr Cardiol Rep*. 2014;16(8):511.

Henrichs B, Walsh RP. Intraoperative MRI for neurosurgical and general surgical interventions. *Curr Opin Aanesthesiol*. 2014;27:448-452.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:2660-2661.

B. Preoperative Evaluation and Preparation

B.1. What type of patients may require sedation or general anesthesia for a magnetic resonance (MR) examination?

Although MRI is painless, patients must remain still throughout the time required to make each scan (as much as 15 minutes) in order to obtain images free of movement artifacts. Patients who are unable to cooperate adequately (e.g., infants, young children, and adults who are confused, mentally ill, or intellectually subnormal) usually require an anesthesiologist to help reduce movement during the examination. Small infants may tolerate the procedure well if fed before the examination and swaddled in a blanket. Oral chloral hydrate is an excellent agent for sedation by

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nonanesthesiologists. Especially with CT scans, chloral hydrate has been shown to be effective in children younger than 3 years, although caution is needed in neonates since they have impaired metabolism. Side effects of this drug may include unpleasant taste, skin irritation, excessive sedation, agitation, or respiratory depression. Most children younger than 5 years of age and as old as 11 years of age require some form of sedation or general anesthesia. Not only children need anesthesia; 30% of adult patients experience some form of anxiety during MR scanning. Anesthesiologists are frequently managing claustrophobic or anxious adults as well as those requiring either airway protection (unconscious or critically ill patients) or mechanical ventilation (patients with head injuries or elevated intracranial pressure) to ensure that an adequate examination is obtained safely and efficiently.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:884.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:41.

Wu J, Mahmoud M, Schmitt M, et al. Comparison of propofol and dexmedetomedine techniques in children undergoing magnetic resonance imaging. *Pediatr Anaesth*. 2014;24:813-818.

B.2. What preoperative laboratory testing would you require for this patient?

For a routine MRI examination in this child, no preoperative laboratory tests would be required as long as anticonvulsant medications have been stable with documented adequate serum levels.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:38.

B.3. How would you premedicate this patient?

The goals of premedication for this child would be to provide anxiolysis and facilitate the induction of anesthesia without exacerbating a seizure. At Weill Cornell Medical Center, ambulatory pediatric patients are not routinely given pharmacologic premedicants; rather, it is our practice to allow a parent to be present at the time of induction, in order to help allay the child's anxiety and ease the induction. If one elects to administer a sedative drug to this child, a logical choice would be oral midazolam (0.5 mg per kg, maximum 10 mg) in a small amount of cherry or strawberry syrup. We find that oral chloral hydrate is effective in children younger than 12 months of age but not including neonates. It is dosed at 80 to 100 mg per kg, depending on scan duration. Currently, commercially prepared chloral hydrate is no longer available in the United States, but a powdered version is available and can be reconstituted for oral use.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:39-41.

C. Intraoperative Management

C.1. What are some of the anesthetic options for this patient?

Many different anesthetic techniques have been used for anesthetizing children undergoing MRI or other painless radiologic procedures. These range from simple sedation, with orally administered chloral hydrate, rectally administered barbiturates, or intramuscularly administered meperidine/promethazine/Thorazine, to deep sedation, with intravenous ketamine/propofol/dexmedetomidine, or general anesthesia, with inhaled anesthetics.

Because conscious sedation of children is frequently insufficient to prevent patient movement, deeper levels of sedation or general anesthesia are required to successfully anesthetize the pediatric patient for MRI. The ideal anesthetic should allow the anesthesiologist the ability to titrate and maintain stable drug concentrations in order to prevent undesired patient movement during the scan and to provide rapid rates of induction and recovery with a minimal requirement for special MRI-compatible equipment.

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Intravenous anesthesia with propofol meets several of the aforementioned criteria, and it can be an excellent technique for MRI. Continuous intravenous infusion of propofol allows for a precise, rapid titration to the desired effect and provides for a rapid recovery. Propofol use eliminates the need for a nonferromagnetic, MRI-compatible anesthesia machine and for a scavenger of waste anesthetic gases, both of which are the major drawbacks of an inhalational technique. Ketamine, although considered a potent bronchodilator with minimal respiratory depression, can increase salivation. This, especially in children, can cause upper airway obstruction, laryngospasm, and microaspiration, even in the presence of relatively intact upper airway reflexes. In addition, ketamine may elicit undesirable myoclonic movements, increased intracranial pressure, and ED, especially at higher intravenous dosages and in ages younger than 2 and older than 13 years. Recently, dexmedetomidine is another alternative for sedation. No major respiratory effects are known with this agent, although hemodynamic side effects can occur, especially at higher dosing regimens. Wu et al. compared propofol and dexmedetomidine infusions for sedation in MRI and concluded that for longer scans, the dexmedetomidine group had longer induction times and overall hospital times than the propofol group. Due to potential hemodynamic side effects, such as hypotension and bradycardia, and with life-threatening complications when used with digoxin, dexmedetomidine should be used cautiously in patients with cardiac compromise.

Another viable alternative to deep sedation with intravenous agents would be general anesthesia with inhalational anesthetics. In children younger than 3 years of age or in patients with comorbidities requiring or necessitating airway management, general anesthesia may be the preferred choice.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:884-885.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:966, 971-973.

Schulte-Uentrop L, Goepfert MS. Anaesthesia or sedation for MRI in children. *Curr Opin Anaesthesiol*. 2010;23:513-517.

Wu J, Mahmoud M, Schmitt M, et al. Comparison of propofol and dexmedetomedine techniques in children undergoing magnetic resonance imaging. *Pediatr Anaesth*. 2014;24:813-818.

C.2. How is an MRI conducted?

The patient is placed on a long, thin table outside the scanner. After obtaining an adequate level of anesthesia, the patient is positioned. If the head is to be examined, it is often enclosed within a small coil or tube. Next, the table with the patient is fed into the long tube of the MRI magnet. The portion of the body to be examined is usually centered in the magnet approximately 1 m from the end of the tube. During the examination, the delivery of the RF pulses produces a loud thumping noise, which can average 95 dB in a 1.5 T scanner. To obtain a high-quality scan, the patient must refrain from moving during the acquisition of an individual cut or from changing position at any time during the entire examination. An individual scan can take several minutes, and the total scanning time may be from 1 to 3 hours. Body surfaces can absorb some of the RF energy during the sequence, but this is unlikely to increase the patient's core temperature by more than 1°C. Nevertheless, the SAR of energy in the body as measured in watt per kilogram is monitored. Depending on the patient, if the SAR is too high, the sequence may need to be aborted and adjusted.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:884.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:966, 971-973.

Peden CJ, Menon DK, Hall AS, et al. Magnetic resonance for the anaesthetist. Part II. Anaesthesia and monitoring in MR units. *Anaesthesia*. 1992;47:508-517.

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C.3. How would you monitor this patient?

Reliable and accurate monitoring of an unconscious individual during an MRI is essential because the patient cannot be seen adequately or accessed easily by the anesthesiologist. During sedation, the ASA standard monitors including blood pressure, pulse oximetry, and ECG need to be used. ECG electrodes should be placed together and toward the middle of the magnetic field, and the leads should be insulated from the patient's skin to avoid any potential thermal injuries. During general anesthesia, capnography and temperature should also be monitored. The assessment of ventilation in a spontaneously breathing patient may be difficult especially when the patient is within the magnet and far from view. Monitoring end-tidal carbon dioxide from one limb of the nasal oxygen prongs or through a nasal catheter is frequently successful. Pulse oximetry is a marker for oxygenation and should not be used as a marker for ventilation. Use of an MRI-compatible precordial stethoscope may be unsatisfactory due to the length of tubing required and the loud noise of the MRI scanner. Hypothermia can be problematic, especially in the pediatric patient. Because of the high airflow through the scanner cavity, the patient should be covered in blankets. Hyperthermia can also occur, and if suspected based on SAR, the sequence may need to be temporarily stopped. Temperature monitoring can be accomplished by using nonferromagnetic temperature strips or probes with RF filters when feasible. It is currently not mandatory for the anesthesiologist to remain in the scanner room during the examination as long as remote monitoring with direct vision of the patient is possible.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:884.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:2660.

Practice advisory on anesthetic care for magnetic resonance imaging: a report by the American Society of Anesthesiologists task force on anesthetic care for magnetic resonance imaging. *Anesthesiology*. 2009;110:459-479.

C.4. What special considerations apply to the monitoring equipment used during MRI?

Unshielded ferromagnetic materials within monitors and cables can interfere with imaging signals, causing a distortion of MRI results and burns. Similarly, the RF signals of the scanner can induce currents in ferromagnetic elements of the monitors, causing a distortion of the monitoring signal and making the monitor unusable. Fortunately, the use of MR safe/conditional monitors and equipment (e.g., ECG electrodes) are preferable because they contain shielding nonferromagnetic components and filters to produce satisfactory results without a major distortion of signal. In addition, to avoid magnetic pull, monitors should be placed at least 5 to 8 ft from the magnet bore or be permanently mounted.

The ECG may show significant changes within a static magnetic field. In particular, the T waves and the late ST segments can mimic the ECG changes associated with conditions such as hyperkalemia and pericarditis. This is due to an induced voltage in blood (a conducting fluid) flowing through the magnetic field. These changes are directly related to field strength, but they do not appear to represent any significant physiologic alteration.

In addition, pulse oximeter cables must be nonconducting, fiberoptic, and MRI-compatible. The traditional pulse oximeter probes and attachment may contain metal; when adjacent to the patient, they may cause burns and injury.

The high RF power used in MR poses the risk of excessive heat at the monitoring sites. This can lead to potential thermal injury. To minimize the risk of burns from monitoring cables, one should do the following:

- Inspect the insulation on all monitoring wires to ensure that it is intact.
- Place cables and lead wires in straight alignment. Do not allow monitoring wires to form loops.
- Remove all leads or wires not in use.
- Separate cables from patient's skin.

- Keep the cable and sensor out of the scanning area (e.g., place a pulse oximeter probe on the toe of a patient whose chest is being examined).

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- Avoid excessive power.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:884.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:3226.

Peden CJ, Menon DK, Hall AS, et al. Magnetic resonance for the anaesthetist. Part II. Anaesthesia and monitoring in MR units. *Anaesthesia*. 1992;47:513-517.

C.5. How would you induce and maintain general anesthesia in this patient?

There are many different ways anesthesia can be induced in this child. Since this child does not have aspirational risk, an inhalational induction can be performed safely. With a parent present and pulse oximetry monitored, induction of anesthesia may be accomplished with an inhalational agent (e.g., sevoflurane) in nitrous oxide and oxygen through face mask in a room adjacent to the MRI scanner or at the greatest possible distance from the magnetic field within the scanner room. After the child has lost consciousness, the parent is escorted back to the waiting room. Intravenous access is then established, and all remaining monitors are placed. The anesthetic level is deepened with a loading dose of propofol (e.g., 1 to 2 mg per kg), and if needed, the airway is secured. If a breathing device such as an SGA or ETT is used, the pilot balloon on the cuff must be taped away from the patient to minimize artifact from the cuff's spring. Once under general anesthesia, the child is then moved into the scanner room and placed on the MRI table. The patient and monitors are carefully positioned before attempting to advance the table into the magnet bore. Anesthesia is maintained with either a continuous intravenous infusion of propofol or an inhalational agent combined with oxygen.

Alternatively, an intravenous catheter may be inserted first or after oral sedation with a sedative, and anesthesia induced with either intravenous propofol 3 mg per kg followed by a continuous infusion or any other intravenous induction agent, such as dexmedetomidine 2 to 3 μg per kg load over 10 minutes followed by an infusion of 1 to 2 μg/kg/hr.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:966, 971-974.

Frankville DD, Spear RM, Dyck JB. The dose of propofol required to prevent children from moving during magnetic resonance imaging. *Anesthesiology*. 1993;79:953-958.

Schulte-Uentrop L, Goepfert MS. Anaesthesia or sedation for MRI in children. *Curr Opin Anaesthesiol* . 2010;23:513-517.

Wu J, Mahmoud M, Schmitt M, et al. Comparison of propofol and dexmedetomedine techniques in children undergoing magnetic resonance imaging. *Pediatr Anaesth*. 2014;24:813-818.

C.6. How would you maintain the airway during the scan?

Limited access to the patient's airway is one of the greatest challenges for the anesthesiologist during an MR scan. In light of this, many propose that the airway be secured with either an ETT or SGA, especially in those whose airway might potentially be problematic. Respiration can be spontaneous or controlled depending on personal preference and the needs of the patient. According to the ASA Task Force, the literature is silent in regard to the management of airway problems (e.g., obstruction, hypoventilation, laryngospasm) during an MRI scan. As long as a plan is prepared should emergencies occur, any type of anesthetic can be used to accomplish the scan. Alternatively, total intravenous anesthetic with nasal cannula can be used in lieu of an intubation. This should be considered in patients with good natural airways whose ventilation is being monitored adequately. Infusions of propofol or dexmedetomidine can be considered in this situation. Placing a shoulder roll under the patient with the chin taped up may help prevent future airway obstruction during the MR scan. This should only be performed when there are no contraindications, such as potential spinal injuries with head and neck manipulations.

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Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:966, 971-974.

Practice advisory on anesthetic care for magnetic resonance imaging: a report by the American Society of Anesthesiologists task force on anesthetic care for magnetic resonance imaging. *Anesthesiology*. 2009;110:459-479.

C.7. What are the advantages of the supraglottic airway (SGA) compared with the face mask?

In general, when used as an alternative to the face mask, the SGA gives the anesthesiologist more freedom to perform other tasks (e.g., record keeping, monitoring, and drug administration) and decreases the incidence of operator hand fatigue. The SGA allows for more reliable capnography and is capable of maintaining higher hemoglobin oxygen saturations. The contamination of the MRI scanner room environment with inhalational anesthetics is reduced and less manipulation of the airway is required with an SGA. Furthermore, injury to the eyes and facial nerves may be reduced by the avoidance of a face mask and head strap.

Boehringer LA, Bennie RE. Laryngeal mask airway and the pediatric patient. *Int Anesthesiol Clin*. 1998;36(2):45-60.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:254.

C.8. What are the advantages of the SGA compared with the endotracheal tube (ETT)?

Although the SGA does not replace the ETT (especially in longer cases and when protection from aspiration is important), it has some advantages. The ease placement and a decreased in stimulation (i.e., less coughing, gagging, swallowing, breath holding, bronchospasm, and cardiovascular response) are two advantages of SGA over the ETT. Lighter levels of anesthesia can, therefore, be better tolerated with an SGA than with an ETT. In inexperienced hands, the SGA can be more rapidly and reliably placed than an ETT, suggesting a role in resuscitation. Trauma to the vocal cords is limited because the SGA does not pass through this area. In adults, the incidence of sore throat after SGA usage is reduced when compared with the ETT.

Brimacombe JR, Berry AM, White PF. The laryngeal mask airway: limitations and controversies. *Int Anesthesiol Clin*. 1998;36(2):155-182.

Landsman IS. The laryngeal mask airway. *Int Anesthesiol Clin*. 1997;35(3):49-65.

C.9. What complications are associated with the use of the SGA?

The most serious potential problem of the SGA device is the lack of tracheal protection from aspiration of gastric contents. In patients at low risk of regurgitation, the rate of aspiration during general anesthesia using an SGA is similar to that in all non-SGA general anesthetics (2 per 10,000 cases). Most authors recommend that it not be used in patients at high risk of regurgitation. Conversely, aspiration of pharyngeal contents has not been shown to be a problem with the SGA, and the use of the device has been reported to be suitable during ear, nose, and throat procedures and dental procedures. Odynophagia occurs in 4% to 12% of patients after SGA use, an incidence that is comparable to the use of a face mask with an oropharyngeal airway. This is still less than that associated with tracheal intubation, which is associated with a 30% incidence of odynophagia. Hoarseness, dysphagia, and several cases of recurrent, hypoglossal, and lingual nerve injury have been reported with SGA use. Cuff overinflation, unmonitored increases in cuff pressure secondary to nitrous oxide diffusion, light anesthesia with constriction of pharyngeal musculature, venous engorgement and tissue edema associated with the head-down position, and lidocaine gel lubricant have all been cited as causes of nerve injury.

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One fatal case has been reported with the use of an intubating SGA; an unrecognized esophageal tear from an accidental blind esophageal intubation resulted in septic shock and death 9 weeks postintubation. Although this complication was a result of the blind intubation, it nevertheless was associated with an SGA device.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:772.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:256.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:1662-1664.

C.10. What are the contraindications to the use of the SGA?

The following conditions contraindicate the use of the SGA:

- Increased risk of gastric regurgitation (i.e., full stomach, hiatal hernia, bowel obstruction, delayed gastric emptying, etc.)
- Limited ability to open the mouth or extend the neck (e.g., severe rheumatoid arthritis and ankylosing spondylitis), making advancement of the SGA into the hypopharynx difficult
- Low pulmonary compliance or high airway resistance
- Airway obstruction at or below the level of the larynx
- Oropharyngeal pathology (e.g., hematoma, abscess, and tissue disruption)
- Single-lung ventilation

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:772.

Landsman IS. The laryngeal mask airway. *Int Anesthesiol Clin*. 1997;35(3):49-65.

C.11. What are the indications for the use of the SGA?

The SGA is best suited for use in any patient in whom anesthesia can be safely maintained through a face mask (except in a patient with oropharynx pathology). It has been used routinely in various surgical procedures including minor gynecologic, urologic, orthopedic, bronchoscopic, and endoscopic diagnostic procedures. In addition, the device may be useful in surgery around the face in which the trachea is intubated solely due to the physical interference imposed by the face mask. Other types of surgery in which the SGA has been used successfully include dental extraction, adenotonsillectomy, repair of cleft palate, myringotomy and placement of tympanostomy tubes, and eye surgery. Furthermore, use of the SGA in the management of the difficult airway is increasing.

Asai T, Morris S. The laryngeal mask airway: its features, effects and role. *Can J Anaesth*. 1994;41:930-960.

C.12. Examination of the patient before the table is fed into the MRI scanner reveals wheezing. What most likely is happening, and what do you do?

Wheezing in the setting of an SGA can be caused by light anesthesia resulting in partial laryngospasm, bronchospasm, or malposition of the device with the tip of the mask encroaching on the glottis. This can be a result of inadequate depth of anesthesia. One should deepen the anesthetic either with topical, inhaled, or intravenous agents in the spontaneously breathing patient or administer muscle relaxant in the mechanically ventilated patient as an initial treatment. If the problem is not relieved, despite an adequate level of anesthesia and/or paralysis, the device should be removed and repositioned.

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Brimacombe JR. Problems with the laryngeal mask airway: prevention and management. *Int Anesthesiol Clin*. 1998;36(2):139-154.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:1663.

D. Postoperative Management

D.1. When is the SGA removed?

The removal of an SGA during the excitation stages of emergence may cause coughing and/or laryngospasm; therefore, it should be removed either when the patient is deeply anesthetized or awake. Suctioning of secretions from the pharynx is usually not necessary before removal of the SGA. If suctioning is to be performed, it is important to ensure that an adequate level of anesthesia is maintained to avoid unnecessary airway stimulation. The cuff of the SGA may be deflated before removal, or alternatively, it may be left fully inflated to scoop out the secretions collected above the mask as it is withdrawn. As with extubation of the trachea, equipment for managing airway emergencies must be immediately available.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:772.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:256-257.

D.2. How will you have the patient recover from anesthesia?

Postanesthesia recovery care after MRI is the same as that required after an anesthetic in the operating room. This can be accomplished in a designated area of the MRI suite provided that adequate facilities and trained personnel are available. For most, such a facility may not be available, and the patient will require transport to the main recovery room. To transport the patient quickly and safely, one must ensure that adequate personnel and the proper equipment are organized in advance. It is useful to have the location of recovery and logistics of transport (if necessary) planned before the procedure begins.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:981-982.

Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier/Churchill Livingstone; 2015:2925-2927.

D.3. What is emergence delirium (ED) and how do you evaluate it? What has been shown to help decrease ED?

ED is characterized as a maladaptive behavioral change in children, usually after surgery or anesthesia. It can be non-purposeful restlessness with agitation, and the patient may be thrashing about, crying uncontrollably, and disoriented. Some studies have reported that up to 18% of all pediatric patients undergoing surgery and anesthesia experience ED, especially when preoperative anxiety was present. Some studies have shown that oral premedication with midazolam decreases perioperative anxiety.

The severity of ED can be determined by applying the Paediatric Emergence Delirium Scale (PAED). Five items are examined: level of eye contact, purposeful actions, awareness of surroundings, restlessness, and inconsolability; scores are attributed from 0 to 4. It is understood that the higher the score, the more likely it is that the patient is experiencing ED. Scores of 12 or greater have shown greater sensitivity and specificity for ED. Some attributable risk factors may be of ages 2 to 5 years old and procedures involving the head, such as ear, nose, and throat (ENT) procedures. Some have shown that in nonpainful procedures, such as MRI, propofol for maintenance decreased the incidence of ED when compared to a sevoflurane maintenance group. Other agents such as dexmedetomidine and midazolam have been used

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as well to help decrease ED in pediatric patients, although there are many conflicting results regarding their effectiveness. Some report that an infusion of 0.2 μg/kg/hr of dexmedetomidine is effective in decreasing the incidence of ED without prolonging the time to extubation and discharge after a sevoflurane-based general anesthetic.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children* . 5th ed. Philadelphia, PA: Elsevier/Saunders; 2013:983-984.

Pieters BJ, Penn E, Nicklaus P, et al. Emergence delirium and postoperative pain in children undergoing adenotonsillectomy: a comparison of propofol vs sevoflurane anesthesia. *Paediatr Anaesth*. 2010;20:944-950.

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Chapter 63

Morbid Obesity, Obstructive Sleep Apnea, and Bariatric Anesthesia

Jon D. Samuels

Fun-Sun F. Yao

A 46-year-old woman was scheduled for elective laparoscopic sleeve gastrectomy. She had a past medical history significant for morbid obesity (MO) (height, 162.5 cm; weight, 176 kg; body mass index [BMI], 66.6 kg per m^2), Pickwickian habitus, mild rheumatoid arthritis, osteoarthritis, mild asthma, hypertension, adult-onset diabetes mellitus, peptic ulcer disease with symptomatic gastroesophageal reflux, and obstructive sleep apnea (OSA). She experienced daytime somnolence, heavy nighttime snoring, and had slept in a seated position for the previous 2 years. She was able to walk around the house with a cane but was unable to climb any stairs. A preoperative diagnostic polysomnogram was performed, and an apnea-hypopnea index (AHI) of 42 was calculated. Two weeks prior to surgery, home oxygen therapy with bilevel positive airway pressure (BIPAP) settings had been started at the following settings, with symptomatic improvement: FIO_2 of 0.40, respiratory rate 10 breaths per minute, inspired positive airway pressure (IPAP) of +12 cm H_2O, and expired positive airway pressure (EPAP) of +4 cm H_2O, spontaneous mode. Cardiology clearance was obtained as a high-risk candidate, after an echocardiogram revealed mild right-sided cardiomegaly and mild pulmonary hypertension. The patient's blood pressure was 155/82 mm Hg, pulse 60 beats per minute, and respirations 20 breaths per minute. The patient was determined to have a difficult airway based on a poor Mallampati score (class 3).

A. Medical Disease and Differential Diagnosis

1. What problems exist with this patient? This patient asks you if she is high-risk. What is the evidence?
2. Define the terms overweight, obesity, morbid obesity (MO), super obesity (SO), normal weight, and ideal body weight (IBW).
3. What is obstructive sleep apnea (OSA)? What are the risk factors for OSA?
4. How is OSA diagnosed? What is a sleep study, or polysomnogram (PSG)? How are results obtained from a PSG used to grade the severity of OSA?
5. How does OSA differ in the pediatric population in clinical presentation and pathogenesis?
6. What is the Pickwickian syndrome (PS)? What is the pathogenesis of severe OSA?
7. What is the association between obesity and OSA? What is the etiology of pharyngeal pathology in severe obesity?
8. What are the anesthetic implications of OSA?
9. What type of metabolic problems would you expect to find in morbidly obese patients? What is the role of leptin in obesity?

10. Describe the changes that occur in the following respiratory parameters in morbidly obese patients:
    - Pulmonary mechanics: tidal volume (V_T), functional residual capacity (FRC), residual volume (RV), vital capacity (VC), inspiratory reserve volume (IRV), expiratory reserve volume (ERV), and total lung capacity (TLC)
    - Flow volume loops
    - Pressure volume loops
    - Diffusing capacity for carbon monoxide (DLCO)
    - Compliances: lung (C_L), chest wall (C_{CW}), and total (C_{RS})

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- Resistance: airway and total respiratory system
- Closing capacity (CC)
- Work of breathing (WOB)

11. What changes occur in PaO_2 and $PaCO_2$ in morbidly obese patients?
12. What changes occur in intrapulmonary shunt (Q_S/Q_T) and dead space (V_D/V_T)? Describe the equations.
13. What changes occur in the cardiovascular system of the obese patient? Discuss cardiac output, blood volume, blood pressure, and pulmonary arterial pressure.
14. Are there any other disease entities commonly associated with obesity? What is their relationship?
15. What anatomic changes that affect the airway are associated with MO?
16. What derangements of the gastrointestinal system are associated with MO?

B. Preoperative Evaluation and Preparation

1. How would you prepare this patient preoperatively? Would you use preoperative screening questionnaires to diagnose OSA?
2. How would you premedicate this patient? Why?
3. How would you adjust doses of anesthetics in the morbidly obese?

C. Intraoperative Management

1. How would you monitor this patient?
2. The American Society of Anesthesiologists' (ASA) Difficult Airway Algorithm provides a guideline for management of the difficult airway. How do the comorbidities of MO and OSA modify implementation of the algorithm?
3. How would you induce anesthesia? Describe the intubation technique.
4. Why is it important to preoxygenate the obese patient? How would you do it? Compare the effectiveness of the four-maximum-breath and 3-minute techniques.
5. There are many new airway devices on the marketplace. Which of these devices have been particularly successful on the morbidly obese or OSA patient?
6. How would you maintain general anesthesia? What agents would you choose? How would you prepare for emergence?
7. Which muscle relaxants would you use?
8. Can regional anesthesia be used intraoperatively and postoperatively to decrease opioid requirements for bariatric surgery? What are the advantages and disadvantages of regional anesthesia? What are some of the newer techniques available?
9. What is the pathophysiology of pneumoperitoneum (PNP)? What is the effect on the cardiopulmonary system? How does it change perioperative care? What are the optimal ventilator strategies for morbidly obese patients undergoing bariatric surgery?
10. What are the devices that anesthesiologists place in the upper gastrointestinal canal during laparoscopic bariatric surgery? Are there risks associated with placement and management of these devices?
11. When will you extubate this patient? What are the extubation criteria?

12. What is apneic oxygenation?
13. What is diffusion hypoxia? How do you prevent it?

D. Postoperative Management

1. What are the major early postoperative complications in the morbidly obese patient?
2. How does position affect respiratory function in the obese patient?

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3. How would you prevent postoperative atelectasis?
4. How long would you prescribe supplementary oxygen postoperatively?
5. How would you control postoperative pain?

A. Medical Disease and Differential Diagnosis

A.1. What problems exist with this patient? This patient asks you if she is high-risk. What is the evidence?

Preoperative significant past medical history in this patient consists of MO, OSA, possible PS, right ventricular hypertrophy, mild pulmonary hypertension, systemic hypertension, adultonset diabetes mellitus, osteoarthritis, mild rheumatoid arthritis, and severe gastroesophageal reflux disease (GERD). Epidemiologically, this patient is at increased risk of coronary artery disease, cardiac arrhythmias, left- and right-sided congestive heart failure, peripheral vascular disease, venous thrombosis and pulmonary emboli, cerebrovascular disease, biliohepatic disease, hepatic steatosis, hepatic cirrhosis, degenerative joint disease, metabolic syndrome, and socioeconomic and psychosocial impairment.

This is a high-risk patient, with increased risk of both perioperative morbidity and mortality. Major anesthetic concerns include risk of difficult airway, difficult mask ventilation, decreased apneic threshold to trace amount of anesthetics, sedatives and narcotics, prolonged anesthesia emergence, postemergence resedation, positional ventilatory collapse, restrictive and obstructive lung disease, ventilation/perfusion mismatch, and worsening of reactive pulmonary hypertension and cor pulmonale. This patient must receive continuation of her preoperative oxygen therapy with continuous positive airway pressure (CPAP) in the immediate recovery period, at the values determined by her sleep study (PSG), or greater. Additional anesthetic concerns include difficult monitoring, difficult vascular access, and positioning issues. Additionally, there is a rare risk of postoperative massive pharyngeal collapse, rhabdomyolysis with renal failure, increased risk of infection including pneumonia, and positional injuries. Meticulous attention to acute pain management is essential.

Safe perioperative care for this patient requires triage to a specialized facility, additional personnel, surgeons with advanced laparoscopic training, and anesthesiologists with advanced airway skills and optimal equipment.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:208-212.

American Society of Bariatric Surgery. The largest dedicated site to weight reduction surgery. http://www.asbs.org. Accessed October 22, 2015.

Kaw R, Chung F, Pasupuleti V, et al. Meta-analysis of the association between obstructive sleep apnoea and postoperative outcome. *Br J Anaesth*. 2012;109(6):897-906.

Kopelman PG, Caterson ID, Dietz WH, eds. *Clinical Obesity in Adults and Children*. 3rd ed. West Sussex, United Kingdom: Wiley-Blackwell; 2010;228-243, 267-274.

Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient*. Milan, Italy: Springer-Verlag Italia; 2013:33-40.

A.2. Define the terms overweight, obesity, morbid obesity (MO), super obesity (SO), normal weight, and ideal body weight (IBW).

Obesity is a multifactorial chronic disease involving social, cultural, physiologic, psychological, metabolic, endocrine, genetic, and behavioral components, resulting in excess adipose and tissue mass. The modern basis for the determination of demographics is the BMI, or Quetelet's

Index, after the Belgian statistician, Adolphe Quetelet, published in 1842, and is measured in body weight in kilograms divided by the height in meters squared (kg per m^2). The standard for *ideal body weight* (IBW), the sex-specific desirable weight for persons with small, middle, and large frames, is published in the Metropolitan Life insurance tables.

- *Anorexia* is defined as a BMI of less than 17.5 in males or females.

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- *Underweight* is defined as a BMI of 17.6 to 19.0 in females or 17.6 to 20.6 in males.
- *Ideal (normal) weight* is defined as a BMI of 19.1 to 25.8 in females and 20.7 to 26.4 in males.
- *Marginally overweight* is defined as a BMI of 25.9 to 27.2 in females and 26.5 to 27.8 in males.
- *Overweight* is defined as a BMI of 27.3 to 32.3 in females and 27.9 to 31.1 in males.
- *Obesity* is defined as a BMI of greater than 20% of IBW, 32.4 to 34.9 in females and 31.2 to 34.9 in males.
- *Severe obesity* is defined as a BMI of 35.0 to 39.9 in both sexes.
- *Morbid obesity* is defined as a BMI of greater than 40 or greater than 35 with associated comorbidites such as hypertension and diabetes mellitus.
- *Super obesity*, a relatively new term, is defined as a BMI greater than 50.

There exist imperial and metric system BMI tables and web-based calculators.

Occasionally, an approximate, non-sex-specific system is used. In this system, a *healthy (normal) weight* is a BMI of 18.6 to 24.9, *overweight* is a BMI of 25 to 29.9, *obesity* is a BMI of 30 to 34.9, *severe obesity* is a BMI of 35 to 39.9, *morbid obesity* is a BMI of more than 40.0.

The older definitions of obesity may occasionally suffice. Overweight was formerly defined as a body weight of up to 20% greater than the predicted ideal weight, and obesity of more than 20%. MO was formerly defined as a body weight of 100 lb above the IBW, or alternatively, of twice the IBW. These definitions involved value judgments and inaccuracies and were later abandoned in favor of more objective terminology.

Alternative systems for the determination of obesity exist. In the triceps skinfold thickness test, for example, obesity is defined as a value of greater than 23 mm in males or greater than 30 mm in females. In the Broca's index (height in centimeters minus 100 for males and minus 105 for females), the IBW is calculated in kilograms.

- Males: ideal body weight (kg) = height (cm) - 100
- Females: ideal body weight (kg) = height (cm) - 105

There are different patterns of distribution of obesity. In *peripheral obesity* (e.g., gynoid or gluteal pattern), the individual has a pear shape, and adipose tissue deposition is predominantly in the lower body. In *central obesity* (e.g., android, or cushingoid), and especially upper body obesity, the individual has an apple shape, and adipose tissue deposition occurs predominantly in the upper body. Central obesity has greater associations with perioperative risk and OSA.

Halls SB. The “Metropolitan Life” tables. http://www.halls.md/met-life-ideal-weight/. Accessed July 1, 2015.

Kopelman PG, Caterson ID, Dietz WH, eds. *Clinical Obesity in Adults and Children*. 3rd ed. West Sussex, United Kingdom; Wiley-Blackwell; 2010:3-14.

The New Image Weight Loss Center. Imperial system BMI calculator. http://www.newimageweightloss.com. Accessed July 1, 2015.

What Health. Metric system BMI calculator. http://www.whathealth.com/bmi/chart-metric2.html. Accessed July 1, 2015.

A.3. What is obstructive sleep apnea (OSA)? What are the risk factors for OSA?

OSA is a sleep disorder. Sleep disorders may be grouped into the following types: conditions with excessive daytime somnolence (e.g., OSA), conditions with disorders initiating and maintaining sleep (e.g., insomnia), and circadian rhythm disorders (e.g., jet lag).

In the older terminology, OSA referred to both OSA proper and to obstructive sleep hypopnea (OSH) syndrome, a milder variant. Today, it is more precise to refer to obstructive sleep apnea and hypopnea syndrome (OSAHS) when naming the general condition.

OSA is defined as cessation of airflow for more than 10 seconds despite continuing ventilatory effort, five or more times

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per hour of sleep, associated with a decrease in arterial oxygen saturation (SpO_2) of greater than 4%. OSH is defined as a decrease in airflow of more

than 50% for more than 10 seconds, 15 or more times per hour of sleep, associated with a decrease in SpO_2 of greater than 4%. Both forms of OSAHS are usually associated with snoring, sleep disruption from increased ventilatory effort-induced arousal, hypersomnolence (daytime sleepiness), altered cardiovascular function, and pathophysiologic alterations, of which hypoxemia and hypercarbia are primary events, and polycythemia, systemic and pulmonary hypertension, various cardiac arrhythmias, myocardial ischemia, right and left ventricular hypertrophy, and eventually failure are secondary events.

Severe obesity is a strong independent risk factor for OSAHS. Other risk factors include male gender, middle age, evening ingestion of alcohol, and drug-induced sleep. In nonobese individuals, risk factors are craniofacial dysostoses, particularly micrognathia (absolute or relative), cartilaginous abnormalities (e.g., lingual tonsillar hyperplasia), chronic nasal obstruction, and tonsillar hypertrophy.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:19-27.

Sugerman HJ, Nguyen NT, eds. *Management of Morbid Obesity* . New York; Taylor and Francis; 2006:14, 52.

A.4. How is OSA diagnosed? What is a sleep study, or polysomnogram (PSG)? How are results obtained from a PSG used to grade the severity of OSA?

OSA may be suspected by history, physical examination, or comorbidities, but definitive diagnosis requires a sleep study. The hallmark of OSA is a history of heavy snoring. Nocturnal apnea, arousal during sleep, and daytime somnolence are commonly reported. Most adults with OSA have upper body obesity, increased neck circumference, micrognathia, and poor Mallampati scores on physical examination. Patient characteristics typically associated with OSA are a higher BMI, hypertension, and certain cephalometric measurements. In 90% of cases, the patient has a BMI in excess of 28 kg per m^2. OSA, however, may result from any condition that predisposes to upper airway obstruction. Some examples are pregnancy, upper airway abnormalities (e.g., deviated nasal septum, hypertrophic tonsils, and adenoids), cartilaginous abnormalities (e.g., lingual tonsillar hyperplasia), craniofacial dysostoses, certain congenital and genetic conditions (e.g., Prader-Will syndrome, Down syndrome, Marfan syndrome, Pierre Robin sequence, acromegaly, muscular dystrophy), as well as certain medical conditions (hypothyroidism). The absence of a typical or compelling presentation, however, does not rule out the possibility of OSAHS.

Definitive diagnosis of OSA is made by sleep specialists with a formal sleep study or a PSG. A PSG is an involved study, performed at sleep study centers, that examines nocturnal sleeping patterns by monitoring physiologic parameters. In its most comprehensive form, the following parameters are studied: two to six electroencephalographic (EEG) channels to measure electrical activity of the brain and to document sleep cycles, two electrooculogram (EOG) channels to distinguish rapid eye movement (REM) from non-REM sleep, chin electromyogram (EMG) to monitor arousal and activity of the upper airway (genioglossus and digastric muscles), an airway microphone to monitor airflow from the nose and mouth, elastic belts placed on the chest and abdomen to monitor respiratory effort, an infrared video camera to monitor body position, one channel of electrocardiogram (ECG) to monitor cardiac activity, a pulse oximeter to monitor oxygen saturation, and two-leg EMG channels to monitor leg movements. A PSG may be ordered to definitively diagnose a sleep disorder, as part of medical management, or in the surgical work-up of a high-risk population (e.g., preoperative screening of bariatric surgical candidates).

A PSG will diagnose the presence of OSAHS, type (central, peripheral, or mixed), and grade severity. Results are reported in as the total number of apneas and hypopneas per hour of sleep or the AHI. AHI values correspond to OSA severity as follows: 6 to 20 (mild), 21 to 40 (moderate), and greater than 40 (severe). The total number of arousals hourly is the Arousal Index (AI), which is the number of hourly arousals. The sum of the AHI and the AI is the Respiratory Disturbance Index (RDI).

As the PSG is an expensive and time-consuming study that not covered by all insurance plans, simpler tests have been proposed, such as a partial (level 2) portable polysomnography and nocturnal oximetry. OSA is primarily a clinical diagnosis. Because only a very small

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percentage of patients presenting for surgery have been tested, have available results, and are compliant with recommendations, great importance is placed on preoperative sleep apnea screening tools and questionnaires.

Abishami A, Khajehdehi A, Chung F. A systematic review of screening questionnaires for obstructive sleep apnea. *Can J Anaesth*. 2010;57:423-438.

American Sleep Apnea Association. http://www.sleepapnea.org/learn/sleep-apnea.html. Accessed July 1, 2015.

Kopelman PG, Caterson ID, Dietz WH, eds. *Clinical Obesity in Adults and Children*. 3rd ed. West Sussex, United Kingdom: Wiley-Blackwell; 2010:251-253.

Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient.* Milan, Italy: Springer-Verlag Italia; 2013:103-104.

National Heart, Lung, and Blood Institute. Introduction to types of polysomnograms. http://www.nhlbi.nih.gov/health/health-topics/topics/slpst/types.html. Accessed July 1, 2015.

Practice Guidelines for the Perioperative Management of Patients with Obstructive Sleep Apnea . Washington, DC: American Society of Anesthesiologists; 2005.

A.5. How does OSA differ in the pediatric population in clinical presentation and pathogenesis?

Sleep-disordered breathing in children and adults is distinct in pathophysiology, clinical presentation, and therapy.

Childhood OSA (COSA) consists of a continuum from snoring, to upper airway resistance syndrome, to the fully expressed syndrome. The pathophysiology of COSA is most commonly peripheral in origin due to nocturnal airway blockage from nasal pathophysiology, hypertrophic tonsils and adenoids, or craniofacial dysostoses. The symptomatology in COSA consists of snoring (usually continuous), rare daytime sleepiness, and frequent behavioral disturbances (e.g., attention deficit hyperactivity disorder [ADHD]). It is distinguished from adult OSA by the following: Snoring is more continuous, there is no sex predilection, and surgery (commonly adenotonsillectomy, rarely uvulopalatopharyngoplasty [UPPP]) is curative. There is no gold standard for the PSG diagnosis in children.

Adult OSA or OSAHS consists of a continuum from asymptomatic, to paroxysmal snoring, to severe nocturnal airway closure, requiring the patient to sleep in a sitting position, and daytime somnolence. The pathophysiology of OSAHS is central, peripheral, or mixed. Peripheral disease is caused by redundant adipose tissue in the upper airway, in the setting of severe obesity, sometimes with a superimposed craniofacial dysostosis. The symptomatology of OSAHS consists of intermittent snoring, apneic episodes, with daytime somnolence. *OSH*, a milder form of OSA, may be clinically indistinguishable. *Obesity-hypoventilation syndrome (OHS)* is severe OSA with chronic daytime hypoventilation, super obesity, and hypercapnia not related to pulmonary disease. *Pickwickian syndrome* is OHS with cor pulmonale.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:222-232.

Kopelman PG, Caterson ID, Dietz WH, eds. *Clinical Obesity in Adults and Children*. 3rd ed. West Sussex, United Kingdom: Wiley-Blackwell; 2010:392-407.

A.6. What is the Pickwickian syndrome (PS)? What is the pathogenesis of severe OSA?

The PS was so named by Burwell in 1956, as a reference to Joe, an obese, somnolent boy in the *Posthumous Papers of the Pickwick Club*, written in 1837 by Charles Dickens. In Joe, Dickins provided the first accurate description of the most severe type of OSA, consisting of a BMI over 50 kg per m^2 or SO, alveolar hypoventilation (hypoxemia and hypercarbia), heavy nighttime snoring with periodic respiration, hypersomnolence (daytime somnolence), secondary polycythemia, right

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and left ventricular hypertrophy, and right-sided heart failure. This syndrome may occur with or without pulmonary hypertension.

In these individuals with PS, there are repeated cycles of sleep, arousal, and sleep, accompanied by obstructed breathing, with snoring and restlessness. Hypoxemia and hypercarbia result from disruption of a normal sleep pattern, with loss of REM sleep and cardiovascular changes. Loss of REM sleep induces hypersomnolence, personality, behavior, and cognitive changes, and predisposes these individuals to be accident-prone. Eventually, severe

OSA leads to OHS, with nocturnal, and later diurnal alterations in the control of breathing, manifested as central apneic events, or apnea without ventilatory efforts. They also develop an alveolar-arterial oxygen gradient by ventilation/perfusion mismatch. The major factor in the pathogenesis of this syndrome is unknown but may be due to decreased hypoxic and hypercarbic ventilatory drive. Late in the disease process, there is progressive daytime hypoxia and hypercarbia. When cor pulmonale supervenes, PS is complete. Recently, the term Pickwickian syndrome has been abandoned in favor of obesity hypoventilation syndrome.

There are several cardiovascular changes in severe OSA, all related to the episodic airway closure, with hypoxemia and hypercarbia. Hypoxemia and alterations in autonomic tone may induce bradycardia during apneic episodes; in half of these patients, long sinus pauses, second-degree heart block, and ventricular ectopy may result. These arrhythmias may lead to nocturnal angina and myocardial infarction in susceptible individuals. Pulmonary hypertension may be caused directly by hypoxic pulmonary vasoconstriction, or indirectly by either increased transmural pulmonary artery pressures from negative thoracic pressure created by a sustained ventilatory effort against the upper airway obstruction, or by increases in pulmonary artery tone from increased sympathetic tone created by episodic hypoxemia. Pulmonary hypertension initially causes right ventricular hypertrophy, resulting in a higher right ventricular end-diastolic pressure (RVEDP), and later culminates in right ventricular failure, or cor pulmonale. The systemic circulation is also affected by episodic increases in sympathetic tone, with systemic hypertension presenting early, and left ventricular hypertrophy, followed by left ventricular failure, presenting much later. Systemic hypertension may also lead to increased stroke volume.

Chau EHL, Lam DB, Wong J, et al. Obesity hypoventilation syndrome: a review of epidemiology, pathophysiology, and perioperative considerations. *Anesthesiology*. 2012;117(1):188-205.

A.7. What is the association between obesity and OSA? What is the etiology of pharyngeal pathology in severe obesity?

Obesity and OSAHS are both common, coexisting diseases. Obesity has reached epidemic proportions in the industrialized world and currently poses a greater worldwide health risk than malnourishment. In the United States alone, obesity is annually responsible for 300,000 premature deaths and an annual health care cost of $100 billion dollars. Sixty-five percent of the U.S. population, or 127 million adults, are obese. The prevalence of severe obesity, a strong risk factor for OSAHS, is 3.15% in males and 6.70% in females, according to U.S. population data.

Incidence and severity of OSAHS correlates loosely with BMI, better with neck circumference, and most closely with waist circumference. OSAHS is 2.6 times more likely when the waist-to-hip ratio exceeds 1.0 in obese males and 0.85 in obese females.

Sixty percent to 90% of OSA patients are obese, and it has been estimated that 9% of women and 24% of men in the United States suffer from the syndrome, a total of 18 million individuals, of which 2% of women and 4% of men are symptomatic. These figures will almost certainly increase, as the demographics shift toward an older and more obese population. Many of these patients are undiagnosed at the time of surgery, representing potential perioperative complications. The prevalence of OSA in morbidly obese patients presenting for weight loss surgery is 78%.

There are three reasons why severe obesity per se may cause or exacerbate OSAHS. First, there is an inverse relationship between obesity and pharyngeal volume. The pharyngeal area decreases in obesity from deposition of adipose tissue into pharyngeal structures, in particular, the uvula, the tonsils, the tonsillar pillars, the tongue, the aryepiglottic folds, and, most importantly, the lateral pharyngeal walls. The volume of adipose in the lateral pharyngeal walls correlates with the clinical severity of airway obstruction. Increased deposition of pharyngeal adipose increases the likelihood that relaxation of the upper airway muscles will result in collapse of the soft-walled retroglossal space, or the oropharynx, between the uvula and the epiglottis. The shape of the pharynx remodels from an ellipse with the long axis transverse to an ellipse with the long axis anterior-posterior. The muscles that open the collapsible pharynx on expiration during sleep (e.g., tensor palatini, genioglossus, hyoid

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muscles) in response to stretch receptors in the pharynx are located in the anterior pharynx, and do not function well with a remodeled pharynx.

Second, patency of the collapsible pharynx is determined by the transmural pressure (the difference between the extraluminal and intraluminal pressure) and compliance of its wall. If the compliance of the pharyngeal wall and intraluminal pressure (inspiratory pressure) is constant, then the remaining important determinant of upper airway patency is extraluminal pressure. In obese patients, extraluminal pressure is increased by superficially located fat masses; that is, the upper airway is compressed externally. Therefore, neck circumference is greater in obese patients with OSAHS compared with obese non-OSAHS patients.

Third, pharyngeal patency is partially determined by lung volume. The collapsible (particularly in a supine position), soft-walled pharynx is kept patent during sleep by lung volumes above the FRC, which pulls on the carina, tenting open the pharynx. This is known as *the lung volume hypothesis*. Smaller lung volumes allow a cephalad displacement of the carina, approximately 0.5 to 1.5 cm, resulting in collapse or even telescoping of the pharynx, with a smaller circumferential area.

Amatoury J, Kairaitis K, Wheatley JR, et al. Peripharyngeal tissue deformation and stress distributions in response to caudal tracheal displacement: pivotal influence of the hyoid bone? *J Appl Physiol (1985)*. 2014;116(7):746-756.

Hillman DR, Walsh JH, Maddison KJ, et al. The effect of diaphragm contraction on upper airway collapsibility. *J Appl Physiol (1985)*. 2013;115(3):337-345.

Lopez PP, Stefan B, Schulman CI, et al. Prevalence of sleep apnea in morbidly obese patients who presented for weight loss surgery evaluation: more evidence for routine screening for obstructive sleep apnea before weight loss surgery. *Am Surg*. 2008;74:834-838.

Martinez-Rivera C, Abad J, Fiz JA, et al. Usefulness of truncal obesity indices as predictive factors for obstructive sleep apnea syndrome. *Obesity (Silver Spring)*. 2008;16:113-118.

Squier SB, Patil SP, Schneider H, et al. Effect of end-expiratory lung volume on upper airway collapsibility in sleeping men and women. *J Appl Physiol (1985)*. 2010;109:977-985.

A.8. What are the anesthetic implications of OSA?

Management of anesthesia in patients with severe OSAHS poses significant risks. These patients are extremely sensitive to minimal doses of central nervous system-depressant drugs, such as anesthetics, sedatives, and analgesics, and may exhibit prolonged sedation, resedation, or apnea as well as upper airway obstruction or, rarely, massive pharyngeal collapse. For these reasons, premedication with benzodiazepines or narcotics is used sparingly if at all, and sedation is generally reserved for painful or unpleasant situations (e.g., placement of invasive lines) where the patient is under the direct observation of a trained clinician.

Difficult tracheal intubation is expected in 13% to 24% of obese patients with OSAHS. In this particular case, the patient presents for laparoscopic bariatric surgery. Although the “ideal general anesthetic” regimen for these patients is a matter of some discussion, the literature does support the following: a safe induction, a deep maintenance anesthetic with muscle relaxants, and a smooth emergence with rapid offset devoid of active metabolites or trace anesthetic. Anesthetic gases should be insoluble, resistant to metabolic degradation, and without lipid depot compartmentalization, combined with rapid return of airway reflexes. The only weak inhalation anesthetic, nitrous oxide (N_2O), has the advantage of being relatively insoluble, as measured by blood-gas solubility coefficient (0.46), but it causes intestinal inflation, may be emetic, and is not recommended in the presence of pulmonary hypertension, a condition that is more common in MO. Of the available potent inhalation anesthetics (desflurane, sevoflurane, and isoflurane), desflurane combines the quickest wake-up, fastest return of airway reflexes, lowest solubility, as measured by the blood-gas solubility coefficient (desflurane, 0.45; sevoflurane, 0.65; isoflurane, 1.4), and lowest percentage of hepatometabolization (desflurane, 0.02%; isoflurane, 0.2%; sevoflurane, 2% to 3%). Intravenous agents should be either lipophobic (hydrophilic), spontaneously degrade in vivo or be ultrashort-acting.

Sedation or awake fiberoptic intubation: Ketamine and dexmedetomidine are optimal agents. *Induction of general anesthesia*: All agents have been utilized. *Maintenance agents*: air/oxygen mixtures, desflurane, cisatracurium, and

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and emergence: nitrous oxide (except in the presence of pulmonary hypertension), remifentanil, and morphine sulfate.

When feasible, regional anesthesia is useful. Tracheal extubation is considered only when patients are fully awake with intact upper airway reflexes. Episodic arterial hypoxemia may occur early, in the first 24 hours, or late, from the second to the fifth day, postoperatively.

Discharge from the postanesthetic care unit (PACU) may be made in the morbidly obese OSA, per protocol, after they have been started on CPAP or BIPAP, and have been observed for at least 30 minutes, without stimulation, and found to be free of respiratory arrests. If they have even one respiratory arrest, PACU stay is extended for an additional 3 hours, and consideration is made to transfer the patient to a monitored bed.

Intravenous patient-controlled analgesia (PCA) appears to be well tolerated in the morbidly obese, without deleterious effects on oxygen saturation, respiratory function, blood pressure, or heart rate. Dosing is based on IBW, without continuous rate. The most common drug used is morphine sulfate, starting at 20 μg per kg every 10 minutes with a 4-hour dose of 80% of the calculated maximum dose. Hydromorphone is an excellent second-line agent. It is important to individualize therapy. There is a paucity of literature on the safety and efficacy of intravenous PCA in the morbidly obese severe OSAHS patient. There are case reports of respiratory complications in this population; postoperative pain management must take into account the exquisite sensitivity of these patients to the ventilatory-depressant effects of opioids.

American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. *Anesthesiology*. 2014;120:268-286.

Apfelbaum JL, Hagberg CA, Caplan RA, et al. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology*. 2013;118:251-270.

A.9. What type of metabolic problems would you expect to find in morbidly obese patients? What is the role of leptin in obesity?

In MO, there is an increase in both low metabolically active tissue (e.g., adipose) and normally active tissue (e.g., muscle). In general, lean body weight (LBW) is equal to IBW plus 20% to 40% IBW. IBW is a value, based on population demographics, which could never be realized through weight reduction, in a severely obese individual.

Morbidly obese individuals have an increase in total oxygen consumption and carbon dioxide production due to an increased tissue mass. Increased metabolism demonstrates a linear relation with body weight and body surface area. Basal metabolic rate, however, remains normal in obese individuals.

Severely obese patients often have nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH), increasing long-term risk of hepatic cirrhosis, dyslipidemia, inflammation, insulin resistance, and atherosclerosis. Metabolic syndrome, defined as a collection of central obesity, hypertension, dyslipidemia, and impaired glucose tolerance, is present in severe cases and increases perioperative risk of morbidity and death. Metabolic syndrome is mediated through adipocytokines, such as acute phase reactants (increases in C-reactive protein and serum amyloid A [SAA]), adipokines (decreased adiponectin, or increases in leptin or resistin), macrophage-derived factors (increased resistin or interleukin-1 beta [IL-1β beta]), proinflammatory cytokines and chemokines (increases in tissue necrosis factor-alpha [TNF-α], several interleukins [IL-1, IL-6, IL-8, IL-10, IL-18]), chemokine [C-C motif], and prothrombotic factors (increases in plasminogen activator inhibitor-1 [PAI-1], fibrinogen and Factor VII).

Leptin is a satiety hormone secreted by adipocytes. Most obese adults have high inappropriate leptin levels or hyperleptinemia. Leptin levels are increased by overfeeding, insulin, glucocorticoids, endotoxin, and cytokines and are decreased by fasting, testosterone, thyroid hormone, and exposure to cold temperature. In the heart, increased leptin expression is seen following reperfusion after ischemia, and leptin concentration in cardiomyocyte culture serum is increased with endothelin (ET)-1 and angiotensin II treatment. Congenital leptin

deficiency is a rare cause of obesity, caused by mutations in the LEP gene in an autosomal recessive pattern.

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Genetics Home Reference. http://ghr.nlm.nih.gov/condition/congenital-leptin-deficiency. Reviewed December 2013. Accessed July 1, 2015.

Martyn JA, Kaneki M, Yasuhara S. Obesity-induced insulin resistance and hyperglycemia: etiologic factors and molecular mechanisms. *Anesthesiology*. 2008;109:137-148.

Matsuzawa Y. Therapy insight: adipocytokines in metabolic syndrome and related cardiovascular disease. *Nat Clin Pract Cardiovasc Med*. 2006;3:35-42.

Yang R, Barouch LA. Leptin signaling and obesity: cardiovascular consequences. *Circ Res*. 2007;101:545-559.

A.10. Describe the changes that occur in the following respiratory parameters in morbidly obese patients:

- **Pulmonary mechanics: tidal volume (V_T), functional residual capacity (FRC), residual volume (RV), vital capacity (VC), inspiratory reserve volume (IRV), expiratory reserve volume (ERV), and total lung capacity (TLC)**
- **Flow volume loops**
- **Pressure volume loops**
- **Diffusing capacity for carbon monoxide (DLCO)**
- **Compliances: lung (C_L), chest wall (C_{CW}), and total (C_{RS})**
- **Resistance: airway and total respiratory system**
- **Closing capacity (CC)**
- **Work of breathing (WOB)**

Morbidly obese patients have reduced lung volumes, increased WOB, and alterations in control of breathing and gas exchange. Body fat distribution, as well as BMI, determines the effect of obesity on pulmonary function.

Pulmonary mechanics. Pulmonary function tests (PFTs), or lung volumes, are uniformly altered in obesity. V_T is normal or increased in the obese and is decreased in Pickwickian obesity. IRV is decreased. ERV is markedly decreased because the increased weight of the torso decreases the normal expansive tendency of the rib cage and pulmonary parenchyma. RV is normal. FRC or ERV plus RV is markedly decreased because of the decrease in ERV. VC or ERV + V_T + IRV is decreased because of decreased ERV. TLC or RV + ERV + V_T + IRV is decreased for the same reason as VC. Individuals with central, as opposed to peripheral fat distribution, have greater decreases in the forced vital capacity (FVC), forced expiratory volume (FEV), and TLC. The maximum voluntary ventilation (MVV) may also be reduced.

Diffusing capacity for carbon monoxide. The DLCO is usually normal in individuals with obesity and mildly reduced in those with OHS because the lung parenchyma is normal, and changes in PFTs are due to abnormal chest wall mechanics and lower lung volumes. DLCO is a useful test to separate intrinsic lung pathology from obesity.

Compliance. There is a decrease in the total respiratory system compliance ($1 / C_{RS} = 1 / C_L + 1 / C_{CW}$), where C_{RS} is the total compliance, C_L is the compliance of the lung, and C_{CW} is the compliance of the chest wall. Total compliance is always decreased because of the weight of the torso and abdominal contents pressing against the diaphragm creating a restrictive component, markedly decreasing the chest wall compliance. Lung compliance is often normal but is decreased when pulmonary and circulatory comorbidities are present (e.g., pulmonary hypertension).

Resistance. There are increases both in the airway resistance (reduced elastic tension of the lung) and in the total respiratory system resistance (increased elastic tension of chest wall) at lower lung volumes, which leads to reduction in the caliber of the smaller airways. The increase in total resistance is approximately 30% in simple obesity and 100% in OHS. Resistance increases further in the supine position, possibly due to extrinsic adipose pressure of the supralaryngeal airway, and a decreased FRC.

Closing capacity. FRC is reduced in the morbidly obese patient and may be below the closing capacity (CC), resulting in

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small airway closure, ventilation/perfusion mismatch, right-to-left shunting, and possibly hypoxemia, the so-called positional ventilatory collapse. This may be worsened in the supine position, Trendelenburg position, by general anesthesia

and muscle relaxants, and improved by the use of lung recruitment strategies (e.g., positive end-expiratory pressure [PEEP]), and reverse Trendelenburg position.

Increased work of breathing. MO is associated with a 70% increase in the work of breathing, and a fourfold increase in the oxygen cost of breathing (oxygen consumed by the respiratory muscles per liter of ventilation, used as a surrogate for the energy cost of breathing). This is due to decreased lung compliance, increased respiratory resistance, and threshold inspiratory load from adipose tissue mass. Obese individuals with obstructive sleep apnea syndrome (MO-OSAHS) have elevated pharyngeal and nasopharyngeal resistance, raising the work of breathing 60% above the obese and 250% above the nonobese.

Al Ghobain M. The effect of obesity on spirometry tests among healthy non-smoking adults. *BMC Pulm Med*. 2012;12:10.

Lumb AB, ed. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2010:28-40, 43-55, 92-96.

Salome CM, King GG, Berend N. Physiology of obesity and effects on lung function. *J Appl Physiol (1985)*. 2010;108:206-211.

A.11. What changes occur in PaO_2 and $PaCO_2$ in morbidly obese patients?

In the awake patient, positional reduction in lung volume and respiratory system compliance occur when moving from an upright position to a supine position. These changes are exaggerated in the severely obese patient, particularly ERV and FRC. FRC declines both with obesity and with induction of general anesthesia.

Hypoxemia is the most common blood gas abnormality in the severely obese patient. The etiology is most commonly due to a low ventilation/perfusion ratio ([V with dot above]/[Q with dot above]) and less commonly as a result of hypoventilation. Pulmonary perfusion is increased in the obese as a result of increased cardiac output, increased circulating blood volume, and, occasionally, pulmonary hypertension. Alveolar ventilation is decreased in the obese as a result of upper airway closure, and spirometric changes (decreased ERV and FRC). In addition, the closing volume is often greater than the expiratory reserve volume, particularly in the supine position, causing airway closure, resulting in right-to-left shunt and hypoxemia. These patients frequently develop atelectasis, both from cephalad position of the diaphragm and increased weight of thoracic adipose tissue. Many obese patients develop a restrictive respiratory pattern, with mild small volume tachypnea, and increased use of accessory muscles of respiration.

The second most common blood gas abnormality in the severely obese is a variable change in the carbon dioxide tension ($PaCO_2$), not related to lung disease, and dependent on the alveolar ventilation. There are three patterns of ventilatory derangement described:

- *Alveolar hyperventilation* in response to a hypoxic drive. This occurs in young, active subjects. $PaCO_2$ is approximately 35 mm Hg.
- *Periodic, nocturnal, alveolar hypoventilation* with normal daytime values. This is the hallmark of OSAHS.
- *Daytime, or constant, alveolar hypoventilation*. This occurs in OHS and PS.

In addition, lung disease, such as asthma and chronic obstructive pulmonary disease (COPD), is more common in the obese patient population, when compared with age- and sex-matched controls. Preexisting lung disease may become exacerbated perioperatively.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:125-126.

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A.12. What changes occur in intrapulmonary shunt (Q_S/Q_T) and dead space (V_D/V_T)? Describe the equations.

Q_S/Q_T is normally less than 5%. In the MO, this is increased, because of the following:

- Lower ventilation/perfusion ([V with dot above]/[Q with dot above]) ratio
- Upper airway closure (e.g., OSAHS)
- Decreased FRC from abdominal compression
- Hypoventilation (e.g., OSAHS)

- Increased pulmonary circulation, from increased cardiac output, increased blood volume, and occasionally pulmonary hypertension

Shunt equation: $Q_S / Q_T = (CCO_2 - CaO_2) / (CCO_2 - CVO_2)$

where CCO_2 is pulmonary capillary oxygen content, CaO_2 is arterial oxygen content, and C_VO_2 is mixed venous oxygen content.

Dead space is anatomic, alveolar, or physiologic. *Anatomic dead space* is the volume of the lung and upper airway that is not involved in gas exchange. Ventilation of this area does not result in gas exchange. The volume of the anatomic dead space in milliliters is approximately equal to the IBW in pounds. Fowler's method of measuring anatomic dead space is by analyzing nitrogen concentration after single breath 100% oxygen. *Alveolar dead space* is the area of alveoli with ventilation and no perfusion, which has a [V with dot above]/[Q with dot above] equal to infinity, or West Zone 1. *Physiologic dead space*, the sum of anatomic and alveolar dead space, is the total area of lung plus airways not involved in gas exchange. Physiologic dead space is approximately 30% of the V_T. It is decreased in the supine position, and increased with disease states that alter [V with dot above]/[Q with dot above], and in OHS, because the latter individuals adopt a shallow ventilatory pattern. Physiologic dead space is decreased in SO due to increased V_T ventilation and unchanged anatomic dead space. Physiologic dead space, or V_D/V_T, is measured by the Bohr equation.

Bohr equation: $V_D/V_T = (PaCO_2 - PECO_2) / PaCO_2$

where $PECO_2$ is mixed expired CO_2 tension.

There are no changes in the physiologic dead space-to-tidal volume ratio or the alveolar-arterial oxygen gradient in obese patients undergoing laparoscopic gastric bypass surgery during general anesthesia compared with baseline.

Lumb AB, ed. *Nunn's Applied Respiratory Physiology*. 7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2010:119-137.

A.13. What changes occur in the cardiovascular system of the obese patient? Discuss cardiac output, blood volume, blood pressure, and pulmonary arterial pressure.

MO produces changes in cardiac morphology and ventricular function.

As BMI increases, both total and circulating blood volume increase. Although absolute blood volume is expanded, relative blood volume is decreased. Increase in circulating blood volume and decrease in systemic vascular resistance results in augmentation in cardiac output. Cardiac output increases by increased stroke volume, and heart rate remains unchanged. Cardiac output and stroke volume increase in proportion to oxygen consumption and the degree of obesity but more closely to the LBW. Left ventricular (LV) wall stress increases according to the law of Laplace ($P_2 - P_1 = 2T / R$), where P is the change in pressure produced by the increased volume, T is the LV wall stress, and R is the radius. Increase in afterload from hypertension produces eccentric LV hypertrophy and eventually LV dysfunction. They are thus sensitive to acute changes in preload and afterload. Morbidly obese patients presenting to the operating room (OR) require an ECG, chest x-rays, and an echocardiogram. Seventy percent of the echocardiograms in morbidly obese patients contain abnormalities.

Hypertension is more prevalent because of increased cardiac output and increased blood volume. Hypertension is more

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commonly systolic than diastolic in the obese. Obese patients without comorbidity have normal pulmonary artery filling pressures. Those individuals with OHS and PS, however, commonly have pulmonary hypertension, as a result of hypoxic pulmonary vasoconstriction and increased cardiac output. Hypertension and increased cardiac output lead to congestive heart failure in approximately 10% of obese individuals. There are two mechanisms in the pathogenesis of heart failure. In the first, pulmonary and systemic vascular congestion develops as a consequence of chronic volume overload superimposed on diminished diastolic compliance, caused by long-standing ventricular hypertrophy. In the second, chronic volume overload and high cardiac output results in LV hypertrophy. The ventricular wall/cavity ratio decreases, and LV systolic dysfunction results.

Echocardiography demonstrates LV hypertrophy in these patients, often in the absence of electrocardiographic evidence. Obesity leads to fatty infiltration of the cardiac conduction system, predisposing to sudden death, with a peak incidence occurring at 2:00 AM. Obesity is not a direct predictor of coronary artery disease. As an indirect predictor, obesity is linked to coronary artery disease via hyperlipidemia and systolic hypertension. Incidence of congestive heart failure and stroke are elevated.

Obese patients develop a particular pattern of ventricular remodeling. Centrally obese normotensives develop eccentric ventricular remodeling from chronic volume overload, increased diastolic pressure, increased diastolic wall stress, and chamber enlargement. This is in contrast to lean hypertensives, with concentric hypertrophy. The hypertensive obese may have both systolic and diastolic pressure overload and potentially earlier heart failure.

The term “syndrome Z” has been used to describe the association of components of the metabolic syndrome, including central obesity, type 2 diabetes with insulin resistance, hypertension, atherogenic dyslipidemia, increased sympathetic nerve activity, and OSA.

Kopelman PG, Caterson ID, Dietz WH, eds. *Clinical Obesity in Adults and Children*. 3rd ed. West Sussex, United Kingdom: Wiley-Blackwell; 2010:228-237.

Poirer P, Giles TD, Bray GA, et al. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss. *Circulation*. 2006;113:898-918.

Silventoinen K, Magnusson PKE, Neovius M, et al. Does obesity modify the effect of blood pressure on the risk of cardiovascular disease? A population-based cohort study of more than one million Swedish men. *Circulation*. 2008;118:1637-1642.

A.14. Are there any other disease entities commonly associated with obesity? What is their relationship?

Secondary obesity may be associated with hypothyroidism, Cushing disease, insulinoma, hypogonadism, and hypothalamic disorders. Although most obese patients are not diabetic, 80% to 90% of nonketotic diabetics are obese. Increased insulin secretion and insulin resistance resulting from peripheral tissue insensitivity are well-characterized features of obesity. Obesity exacerbates the diabetic state. Furthermore, malignancies of breast, prostate, cervix, uterus, colon, and rectum are more common in the obese.

In addition, there is a disproportionate increase in health-related risks from obesity. Above a BMI of 25, the risk of coronary artery disease more than doubles. Above a BMI of 29, there is an increased perioperative risk of pulmonary embolus. Above a BMI of 35, there is more than a 40-fold increase in adult-onset diabetes mellitus, respiratory disease, osteoarthritis, and OSAHS. Perioperative mortality during weight reduction surgery is statistically correlated with BMI, preoperative hypertension, anastomotic leak, and pulmonary embolus.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010;124:28-38.

Kopelman PG, Caterson ID, Dietz WH, eds. *Clinical Obesity in Adults and Children*. 3rd ed. West Sussex, United Kingdom: Wiley-Blackwell; 2010:82-90, 167-179, 200-206, 212-216.

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A.15. What anatomic changes that affect the airway are associated with MO?

Patient-specific anatomic changes in the MO are related to the BMI, type of obesity (peripheral vs. central), and presence or absence of OSAHS. Not all MO patients have airway involvement. The anatomic changes affecting the airway are not always easily diagnosed on routine physical examination. At a given BMI, there is more airway involvement in central obesity compared with peripheral obesity, and the most severe involvement airway involvement occurs in patients with OSAHS.

Significant anatomic alterations in the airway of the morbidly obese include the following:

- Deposit of adipose tissue in the lateral pharyngeal walls, and to a lesser extent in the uvula, the tonsillar pillars, the tongue, and the aryepiglottic folds, causing a decreased in the pharyngeal area
- Deposit of adipose tissue external to the upper airway (lateral parapharyngeal fat pads or jowls), extrinsically compressing the airway
- Presence of hypopharyngeal adipose tissue not evident on external examination that acts as a ball valve, obstructing the upper airway and interfering with the line-of-sight (LOS) at direct laryngoscopy

- Presence of pretracheal adipose tissue, which pushes the hyoid bone posteriorly into a less favorable position, causing the epiglottis to partially override the glottic entrance, worsening the laryngoscopic view
- Alteration in shape of the pharynx from an ellipse with the long axis lateral transverse to an ellipse with the long axis anterior-posterior
- Decreased efficiency of the anterior pharyngeal dilator muscles (tensor palatini [nasopharynx], genioglossus [oropharynx], hyoid muscles [laryngopharynx]), which promotes snoring

The anatomic changes that occur with MO are important for three reasons. First, these patients may obstruct their airway with light to moderate sedation (peripheral OSAHS). Various surgical procedures have been developed to improve this problem, such as the UPPP. Second, these patients may be difficult to mask ventilate, both because of external adipose tissue, and internal collapse of redundant upper airway adipose. Third, there is a higher incidence of difficult intubation (DI) and failed intubation in the MO. When coupled with the precipitous desaturation, there is a need to revise the ASA Difficult Airway Algorithm.

The literature is inconclusive on the relationship between obesity and difficult airways. According to some authorities, obesity is an independent risk factor for DI due to a disproportionately large tongue base, or a short, thick neck. Other authors found that a higher BMI is not an indicator of DI but that increased neck circumference and poor Mallampati scores (classes 3 and 4) are. MO-OSAHS patients with other risk factors for DI (e.g., micrognathia) develop worsening of airway closure to an even greater degree than their counterparts.

Hagberg CA, Vogt-Harenkamp C, Kamal J. A retrospective analysis of airway management in obese patients at a teaching institution. *J Clin Anesth*. 2009;21:348-351.

Isono S. Obstructive sleep apnea of obese adults: pathophysiology and perioperative airway management. *Anesthesiology*. 2009;110:908-921.

Kheterpal S, Martin L, Shanks M, et al. Prediction and outcomes of impossible mask ventilation: a review of 50,000 anesthetics. *Anesthesiology*. 2009;110:891-897.

Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient.* Milan, Italy: Springer-Verlag Italia; 2013:103-104.

A.16. What derangements of the gastrointestinal system are associated with MO?

There are several changes in the upper gastrointestinal tract that place severely obese individuals at risk of acid aspiration pneumonitis upon induction and emergence of general anesthesia: linear increase in intra-abdominal pressure with increasing body weight, increased incidence of GERD, decreased gastric pH, increased incidence of hiatal hernia,

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and impaired gastroesophageal antireflux mechanism, especially with foregut surgery. Ninety percent of fasting morbidly obese patients exceed Mendelson's criteria, a gastric volume of greater than 0.35 mL per kg total body weight (TBW), with a pH less than 2.5. Severely obese patients have a normal gastric emptying rate with a larger pouch, so that after a controlled fasting (e.g., 2-day liquid diet for bariatric surgery), patients should have an empty stomach.

There is a substantially higher incidence of hepatobiliary disease in the morbidly obese, such as cholelithiasis, hepatitis, intra- and extrahepatic cholestasis, hepatic steatosis, and cirrhosis. Seventy-five percent of the morbidly obese have hepatic steatosis. Although there is a 25% incidence of severe hepatic dysfunction in the morbidly obese, there is no clear correlation between liver function tests (LFTs) and hepatic dysfunction, complicating medical and anesthetic management. There is a natural, step-wise progression from NAFLD, to NASH, to fibrosis and hepatocellular carcinoma. Typically, NAFLD is stable and benign, with 1% to 2% risk of developing cirrhosis over 15 to 20 years. NASH is more progressive, with 3% to 15% progressing to cirrhosis over 10 to 20 years. Pancreatic disease is also more common in this population, specifically gallstone pancreatitis, adult-onset diabetes mellitus, and insulinoma. There is a higher incidence of colorectal malignancies in the morbidly obese.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:28-39.

Kopelman PG, Caterson ID, Dietz WH, eds. *Clinical Obesity in Adults and Children*. 3rd ed. West Sussex, United Kingdom: Wiley-Blackwell; 2010:208-227.

B. Preoperative Evaluation and Preparation

B.1. How would you prepare this patient preoperatively? Would you use preoperative screening questionnaires to diagnose OSA?

Preoperative evaluation should include a detailed history, review of systems, physical examination, and laboratory tests. Special attention should be paid to circulatory, pulmonary, and hepatic functions. Circulatory evaluation includes signs and symptoms of left or right ventricular failure, history of hypertension, and electrocardiographic abnormalities. Respiratory evaluation includes smoking history, exercise tolerance, history of hypoventilation and somnolence, PFTs with spirometry and baseline arterial blood gases, and chest x-ray results. Hepatic function tests include serum albumin and globulin, serum aspartate aminotransferase, serum alanine aminotransferase, direct and total bilirubin, alkaline phosphatase, prothrombin time, and cholesterol levels.

A cardiology consultation is needed, with a noninvasive assessment of function by echocardiogram. Patients without an adequate echocardiographic window require radionucleotide ventriculography to assess ventricular function and morphology. It is important to obtain a full assessment by the cardiologist to determine whether this patient is optimized and which invasive lines, if any, are appropriate. This patient was found to have mild right ventricular hypertrophy and mild pulmonary artery hypertension. Pertinent negatives were the absence of demonstrated coronary artery disease and left or right ventricular failure. In this case, it was determined that the patient was optimized and that an arterial line would be helpful.

Physical examination focuses on the cardiovascular, pulmonary, and the upper airway. The upper airway assessment, in particular, should be thorough. In addition to the routine parameters, atlanto-occipital joint extension, Mallampati classification, temporomandibular joint (TMJ) assessment with interincisor distance, mentohyoid distance, and dentition, the following parameters should be checked: pretracheal adipose thickness, neck circumference, and hypertrophic tonsils and adenoids. Nonreassuring findings related to the latter three variables are a large neck, an abundance of anterior neck soft tissue, and obligate mouth breathing. Neck circumference is an independent predictor of DI; the odds ratio is 1.13 (The odds of a problematic intubation in a particular patient with a neck circumference 1 cm larger than that of another patient are 1.13 times the odds of the patient with a 1-cm smaller neck circumference.). At 40 cm (15.75 in.), there is a 5% chance of DI; at 60 cm (23.62 in.), this increases to 35%. Pretracheal adipose greater than 1 in. (2.5 cm) at the level of the vocal cords, determined by ultrasound, may be an even better independent predictor of DI. Obligate mouth breathing may be a clue that the patient has adenotonsillar hypertrophy, nasal septal blockage, or a craniofacial dysostosis. Factors that render mask ventilation problematic, such as a heavy beard, should be noted.

Prior anesthetic records should be obtained. Patients with a history of heavy snoring should have a formal sleep study or PSG. Severity of OSAHS, AHI, home oxygen therapy with CPAP or BIPAP, response and compliance should be noted.

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The obesity surgery mortality risk score (OR-MRS) is a ratified tool consisting of BMI >50 kg per m^2, male gender, hypertension, pulmonary embolus risk (previous thrombus, IVC filter, right-sided heart failure, obesity hypoventilation syndrome), and age >45 years old. The STOP questionnaire is a widely used ratified tool to screen patients for OSA. An acronym, it consists of response to the following questions:

Snoring: louder than talking, heard through closed doors

Tired: daytime; hypersomnolence

Observed cessation of breathing during sleep

High Blood **P**ressure: with or without treatment

BMI: >35 kg per m^2

Age: >50 years old

Neck circumference: >40 cm

Gender: male

Predictive value of the STOP Questionnaire is as follows. High risk of OSA: yes to three or more items. Low risk of OSA: yes to less than three items. Sensitivity of the underlined

variables (the BANG portion) is particularly good: Out of the sample size of 2,467 patients, when three of the underlined variables are positive, the objective portion, the sensitivity of detecting OSA for a subject with PSG-confirmed AHI >5 is 83.6%, with AHI >15 is 92.9%, and AHI >30 is 100%. Because few patients presenting to the OR have sleep study diagnosis, and even fewer, perhaps 2%, have noninvasive positive pressure therapy prescribed and are compliant. Essentially all severe cases of OSA may be detected based on questionnaire results.

ASA has devised a ratified patient- and procedure-specific perioperative scoring system that measures OSA risk based on points:

A) OSA severity based on clinical indicators (0 to 3)

B) Invasiveness of surgery and anesthesia (0 to 3)

C) Need for postoperative opioids (0 to 3)

Score is based upon A + B versus A + C, whichever is greater. Expert consensus: Agree that patient is at increased perioperative risk of OSA complications if the score is >3.

American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. *Anesthesiology*. 2014;120:268-286.

Brodsky JB, Lemmons JM, Brock-Utne JG, et al. Morbid obesity and tracheal intubation. *Anesth Analg*. 2002;94:732-736.

Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiol*. 2008;108:812-821.

DeMaria EJ, Portenier D, Wolfe L. Obesity surgery mortality risk score: proposal for a clinically useful score to predict mortality risk in patients undergoing gastric bypass. *Surg Obes Relat Dis*. 2007;3:134-140.

B.2. How would you premedicate this patient? Why?

Current practice is not to give sedatives or hypnotics until these patients are on the OR table, as part of preparation for painful procedures (e.g., arterial line placement), or airway management (e.g., airway topicalization and cranial nerve blocks V, IX, and X). A well-conducted preoperative visit is more important than is sedation. This patient was not sedated before surgery.

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Nonrespiratory depressant premedicants may be used as part of multimodal analgesia in patients with MO; this has the potential to decrease preinduction anxiety, lower anesthetic requirements, and decrease immediate postoperative depressant effects of opioids in a high-risk population. A single loading dose of intravenous dexmedetomidine in the OR suite blunts the hemodynamic responses during laryngoscopy, reduces opioid and anesthetic requirements; it also decreases blood pressure and heart rate as well as the recovery time after the operation. Other pre- and perioperative medications that have been considered include acetaminophen, nonsteroidal anti-inflammatory drugs including ketorolac, lornoxicam, diclofenac, pregabalin, tramadol, ketamine, magnesium, and others. More research needs to be conducted in this area before a standard of care emerges; however, preemptive analgesia has not been adopted as a standard in bariatric surgical population.

Other drugs that have been advocated as intravenous premedicants include the anticholinergic, drying agent glycopyrrolate, prokinetic, antiemetic metoclopramide, and H_2-blockers, such as famotidine. Aprepitant, a selective human substance P/neurokinin 1 receptor antagonist, has recently been advocated as prophylaxis of postoperative nausea and vomiting (PONV). PONV is often severe following bariatric surgery and requires polypharmacy, including oral preoperative medications, such as aprepitant.

Cabrera Schulmeyer MC, de la Maza J, Ovalle C, et al. Analgesic effects of a single preoperative dose of pregabalin after laparoscopic sleeve gastrectomy. *Obes Surg*. 2010;20(12):1678-1681.

Jayaraman L, Sinha A, Punhani D. A comparative study to evaluate the effect of intranasal dexmedetomidine versus oral alprazolam as a premedication agent in morbidly obese patients undergoing bariatric surgery. *J Anaesthesiol Clin Pharmacol*. 2013;29(2):179-182.

Jones SB. Multimodal analgesia in patients with morbid obesity. Bariatric Times. http://bariatrictimes.com/multimodal-analgesia-in-patients-with-morbid-obesity. Published November 26, 2013. Accessed July 1, 2015.

Kovac AL. Review article. Update on the management of postoperative nausea and vomiting. *Drugs*. 2013;73(14):1525-1547.

B.3. How would you adjust doses of anesthetics in the morbidly obese?

Anesthetizing MO patients requires careful considerations regarding changes in the pharmacokinetic and pharmacodynamic properties of numerous drugs used in anesthesia. Physiologic and anthropometric changes, such as increases in cardiac output, changes in regional blood flow, and increases in fat mass and lean mass, affect pharmacokinetic properties. In addition, respiratory pathophysiology such as the increased incidence of OSA and fat deposition in the oropharynx and chest wall alters pharmacodynamic properties of anesthetics.

Weight-based dosing scalars other than TBW must be considered when administering drugs to MO patients. Administration of drugs based on TBW can result in an overdose, whereas administration based on IBW can result in a subtherapeutic dose.

With the exceptions of succinylcholine (where TBW might be appropriate) and the nondepolarizing neuromuscular blocking agents (where IBW might be appropriate), learn body weight (LBW) is the optimal dosing scalar for most anesthetic agents including opioids and anesthetic-induction agents, especially as cardiac output is significantly correlated to LBW, except in individuals with obesity cardiomyopathy (Table 63.1).

Volatile anesthetics are sequestered in adipose tissue based on lipid solubility. Desflurane has faster washout and recovery than sevoflurane; sevoflurane is useful for short-duration titration of anesthetic depth and in selected patients (e.g., smokers, asthma).

Hanley MJ, Abernethy DR, Greenblatt DJ. Effect of obesity on the pharmacokinetics of drugs in humans. *Clin Pharmacokinet*. 2010;49:71-87.

Ingrande J, Lemmens HJM. Dose adjustment of anaesthetics in the morbidly obese. *Br J Anaesth*. 2010;105(suppl 1):i16-i23.

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La Colla L, Albertin A, La Colla G, et al. Faster wash-out and recovery for desflurane vs sevoflurane in morbidly obese patients when no premedication is used. *Br J Anaesth*. 2007;99:353-358.

Lemmens HJ, Saidman LJ, Eger EI II, et al. Obesity modestly affects inhaled anesthetic kinetics in humans. *Anesth Analg*. 2008;107:1864-1870.

National Heart, Lung, and Blood Institute. Calculate your body mass index. http://www.nhlbi.nih.gov/guidelines/obesity/BMI/bmicalc.htm. Accessed July 1, 2015.

Vallejo MC, Sah N, Phelps AL, et al. Desflurane versus sevoflurane for laparoscopic gastroplasty in morbidly obese patients. *J Clin Anesth*. 2007;19:3-8.

TABLE 63.1 Weight-Based Dosing Scalar Recommendation for Commonly Used Intravenous Anesthetics

DRUG	DOSING SCALAR	COMMENTS
Thiopental	Induction: LBW Maintenance: TBW	Simulations showed a 60% decrease in peak plasma concentration in MO subjects compared with lean subjects after a 250 mg dose. Induction dose adjusted to LBW results in same peak plasma concentration as dose adjusted to CO. Volumes and clearances increase proportionally with TBW.
Propofol	Induction: LBW Maintenance: TBW	MO subjects given an induction dose based on LBW required similar amounts of propofol and similar times to loss of consciousness compared with lean subjects given propofol based on TBW. Volume of distribution and clearance at steady state increases with increasing TBW.
Fentanyl	LBW	Clearance increases linearly with 'PK mass', an arbitrary scalar highly correlated to LBW.
Remifentanil	LBW	An infusion based on LBW results in similar plasma concentrations as normal weight subjects were given an infusion based on TBW.
Succinylcholine	TBW	Administration of 1 mg kg^{-1} based on TBW resulted in a more profound block and better intubating conditions compared with doses based on IBW or LBW.
Vecuronium	IBW	Doses based on TBW result in a prolonged duration of action in obese vs non-obese subjects.
Rocuronium	IBW	There is an increased duration of action when the drug is given based on TBW *vs* IBW.
Atracurium,	IBW	The duration of action is prolonged in obese subjects when given on the

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Cisatracurium	basis of TBW *vs* IBW.

CO, cardiac output; IBW, ideal body weight; LBW, lean body weight; MO, morbid obesity; PK, pharmacokinetic; TBW, total body weight.

Reprinted from Ingrande J, Lemmens HJM. Dose adjustment of anaesthetics in the morbidly obese. *Br J Anaesth*. 2010;105(suppl 1): i16-i23, with permission.

C. Intraoperative Management

C.1. How would you monitor this patient?

In addition to the routine mandated monitors of ECG, noninvasive blood pressure, pulse oximetry, end-tidal carbon dioxide, and temperature, an arterial line is inserted for frequent assessment of blood gases for continuous blood pressure tracing. An esophageal stethoscope with thermistor is placed in the axilla, or in the nasopharynx, to monitor temperature, because any device placed in the esophagus may be inadvertently included in the surgical anastomosis. Hourly urine output is evaluated to assess fluid balance. A peripheral nerve stimulator is used to monitor the effects of muscle relaxants.

A processed EEG, such as the bispectral index or BIS™ (Aspect Medical Systems, Inc, Newton, MA), was used to monitor depth of anesthesia. BIS monitoring has been shown to be useful in laparoscopic bariatric surgery, both because blood pressure and heart rate are inadequate surrogate proxies of anesthetic depth, due to patients positioned in the standing position with frequent sympathomimetic support (in this case, phenylephrine infusion), and because total intravenous anesthesia (TIVA) is frequently used (in this case. we used dexmedetomidine and remifentanil). Sugammadex appears to be useful and well tolerated in the morbidly obese patient population and may offer the advantages of rapid reversibility in the event of a difficult airway encountered unexpectedly, lower rate of respiratory events due to residual muscular blockade, and decreased residual and maintenance of dense muscle relaxation until the end of surgery. Intraoperative spirometry and the use of flow-volume loops (GE Datex S/5 [System 5] series monitor [GE Datex Ohmeda, Helsinki, Finland]) are highly useful and will alert the anesthesiologist to change in surgical conditions and patient status.

The advantages of invasive monitoring have to be weighed against the possible complications. Laparoscopic bariatric surgeries have minimal blood loss (typically less than 100 to 200 mL) and fluid shifts. These are elective cases, and patients are optimized preoperatively. Invasive arterial monitoring is used for the super obese with severe cardiopulmonary disease or poor fit of the noninvasive blood pressure cuff because of the conical shape of the upper arms or unavailability of appropriately sized cuffs. Accurate blood pressure readings may be obtained from the wrist, as it was in this case, or the ankle. Central venous access is typically used when there are difficulties obtaining peripheral access and was not used here. A pulmonary artery catheter is reserved for patients with documented pulmonary hypertension, cor pulmonale, or LV failure.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:92-99.

Lemons HJ, Brodsky JB. General anesthesia, bariatric surgery, and the BIS monitor. *Obes Surg*. 2005;15(1):63.

Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient*. Milan, Italy: Springer-Verlag Italia; 2013:131-138.

C.2. The American Society of Anesthesiologists' (ASA) Difficult Airway Algorithm provides a guideline for management of the difficult airway. How do the comorbidities of MO and OSA modify implementation of the algorithm?

The ASA's Difficult Airway Algorithm provides a guideline for management of the difficult airway. It was created by a panel of experts under the direction of the ASA in 1993 and modified in both 2003 and 2013. Implementation of the Algorithm will be altered in different patient populations, according to factors such as patient demographics, comorbidities, surgical requirements, equipment availability, presence of additional personnel, and probably most importantly the skill set of the

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anesthesiologist.

In the severely obese patient population, with demonstrated or suspected OSA, the following considerations are relevant: Patients may be “full stomach” by demographics, they are vulnerable to precipitous apneic deoxygenation, the standard airway assessment may not be sufficient, there is a higher incidence of difficult mask ventilation and DI, and redundant adipose tissue may obstruct the line of sight on laryngoscopy.

In this patient population, the Difficult Airway Algorithm is biased toward awake induction techniques, traditional preoxygenation is preferable to fast track (four breaths), and extra precautions should be taken prior to induction of anesthesia. These include recruitment of additional personnel during the induction of general anesthesia, immediate availability of the full complement of noninvasive and invasive airway management devices, including an unopened tracheostomy set.

Apfelbaum JL, Hagberg CA, Caplan RA, et al. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology*. 2013;118(2):251-270.

Kheterpal S, Martin L, Shanks A, et al. Prediction and outcomes of impossible mask ventilation: a review of 50,000 anesthetics. *Anesthesiology*. 2009;110(4):891-897.

C.3. How would you induce anesthesia? Describe the intubation technique.

Nonsedative premedication, such as glycopyrrolate, an anticholinergic may be used to dry the upper airway, metoclopramide, a prokinetic, and famotidine, an H_2-receptor blocker may be administered preoperatively. In practice, however, they are rarely used because these patients are on a liquid diet for 2 days preoperatively. The OR should be set up, complete with appropriate alternative noninvasive and invasive airway devices.

On arrival in the OR, the patient is positioned on the OR table in a ramp position, placed on monitors, and given supplemental oxygen via a tight-fitting face mask. With moderate sedation, consisting of midazolam, fentanyl, and propofol, the patient is placed on pressure control ventilation, noninvasive positive pressure ventilation (NPPV) by mask for 3 to 5 minutes. Intraoperative spirometry, especially a flow-volume loop is also helpful; look for an open loop without signs of obstruction or restriction. Failure to obtain a capnogram usually indicates upper airway obstruction requiring jaw thrust or an oral airway. The goal is to have an expired V_T of 3 to 5 mL per kg LBW while maximizing FRC and maximizing arterial oxygen, and pulmonary oxygen reserve in preparation for induction of general anesthesia. Once it has been ascertained that mask ventilation is feasible, nondepolarizing neuromuscular blockade is induced.

This patient was considered to be a moderately difficult intubation, and, possibly, difficult mask ventilation. A videolaryngoscope such as channeled King Vision Laryngoscope™ (KVL_C) (Ambu, Ballerup, Denmark) could be used to intubate this patient. A fiberoptic bronchoscope was set up as a backup. If needed, the FOB could either be utilized to “peer and steer” the channeled tracheal tube, or, more rarely, to cannulate the upper trachea and advance the tracheal tube in a Seldinger maneuver over the KVL_C blade.

If the physical examination and past anesthetic record demonstrated easy orotracheal intubation or the patient was at high risk of aspiration, a rapid sequence intubation could be contemplated using either thiopental (3 to 5 mg per kg TBW) or propofol (2 mg per kg TBW) with succinylcholine (1 to 1.5 mg per kg TBW), with the patient positioned on a ramp.

Delay JM, Sebbane M, Jung B, et al. The effectiveness of noninvasive positive pressure ventilation to enhance preoxygenation in morbidly obese patients: a randomized controlled study. *Anesth Analg*. 2008;107:1707-1713.

Hagberg CA, ed. *Benumof and Hagberg's Airway Management* . 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:588.

Murphy LD, Kovacs GJ, Reardon PM, et al. Comparison of the king vision video laryngoscope with the macintosh laryngoscope. *J Emerg Med*. 2014;47(2):239-246.

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Talab HF, Zabani IA, Abdelrahman HS, et al. Intraoperative ventilatory strategies for prevention of pulmonary atelectasis in obese patients undergoing laparoscopic bariatric surgery. *Anesth Analg*. 2009;109:1511-1516.

C.4. Why is it important to preoxygenate the obese patient? How would you do it? Compare the effectiveness of the four-maximum-breath and 3-minute techniques.

Thorough preoxygenation is important because intubation may take longer in morbidly obese than nonobese patients; moreover, because obese patients have a small intrapulmonary store of oxygen (low FRC), which is rapidly depleted (high oxygen consumption), they are at

particularly high risk of hypoxemia. Preoxygenation is more effective in the ramp or back-up position than in the supine position in MO patients.

Maximal total body preoxygenation, or denitrogenation, requires that the patient breathe 100% oxygen for at least 3 minutes in a well-sealed system to fill the alveolar, arterial, venous, and tissue spaces and to obtain a pulse oximeter saturation (SpO_2) of 99% to 100%. This is superior to fast-track preoxygenation, or four maximum vital capacity breaths.

The rate of apneic desaturation after induction of anesthesia is related to the BMI. In obese patients, three VC breaths of 100% oxygen will allow for 3 minutes of apnea before the onset of hypoxemia. In comparison, without preoxygenation, only 1 minute elapsed before significant desaturation occurred. The effectiveness of the four-maximum-breath and 3-minute preoxygenation techniques in elderly patients has been compared. Peak oxygen saturation values after preoxygenation occurred with these two techniques. However, a significantly shorter time to all levels of desaturation was associated with the four-maximum-breath method when the patients were kept apneic. The average times to 90% saturation were 3.5 minutes in the four-breath group and 6.5 minutes in the 3-minute group. Pulse oximetry has been recommended to achieve a SaO_2 of 99% to 100% during induction to ensure maximal oxygen availability and safe duration of apnea (159 ± 60 seconds) in morbidly obese patients. Oxygen insufflation into the pharynx during laryngoscopy via a nasopharyngeal catheter has been utilized. Most of the studies comparing preoxygenation techniques are older, and more work is required. Some alternative airway devices have an oxygen insufflation sleeve on the blade, such as one version of the C-MAC (Karl Storz Endoskope, Tuttlingen, Germany).

Awake, sedated preinduction CPAP for 3 to 5 minutes has been advocated both to improve oxygenation and to decrease atelectasis. Because apnea tolerance is decreased in both morbidly obese and OSA patients, the triple airway maneuver (mandibular advancement, neck extension, and mouth opening) should be performed if mask ventilation becomes problematic.

Patients exposed to high oxygen concentration during the induction of general anesthesia are at risk of developing atelectasis and may require positive-pressure lung recruitment maneuvers periodically during the perioperative course.

Altermatt FR, Muñoz HR, Delfino AE, et al. Pre-oxygenation in the obese patient: effects of position on tolerance to apnoea. *Br J Anaesth*. 2005;95(5):706-709.

Coussa M, Proietti S, Schnyder P, et al. Prevention of atelectasis formation during the induction of general anesthesia in morbidly obese patients. *Anesth Analg*. 2004;98:1491-1495.

Dixon BJ, Dixon JB, Carden JR, et al. Preoxygenation is more effective in the 25 degrees head-up position than in the supine position in severely obese patients: a randomized controlled study. *Anesthesiology*. 2005;102(6):1110-1115.

Law JA, Broemling N, Cooper RM, et al. The difficult airway with recommendations for management— part 2—the anticipated difficult airway. *Can J Anaesth*. 2013;60(11):1119-1138.

C.5. There are many new airway devices on the marketplace. Which of these devices have been particularly successful on the morbidly obese or OSA patient?

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In the 2003 iteration of the Difficult Airway Algorithm, the laryngeal mask airway (LMA) (Teleflex, Limerick, PN), the most commonly used supraglottic airway at the time, was included. Inclusion of the LMA into the Algorithm emphasized that being able to ventilate through a temporary airway (1) returns the patient to the elective branch of the Algorithm, since they are being ventilated and oxygenated; (2) may often be all that is required for patient management; and (3) provides a bridge for insertion of a definitive airway. As used in the Algorithm, “LMA” should not be interpreted as endorsement of any particular manufacturer or product. In addition, since publication of the first two Difficult Airway Algorithms, many new and diversified LMAs have been developed. Other types of airway devices have been developed as well. The 2013 iteration of the Difficult Airway Algorithm has generalized the term to supraglottic airway and changed the expanded approach of alternative difficult intubation approaches. At the present time, there are no large prospective, randomized studies comparing the newer devices on the MO or OSA subject. The clinical skill set of the clinician still appears to be the most relevant factor until the literature provides more guidance.

In the intervening period since 2003, there have been several advances in airway management devices. The first is the advent of affordable, high-quality video laryngoscopes (VL). The

most promising of these for the MO/OSA patient appears to be the C-MAC™. The C-MAC™ (Karl Storz Endoskope, Tuttlingen, Germany) is a VL based upon CMOS (complementary metal oxide semiconductor) technology, similar to a cell phone camera. The C-MAC™ is an unchannelled device, with high-quality optical resolution, and may be used either for direct laryngoscopy (DL), in which the operator looks in the mouth, or indirect laryngoscopy (IL), in which the operator looks on the screen. It may therefore be referred to as a DL/IL device. The C-MAC™ has the highest quality optics, the brightest image, and is truly a difficult airway device. Reusable blades come in different sizes; most MO/OSA patients may be intubated with either the no. 3 or the D (Doerges) blades. The D-blade is particularly suited to patients with increased neck circumference, who are prone to lateral pharyngeal collapse. The electronic module comes either mounted on an intravenous pole, freestanding, or totally portable (the C-MAC Pocket Monitor™). Digital photographs or video-clips of a C-MAC™ intubation may be easily taken by the laryngoscopist without advance preparation, and uploaded to a memory card. The C-MAC™ electronic module may be used for flexible, fiberoptic, and rigid (Bonfils™) scopes; in addition, a C-HUB adaptor serves as a CMOS-digital convertor for either a fiberoptic intubating tower or the surgeons' operative tower. Other unchannelled VL devices which have been used for the MO/OSA patient population include the McGRATH™ MAC Videoscope Series 5 (Covidien Public Ltd Co, Dublin, Ireland), which is also a DL/IL device, but totally portable, with single-use blades, and the GlideScope™ Videolaryngoscope (GVL) suite of products. Most of the GVL products are IL devices. Although glottic visualization is frequently successful with the GVL, intubation may be problematic, and right palatopharyngeal arch perforation has been reported secondary to blind insertion of the tracheal tube from the back of the pharynx to resurfacing within the camera's visual field at the laryngeal inlet. This complication is more likely to occur when lateral pharyngeal wall crowding occurs, as in MO with jowls, or severe OSA.

The second advance in airway management is the development of a new class of airway devices: the channeled, disposable optical laryngoscope. The Airtraq™ (AT) (Prodol Systems, Viscaya, Spain) and the King Vision™ (KV) (Ambu, Ballerup, Denmark) are in this category. These devices have been very successful in the MO/OSA patient. Advantages include portability, being able to intubate in unusual positions (such as semi-Fowler position or “face-to-face”), with limited access, high retention success rate for the novice or infrequent practitioner, and being an excellent conduit for FOB. Intubating is accomplished in a neutral neck position with little mouth opening, so TMJ limitation and cervical spinal pathology are indications. The KV has technical advantages over the AT. Both the KV and the AT are channeled devices, although they have different operating profiles. The advantages of KV include totally portable organic light-emitting diode (OLED) display (similar to the GVL), needing no special charger (3-AAA batteries provide 1 hour of light), improved channel with J-curve sliding off tracheal tube easily, guiding channel with loaded tracheal tube serving as an ideal fiberoptic ramp, absence of distal “tooth” at end of channel facilitating removal of tracheal tube, possibility of being assembled during intubation in the larynx, distal light and optical inlet with “fish-eye” lens with antifog lens, and wide angle of aperture. However, patients with a short jaw or TMJ dysfunction will benefit from the more compact profile of the original AT, an optical scope similar to a flashlight with two mirrors.

The third advance in airway management is the development of better airway “bridges” and short-term ventilatory support devices. The LMA Fastrach™ (LMA-FT), or intubating LMA™ (Teleflex Medical, Research Triangle Park, NC; LMA, North America, San Diego, CA), provides a method of oxygenating and ventilating while obtaining a definitive airway. The I-Gel™ (Intersurgical Complete Respiratory Systems, Berkshire, United Kingdom) provides a cuffless, high-quality perilaryngeal airway with a gastric decompression lumen. The LMA Supreme™ (Teleflex Medical, Research Triangle Park, NC; LMA, North America, San Diego, CA) is a supraglottic airway salvage device with a gastric decompression

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port that incorporates features of the LMA Unique™, ProSeal™ and LMA-FT.

In practice, these “bridges” are not utilized as often as they were before because the aforementioned devices rarely fail. In the opinion of the author, the LMA-FT is indicated as a backup in locations where “one attempt is all you get,” like the emergent cesarean section induction.

The King Laryngo-Tracheal-Suction-Disposable™ (King LTS-D™) is a disposable supraglottic airways with gastric access. Often used by first responders and military medics, it is a useful airway salvage device in the MO patient, particularly in the event of gastrointestinal bleeding.

The final advance in airway management is the development of high-quality, singleuse metal laryngoscope blades, which appear to have superior success rates compared with reusable metal laryngoscope blades in rapid sequence induction of anesthesia. For the MO/OSA patient with a challenging airway, FOB remains the gold standard. FOB has substantial limitations, however, such as limited availability, a long learning curve, a low retention rate, equipment fragility, longer setup time, longer intubation time, and few absolute indications (mostly lower airway pathology). As the advanced airway management devices improve, and clinician experience grows, the need for FOB should continue to decline.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:111-123.

Amour J, Le Manach YL, Borel M, et al. Comparison of single-use and reusable metal laryngoscope blades for orotracheal intubation during rapid sequence induction of anesthesia: a multicenter cluster randomized study. *Anesthesiology*. 2010;112(2):325-332.

Cavus E, Kieckhaefer J, Doerges V, et al. The C-MAC videolaryngoscope: first experiences with a new device for videolaryngoscopy-guided intubation. *Anesth Analg*. 2010;110:473-477.

Marrel J, Blanc C, Frascarolo P, et al. Videolaryngoscopy improves intubation conditions in morbidly obese patients. *Eur J Anaesthesiol*. 2007;24:1045-1049.

Shippey B, Ray D, McKeown D. Case series: the McGrath videolaryngoscope—an initial clinical evaluation. *Can J Anaesth*. 2007;54(4):307-313.

C.6. How would you maintain general anesthesia? What agents would you choose? How would you prepare for emergence?

Although the ideal maintenance anesthetic for morbidly obese patients undergoing laparoscopic surgical procedures is a matter of some discussion, there is support in the literature for a technique comprising insoluble anesthetic gases resistant to metabolic degradation and without lipid depot compartmentalization, combined with rapid return of airway reflexes, plus intravenous agents that are either hydrophilic, spontaneously degrade in vivo, or are ultrashort-acting.

Of the potent inhalation agents, desflurane has several advantages; it is insoluble, has a faster wake-up, a faster return of airway reflexes, and a decreased amount of hepatometabolism. Obesity increases the biotransformation of the inhalation anesthetics, resulting in increased serum toxic products of metabolism. Because of the frequent presence of coexisting liver dysfunction in the morbidly obese (75% have hepatic steatosis, and 25% have severe hepatic dysfunction), and the absence of a clear correlation between LFTs and hepatic dysfunction, it would seem logical to use the agent with the lowest percentage of hepatometabolism, desflurane (0.02%), compared with isoflurane (0.2%), and sevoflurane (2% to 3%). An agent with a low blood-gas solubility coefficient is better because there will be a smaller body reservoir available for metabolism, and a faster time to steady state at the target organ, the brain. Of the inhaled agents, desflurane has the fastest wake-up, which is followed by sevoflurane and then by isoflurane. Desflurane also has the fastest return of airway reflexes, followed by sevoflurane. All of the inhalational anesthetics will accumulate in the lipid compartment, lengthening the emergence.

Although nitrous oxide, a weak inhalation anesthetic, has certain advantages, such as a low blood-gas solubility coefficient (0.46), it is not recommended for maintenance use because it causes intestinal inflation and is emetogenic. Nitrous oxide use is contraindicated with preexisting severe pulmonary hypertension, a condition more common in the severely obese.

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Short duration use of nitrous oxide, particularly during the surgical closure facilitates offset of relatively lipid soluble agents.

Remifentanil is the intraoperative narcotic of choice because of its rapid onset, consistent profile, and rapid offset. Although it is lipophilic, it has a half-life of 5 minutes, and therefore does not compartmentalize in the lipid compartment. The VD of remifentanil

is therefore calculated as LBW. It is dosed by infusion, in the range of 0.05 to 0.2 μg/kg/min LBW. The lipophilic opioids, fentanyl and sufentanil, that are dosed by TBW and may cause delayed respiratory depression in the high-risk patient, especially OSAHS, are less than ideal in larger doses. They may, however, be used in reasonable doses (fentanyl up to 5 μg per kg TBW).

Anesthetic depth is assessed by hemodynamics, intraoperative spirometry, and a proprietary, processed EEG, such as the BIS monitor. Blood pressure is supported and maintained at the patient's baseline range with a phenylephrine infusion. There are advantages to a total intravenous technique, composed of dexmedetomidine and remifentanil. Addition of these to a desflurane maintenance gas anesthetic allows for the ability to rapidly titrate anesthetic depth, based on BIS values and hemodynamic parameters. They are gradually increased throughout the procedure. Roughly an hour from the end of the procedure, desflurane is discontinued, hydromorphone is administered, fresh gas flow is increased, and switched to O_2/N_2O at 50%, and the BIS is maintained at acceptable levels (under 50) with small boluses of propofol. The ventilator is switched to a patient-assisted modality. Remifentanil is discontinued at skin closure, and dexmedetomidine is maintained at 0.5 μg/kg/hr through the extubation phase and continued until the patient leaves the OR suite.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, England: Cambridge University Press; 2010:100-109.

Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient*. Milan, Italy: Springer-Verlag Italia; 2013:199-206.

McKay RE, Large MJ, Balea MC, et al. Airway reflexes return more rapidly after desflurane anesthesia than after sevoflurane anesthesia. *Anesth Analg*. 2005;100(3):697-700.

Tufanogullari B, White PF, Peixoto MP, et al. Dexmedetomidine infusion during laparoscopic bariatric surgery: the effect on recovery outcome variables. *Anesth Analg*. 2008;106:1741-1748.

C.7. Which muscle relaxants would you use?

For intubation, a nondepolarizing muscle relaxant would be used. Patients presenting for bariatric surgery are generally on a liquid diet for a couple of days. The rate of gastric emptying is identical to that of the nonobese subjects, although MO patients have a larger gastric pouch. Cisatracurium has a predictable dose-response curve, and no prolongation of recovery due to organ-independent recovery, or Hoffman elimination; dosage is by IBW. Cisatracurium is, however, relatively expensive. For this reason, rocuronium and vecuronium are more commonly used; both are dosed by IBW.

For the occasional subject requiring rapid sequence induction, succinylcholine or rocuronium are acceptable choices. Succinylcholine is dosed by TBW because the plasma cholinesterase activity increases in proportion to the BMI. When an awake technique is chosen for securing the airway, a nondepolarizing muscle relaxant may be administered, once tracheal intubation has been confirmed.

Dense muscle relaxation is required for laparoscopic bariatric surgical procedures to facilitate ventilation, to maintain adequate intraperitoneal space for visualization and manipulation of the surgical instruments, and to permit the introduction of surgical instruments and the removal of excised tissues.

Intraoperative contracture of the abdominal musculature, due to inadequate muscle relaxants, may increase intra-abdominal pressure during PNP, driving CO_2 out from the inflated abdominal cavity through the trocar sites. Adequacy of neuromuscular blockade is assessed by the anesthesiologist, by following both the train-of-four and the inflation pressures necessary for excellent surgical conditions.

A peripheral nerve stimulator should be used to monitor the extent of relaxation and to avoid underdosing or overdosing of nondepolarizing neuromuscular blocking agents. Extubation should only occur after documentation of full baseline train-of-four (T_4/T_1 >0.9), and return of extubation criteria. Reversal agents should be given in appropriate doses.

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Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:(11):107-108.

C.8. Can regional anesthesia be used intraoperatively and postoperatively to decrease opioid requirements for bariatric surgery? What are the advantages and disadvantages of regional anesthesia? What are some of the newer techniques available?

Several regional anesthetic techniques may be used intraoperatively and postoperatively to decrease opioid requirements. Thoracic epidural anesthesia and analgesia (TEAA), the best studied of these, has been combined with light general anesthesia and found by some authors to have a good side effect profile and to offer advantages over general anesthesia, such as decreased postoperative drowsiness, nausea, and respiratory depression, improved cardiovascular function (decreased LV stroke work index), decreased oxygen consumption, earlier return of lung function, less pulmonary complications, earlier return of gastrointestinal function, and shorter hospitalization times than intravenous patient-controlled analgesia (IV-PCA). Regional anesthesia/analgesia remains underutilized (IV-PCA is >90%) in this patient population because of the following disadvantages: technical difficulties, logistics (slows OR case flow), increased incidence of epidural failure and catheter dislodgment, decreased epidural space from intra-abdominal pressure causing unpredictable spread of local anesthetics (LAs), variable block level, and increased incidence of wound infection, possibly from microdehiscence. Both patient-controlled epidural analgesia (PCEA) and IV-PCA offer excellent pain reduction scores without respiratory depression when properly used. It is recommended that epidurals be inserted in the sitting position, using ultrasonic guidance. Laparoscopic cases currently comprise approximately 75% of bariatric surgical volume, reducing the need for postoperative analgesic services.

Other regional anesthesia techniques in the morbidly obese that have been less studied include continuous spinal anesthesia and analgesia (CSAA) and intrathecal opioids (ITO). CSAA may be used with or without general anesthesia. The advantages are the same as for TEAA, except that catheter insertion is technically easier, there is a denser block with more motor component, and more predictable and controllable dermatomal spread. With all of these techniques, LA dose is typically 75% to 80% of the dose for the nonobese patient. LA and opioids act synergistically at decreased dosages. Respiratory depression is more common using hydrophilic agents (e.g., morphine) than lipophilic agents (e.g., fentanyl). Respiratory depression induced by morphine follows a longer time course (1 to 18 hours) than with fentanyl (minutes to 2 hours). It is important to identify those individuals with risk factors for neuraxial respiratory depression risk factors: excessive or repeated doses, concomitant sedatives or hypnotics, advanced age, demonstrated lack of opioid tolerance, increased intraabdominal pressure (e.g., PNP), and severe OSAHS patients, who may be at risk for massive pharyngeal collapse. Our patient was not a candidate for regional anesthesia/analgesia for this reason.

Some of the newer techniques available include multimodal perioperative analgesia (MMPA), nonopioid analgesia (NOA), and dexmedetomidine. MMPA, a combination of preincisional LAs, nonsteroidal anti-inflammatory drugs (NSAIDs), and IV-PCA, may also use preemptive analgesia. NOA uses a combination of methylprednisolone, ketorolac, clonidine, lidocaine, ketamine infusion, and magnesium sulfate infusion to decrease side effect profile and speed recovery. Dexmedetomidine, a centrally acting α_2-agonist, may be used intraoperatively and postoperatively to decrease opioid requirements. In current practice, very few cases are performed with the addition of regional anesthesia. Three factors are responsible for this: First, virtually all cases are performed laparoscopically, so postoperative pain scores are lower; second, regional anesthesia even in experienced hands slows patient throughput, in an era where production pressures are paramount; third, and most importantly, today's anesthetic medications are superior, particularly dexmedetomidine and remifentanil, providing a seamless transition to postoperative PCA. There are very few studies on regional anesthesia on bariatric surgical subjects; most studies are on the obese obstetric population.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:(11):138-142.

Brodsky JB, Mariano ER. Regional anesthesia in the obese patient: lost landmarks and evolving ultrasound guidance. *Best Pract Res Clin Anaesthesiol*. 2011;25:61-72.

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Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient*. Milan, Italy: Springer-Verlag Italia; 2013:227-236.

C.9. What is the pathophysiology of pneumoperitoneum (PNP)? What is the effect on the cardiopulmonary system? How does it change perioperative care? What are the optimal ventilator strategies for morbidly obese patients undergoing bariatric surgery?

Currently, the vast majority of bariatric surgical procedures are performed laparoscopically. Benefits of laparoscopy include much smaller surgical incisions, decreased postoperative pain requirements, shorter hospital stay, and faster recovery time to baseline level of activity. CO_2 is the universally accepted gas choice for abdominal insufflation during laparoscopy. CO_2 has documented advantages, including short half-life, due to high tissue diffusion across all tissue beds, and less flammability and morbidity, compared with other agents trialed (oxygen, nitrous oxide).

PNP with CO_2, however, alters physiology and complicates intraoperative anesthetic management. Altered physiology due to PNP is both primary (due to CO_2 absorption) and secondary (due to increased intra-abdominal pressure). Primary physiologic changes arise from acidification of tissues from CO_2 absorption (approximately 30 to 42 mL per minute), which increased ventilator requirements (approximately 30%).

Cerebral effects arise from changes in cerebral vasoregulation from hypercarbia: increased intracranial pressure from increased intrathoracic pressure and cerebral vasodilation, decreased cerebral oxygen saturation, and initiation of a hormonal cascade, with catecholamine and vasopressin release.

Cardiovascular effects arise from CO_2, which mildly depresses myocardial contractility and sensitizes myocardium to the arrhythmogenic effects of catecholamines. Most of the pathophysiologic changes occur as a result of increased intra-abdominal pressure, which decreases venous return, resulting in decreased cardiac output and blood pressure. Other *cardiac effects* are those typical of increased sympathetic output from hypercarbia, although bradycardia may result from initial peritoneal insufflation.

Pulmonary effects are due to cephalad shift of the diaphragm, decreased FRC, increased physiologic dead space, greater ventilation/perfusion mismatch, decreased pulmonary compliance, and increased airway pressures especially peak airway pressure.

Renal effects are due to decreased renal perfusion, decreased urine output, and increased release of antidiuretic hormone, plasma renin, and aldosterone levels. *Hepatic effects* are due to decreased portal venous flow, which may lead to hepatic hypoperfusion, acute hepatocellular injury, and increased transaminase levels. Increased intra-abdominal pressure causes decreased venous drainage of the abdominal viscera and the lower extremities, which may result in deep venous thrombosis.

Most of the intraoperative changes caused by PNP are well tolerated, provided that the insufflation pressure is maintained at the lowest acceptable level, approximately an intraabdominal pressure of 15 mm Hg, an intraoperative recruitment maneuver is provided when indicated, and the following precautions are taken: loading of intravenous fluids, use of sequential compression devices, optimal ventilator settings described below, and intraoperative spirometry to monitor flow- and pressure-volume loops, and plateau airway pressure.

- *Management of ventilation in MO patients*
  - CPAP during induction
  - FIO_2 <0.8
  - Recruitment maneuver after induction, then periodically
  - Pressure control-volume guarantee (PC-VG)
  - V_T = 6 to 10 mL per kg IBW
  - PEEP 10 to 12 cm H_2O
  - I:E = 1:1
  - Inspiratory pressure <30 cm H_2O

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- CPAP or BIPAP after extubation

Blood pressure may need to be supported with a phenylephrine infusion, as the majority of the case is performed in an extreme reverse Trendelenburg position.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010;2:44-50, 124-134.

Cadi P, Guenoun T, Journois D, et al. Pressure-controlled ventilation improves oxygenation during laparoscopic obesity surgery compared with volume-controlled ventilation. *Br J Anaesth*. 2008;100(5):709-716.

Futier E, Constantin JM, Pelosi P et al. Intraoperative recruitment maneuver reverses detrimental pneumoperitoneum-induced respiratory effects in healthy weight and obese patients undergoing laparoscopy. *Anesthesiology*. 2010; 113(6):1310-1319.

Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient*. Milan, Italy: Springer-Verlag Italia; 2013:179-195.

C.10. What are the devices that anesthesiologists place in the upper gastrointestinal canal during laparoscopic bariatric surgery? Are there risks associated with placement and management of these devices?

Various devices have been placed in the upper gastrointestinal tract during laparoscopic bariatric surgery. These devices are usually placed blindly by the anesthesiologist and guided indirectly by the surgeon by laparoscopic visualization. The video image is projected through a video camera, which placed through an abdominal port in the distended abdomen, PNP, and projected onto the video screen. Transit of the device is tracked by watching distension of the esophagus and stomach caused by passage of the particular device. The surgeon guides passage of the device, and determines when the proper location of the tip has been reached, and may help position the device with intraperitoneal devices passed through additional abdominal ports.

Foregut devices are placed by the anesthesiologist: *Orogastric tubes* are used both to decompress the stomach at the beginning of surgery, and for “a leak test” after completion of the anastomosis, in which a vital dye, such as methylene blue, is injected into the orogastric tube, the stomach is inflated, and a watertight seal is documented. Both *bougies* or, less frequently, *calibration tubes* are placed to serve as templates to delineate the landmarks for the anastomosis and choose the staple line. Bougies come as either *graduated-tip*, which are easier to insert, or *blunt-tip*. Esophageal *anvils* are used as templates as internal staplers during laparoscopic Roux-en-Y gastric bypasses. A relatively new device, the ViSiGi 3D (Bariatric Solutions Australia, a division of Sphere Surgical Pty. Ltd, Ormond, Australia) can perform all of these functions. Both the anesthesiologist who places these devices and the surgeon determine that the proper functionality, integrity at removal, and lack of trauma upon removal. When the anesthesiologist is unable to place the indicated device, there are three options: The surgeon may try, gastroscopy may be attempted, or surgery may be converted to an open procedure.

With modern surgical practice, perioperative mortality of bariatric surgery is less than 1% and is usually associated with anastomotic leaks with peritonitis (75%). Because the anesthesiologist places esophageal-gastric devices, they are also culpable. Many of these cases are settled for large amounts, with gag orders; as such, it is difficult to measure anesthetic incidence of settled claims. Clearly, placement of these devices is a crucial portion of the anesthetic and surgical risk. As such, the attending anesthesiologist should be present and document his findings. Orogastric tubes and esophageal temperature probes are strictly prohibited for patient monitoring during bariatric surgery; they may be stapled and left as foreign bodies, resulting in major morbidity or death.

Abu-Gazala S, Donchin Y, Keidar A. Nasogastric tube, temperature probe, and bougie stapling during bariatric surgery: a multi-center survey. *Surg Obes Relat Dis*. 2012;8(5):595-600.

Rosenthal RJ, Diaz AA, Arvidsson D, et al. International Sleeve Gastrectomy Expert Panel Consensus Statement: best practice guidelines based on experience of >12,000 cases. *Surg Obes Relat Dis*. 2012;8(1):8-19.

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ViSiGi 3D. ViSiGi 3D defined. http://www.visigi.com/3d/. Accessed July 1, 2015.

C.11. When will you extubate this patient? What are the extubation criteria?

In the past, prophylactic ventilatory support throughout the first postoperative night was occasionally utilized for the morbidly obese OHS patient having an open abdominal weight reduction procedure. Currently, this is rarely the case due to the huge yearly

increases in the number of bariatric surgeries in the United States (16,000 in the early 1990s to 140,000 in 2010), advanced laparoscopic experience of the surgeons, and advances in the anesthetic care of the morbidly obese. The majority of patients are extubated in the OR at the conclusion of surgery as soon as the following extubation criteria are met:

- Intact neurologic status, fully awake and alert, with head lift >5 seconds.
- Hemodynamic stability
- Normothermia, above 36°C.
- Full reversal of neuromuscular blocking agents confirmed with train-of-four (T_4/T_1 >0.9)
- Respiratory rate (breaths per minute) >10 and <30
- Baseline peripheral oxygenation, as judged by pulse oximeter (SpO_2 >95% on FIO_2 of 0.4)
- Acceptable blood-gas results, if available (FIO_2 of 0.4; pH, 7.35 to 7.45; PaO_2, >80 mm Hg; $PaCO_2$, <50 mm Hg)
- Acceptable respiratory mechanics: negative inspiratory force (NIF) >25 to 30 cm H_2O; vital capacity (VC) >10 mL per kg IBW; V_T >5 mL per kg IBW
- Acceptable pain control
- No demonstrated or suspected laboratory abnormalities

Extubation criteria should be used systematically in obese patients. In all cases, an attending anesthesiologist with advanced airway skills must be in attendance for extubation. Emergency tracheal reintubation may be necessary. Patients with documented difficult airway should be extubated per protocol. Patients with OSAHS, OHS, and PS have higher incidence of postoperative respiratory dysfunction. They require special attention before and after extubation and occasionally warrant a monitored bed for observation.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:(11):124-134.

Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient*. Milan, Italy: Springer-Verlag Italia; 2013:241-253.

Littleton SW. Impact of obesity on respiratory function. *Respirology*. 2012;17:43-49.

Neligan PJ, Malhotra G, Fraser M, et al. Noninvasive ventilation immediately after extubation improves lung function in morbidly obese patients with obstructive sleep apnea undergoing laparoscopic bariatric surgery. *Anesth Analg*. 2010;110:1360-1365.

Talab HF, Zabani IA, Abdelrahman HS, et al. Intraoperative ventilatory strategies for prevention of pulmonary atelectasis in obese patients undergoing laparoscopic bariatric surgery. *Anesth Analg*. 2009;109:1511-1516.

UpToDate. Anesthesia for the obese patient. http://www.uptodate.com/contents/anesthesia-for-the-obesepatient. Accessed July 1, 2015.

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C.12. What is apneic oxygenation?

Draper and Whitehead conducted the pioneer study on apneic oxygenation in 1944. Apneic oxygenation (formerly known as diffusion respiration) is actually caused by mass movement oxygenation. When the lungs are completely denitrogenized with oxygen and the airway is connected to an oxygen source, continuous oxygenation takes place by mass movement. Normally, every minute, 230 mL of oxygen is removed from the alveoli for metabolism, and 200 mL of CO_2 is produced and eliminated from the lungs. When a person is apneic, only 10% of CO_2 accumulates in the alveoli, and 90% of CO_2 stays in the blood as bicarbonate. Consequently, 250 mL of oxygen is removed from the lungs and 20 mL of CO_2 accumulates in the lungs, creating a 230-mL vacuum effect and sucking in oxygen. Carbon dioxide tension continues to rise because no elimination occurs during apnea. The total pressure in the alveoli is constant, so the decrease in PO_2 equals the rise in PCO_2, ranging from 3 to 6 mm Hg per minute. If the patient had been breathing 100% oxygen before respiratory arrest, the starting alveolar PO_2 would be about 650 mm Hg, and therefore, the patient could theoretically maintain PaO_2 above 100 mm Hg for about 100 minutes of apnea provided that the airway remained clear and connected to 100% oxygen. However, patients will die of severe respiratory acidosis (pH <6.80) before hypoxemia occurs. Moreover, as seen in suffocation, gross hypoxia supervenes after about 90 seconds if apnea with airway occlusion follows air breathing at the FRC. When the airway is patent and the ambient gas is air, gross hypoxia

supervenes after about 2 minutes of apnea, as seen during intubation without preoxygenation. However, if the patient is preoxygenated for 3 minutes, gross hypoxia will not occur until 6 minutes of apnea for normal-weight patients and until about 3 minutes of apnea for morbidly obese patients. Apneic oxygenation is an older technique that is not recommended for obese patients. Aside from hypoxia and hypercarbia, it may lead to atelectasis, or derecruitment of West Zone 3.

A much more useful maneuver in severely obese patients is to utilize 100% oxygen and PEEP, during both induction and emergence from general anesthesia.

Coussa M, Proietti S, Schnyder P, et al. Prevention of atelectasis formation during induction of general anesthesia in morbidly obese patients. *Anesth Analg*. 2004;98:1491-1495.

Draper WB, Whitehead RW. Diffusion respiration in the dog anesthetized by pentothal sodium. *Anesthesiology* 1944;5:262.

Edmark L, Kostova-Aherdan K, Enlund M, et al. Optimal oxygen concentration during induction of general anesthesia. *Anesthesiology*. 2003;98:28-33.

Gander S, Frascarolo P, Suter M, et al. Positive end-expiratory pressure during induction of general anesthesia increases duration of nonhypoxic apnea in morbidly obese patients. *Anesth Analg*. 2005;100:580-584.

Jense HG, Dubin SA, Silverstein PL, et al. Effect of obesity on safe duration of apnea in unanesthetized humans. *Anesth Analg*. 1991;72:89-93.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia, PA: Elsevier Butterworth Heinemann; 2005;160-161.

C.13. What is diffusion hypoxia? How do you prevent it?

Fink and colleagues in 1954 first reported diffusion hypoxia during recovery from nitrous oxide-oxygen anesthesia. A mild degree of hypoxia can develop for more than 10 minutes when nitrous oxide-oxygen anesthesia is concluded and the patient is allowed to breathe room air. The arterial oxygen saturation can fall 5% to 10% and often reaches values less than 90% (PaO_2 <60 mm Hg). This occurs at the times when nitrous oxide is eliminated rapidly through the lungs. Nitrous oxide is 35 times more soluble in blood than nitrogen. Therefore, the amount of nitrous oxide diffused from blood to alveoli is much more than the amount of nitrogen diffused from alveoli to blood. Hence, alveolar oxygen is diluted by nitrous oxide. Diffusion hypoxia can be prevented by the inhalation of high concentrations of oxygen for several minutes before the patient is allowed to breathe room air.

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Diffusion hypoxia should not be allowed to occur in obese patients. There is no room for deep extubations in the MO/OSA patient. Patients should be fully awake, with baseline respiratory function. All anesthetics and analgesics, with the possible exception of dexmedetomidine, should be stopped. Many of the newer anesthesia ventilators allow the use of pressure support ventilation during the emergence phase, which minimizes atelectasis. One hundred percent oxygen prior to, and during, extubation followed by a tight-fitting face mask with pressure support aids the patient in reestablishing ventilatory function, and assists in removal of trace anesthetic gas, until the patient is fully recovered.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:124-137.

El-Solh AA, Aquilina A, Pineda L, et al. Noninvasive ventilation for prevention of post-extubation failure in obese patients. *Eur Respir J*. 2006;28:588-595.

Fink BR. Diffusion anoxia. *Anesthesiology*. 1955;16:511-519.

Fink BR, Carpenter SL, Holaday DA, et al. Diffusion anoxia during recovery from nitrous oxide-oxygen anesthesia. *Fed Proc*. 1954;13:354.

Sheffer L, Steffenson JL, Birch AA. Nitrous oxide-induced diffusion hypoxia in patients breathing spontaneously. *Anesthesiology*. 1972;37:436-439.

D. Postoperative Management

D.1. What are the major early postoperative complications in the morbidly obese patient?

The major early postoperative complications in the morbidly obese are mostly related to the pulmonary and cardiovascular systems. Postanesthetic hypoxemia is more common in the

MO patient, with or without the presence of OSA, despite supplemental oxygen therapy. This may be due to atelectasis, or reversion to a restrictive breathing pattern, with increased use of accessory muscles, as well as decreased FRC from pain (“splinting”), residual PNP, parietal peritoneal irritation from carbonic acid, air in the stomach, as well as pain. Other potential early postoperative complications include respiratory depression from residual anesthetic or muscle relaxant, early ventilatory failure with need for reintubation, positional ventilatory collapse, hemodynamic instability, PONV, and venous thromboembolism. Early surgical complications include anastomotic closure with bowel obstruction, anastomotic leak, and wound infection. PONV is distinguished from opioid-induced nausea and vomiting (OINV), which is more severe and more difficult to treat. Bariatric surgical procedures are highly emetogenic and frequently require prophylaxis with multiple agents. They are foregut surgical operations and interrupt peristalsis and the gastroesophageal antireflux mechanism. Severe, resistant or recurrent PONV may be due to anastomotic kink or leak; the surgical team should be called to examine the patient. Late (in-hospital) postoperative ventilatory insufficiency is always a risk; patients should be triaged by the perioperative team to relatively low risk, middle risk, and high risk. High-risk patients include those with severe cardiopulmonary disease, or severe OSA, by either STOP questionnaire, or who are noncompliant with NPPV (CPAP or BIPAP). They should be triaged to an intensive care or step-down unit postoperatively. The standard of postoperative analgesia is IV-PCA. All patients at increased risk of respiratory depression also need to be monitored, in at least a step-down unit. These patients should be transported wide-awake, whenever possible, and with oxygen (nasal cannula or face mask), as well as a NPPV device if needed. Recently, an affordable, lightweight, simple-to-use NPPV device has been marketed, the Boussignac system (Vygon [UK] Ltd, Swindon, Wiltshire, United Kingdom). When connected to an E-cylinder, 10 L per minute produces +5 cm H_2O, and 15 L per minute produces +7.5 cm H_2O, through a virtual valve, by means of the laws of fluid dynamics.

At any given weight, the perioperative risk is greater for central obesity than for peripheral obesity, and for patients with preexisting severe comorbidity, especially OSAHS. The major perioperative risk of death correlates statistically with BMI, preexisting hypertension, pulmonary embolus, and anastomotic leak. Etiology is surgical, anesthetic, mixed, or undetermined.

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Ahmad S, Nagle A, McCarthy RJ, et al. Postoperative hypoxemia in morbidly obese patients with and without obstructive sleep apnea undergoing laparoscopic bariatric surgery. *Anesth Analg*. 2008;107(1):138-143.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:155-159, 161-170.

Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient*. Milan, Italy: Springer-Verlag Italia; 2013:241-253.

Neligan PJ, Malhotra G, Fraser M, et al. Continuous positive airway pressure via the Boussignac system immediately after extubation improves lung function in morbidly obese patients with obstructive sleep apnea undergoing laparoscopic bariatric surgery. *Anesthesiology*. 2009;110(4):878-884.

Vygon. Boussignac CPAP system. http://www.vygon.co.uk/pdf/upload/Boussignac_web.pdf. Accessed July 1, 2015.

D.2. How does position affect respiratory function in the obese patient?

In the supine position, intra-abdominal contents shift the diaphragm rostrally resulting in diaphragmatic dysfunction, decreased FRC, airway closure, increase in venous admixture (Q_S/Q_T), decreased PaO_2, and possibly positional ventilatory collapse. The FRC increases 30% in obese patients by changing from the supine position to the sitting position, both in nonsurgical and post-laparotomy patients. Preoxygenation is more effective in the semi-Fowler position (head up 30 to 45 degrees) than in the supine position in severely obese patients, both for preinduction of general anesthesia, and for eventual postoperative reintubation. Recovery should take place in this position as soon as these patients are hemodynamically stable. Other benefits of a semisitting position are decreased superior vena cava pressure and decreased incidence of positional injuries, which are more common in the MO, especially ulnar neuropathy. Patients recovered in the semi-Fowler position who are in need of eventual emergent mask ventilation or tracheal reintubation present better conditions for the

laryngoscopist. There is a higher incidence of tracheal tube misplacement in the morbidly obese; care should be taken when positioning intubated morbidly obese patients in a semi-Fowler position.

Dixon BJ, Dixon JB, Carden JR, et al. Preoxygenation is more effective in the 25° head-up position than in the supine position in severely obese patients. *Anesthesiology.* 2005;102:1110-1115.

Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient*. Milan, Italy: Springer-Verlag Italia; 2013:141-143.

D.3. How would you prevent postoperative atelectasis?

In the past, bariatric surgical procedures were often performed open, with an incidence of postoperative atelectasis of 45%. Approximately 90% are now performed laparoscopically, so the incidence would be expected to decline substantially.

Early ambulation, chest physical ambulation with incentive spirometry, and effective coughing are encouraged to improve respiratory function. Prolonged recumbency is avoided whenever possible because of its adverse effects on the ventilation/perfusion ratio and to minimize circulatory congestion of the recumbent lung. Careful titration of postoperative analgesics is emphasized to prevent splinting from pain and hypoventilation from excessive sedation.

Reinius H, Jonsson L, Gustafsson S, et al. Prevention of atelectasis in morbidly obese patients during general anesthesia and paralysis: a computerized tomography study. *Anesthesiology*. 2009;111(5):979-987.

D.4. How long would you prescribe supplementary oxygen postoperatively?

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The incidence of postanesthetic hypoxemia (PaO_2 <60 mm Hg) is increased from a baseline of 25% to 30% in the nonobese to 75% in the obese. For a routine case on an otherwise healthy patient with simple obesity, supplemental oxygen in the PACU is probably sufficient. In most MO patients with comorbidities, oxygen should be prescribed for 24 to 72 hours. The MO patient with severe OSAHS on CPAP or BIPAP will usually have continuation of their therapy overnight, be recovered in a semi-Fowler position (30 to 45 degrees), and should have individualized care, in an appropriate setting with continuous pulse oximetry and respiratory monitoring. At the New York-Presbyterian Hospital, the majority of these patients are discharged to home on the second or third postsurgical day.

Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient*. Milan, Italy: Springer-Verlag Italia; 2013:241-253.

D.5. How would you control postoperative pain?

Postoperative analgesia is provided by PCA in more than 90% of bariatric surgical procedures, as it was for our patient. PCA has been shown to be safe and effective in the MO patient population. It has many advantages: PCA is simple to use, saves nursing time, and involves minimal time delay between patient perception of pain and therapy. There is less splinting and derangement of PFTs. PCA also facilitates early ambulation and shortens hospital stay. Hydromorphone is the gold standard. Morphine, once commonly used, has fallen out of favor due to histamine release, higher rates of nausea, and more interpatient variability. Dose regimens need to be individualized according to pain control and side effect profile. There have been rare cases of respiratory complications in the MO-OSAHS patient, so extra vigilance is needed in this group. PCA dosages for the MO in the opioid naive, based on IBW, are as follows:

- MSO_4 20 μg per kg IBW
- Hydromorphone 4 to 5 μg per kg IBW
- Fentanyl 1 μg per kg IBW
- Methadone 20 μg per kg IBW

All settings are every 10 minutes, without continuous rate, at 80% of the calculated maximum doses. Although the opioids have different lipid solubilities, for IV-PCA, all have been dosed by IBW because the doses were originally formulated using IBW. Meanwhile, as we are titrating to individual patient satisfaction, there is room for posttreatment dose modification.

Intravenous infusions of opioids may also be administered in a monitored setting. In the past, opioids have been administered intramuscularly. Although this route has been shown to be effective, intramuscular injection is not advisable in the MO because of unpredictable pharmacodynamics, arising from inadvertent injection into lipid tissue.

There are three regional anesthetic/analgesic options: TEAA/PCEA, intrathecal (IT) opioids, and continuous spinal anesthesia/patient-controlled intrathecal analgesia (CSA/PCIA). All of these may be used with or without light general anesthesia. They offer similar side effect profiles and will be described together. *PCEA*, the most commonly used of these, has numerous theoretical advantages. At a lower dose compared with parenteral opioids, there are few side effects and serious complications, effective analgesia, faster recovery, less respiratory complications, decreased total body oxygen consumption, improved cardiac function, and shorter hospitalization times compared with PCA. PCEA dosages in the MO should be decreased 75% to 80%, due to decreased volume of the epidural space from increased intraabdominal pressure. PCEA is strongly recommended when feasible yet remains underutilized. Patients should be positioned in a sitting position for epidural catheter insertion, and ultrasound guidance is recommended. Disadvantages include a higher rate of wound infection, possibly because of microdehiscence from faster return of gastrointestinal function, and the risk of neural injury. There is frequent technical difficulty with catheter insertion, which slows OR case flow. There is a higher rate of inadequate function, catheter migration and replacement, and variable block level. Side effects include excessive drowsiness, PONV, pruritus, and urinary retention. Respiratory depression occurs rarely and is more common with hydrophilic (e.g., preservative-free morphine sulfate [PFMS]) than with hydrophilic agents. With PFMS, it may occur from 1 hour until 18 hours. With fentanyl or sufentanil, it may occur from minutes until 2 hours. Neuraxial opioid respiratory depression risk factors include advanced age, excessive or repeated doses, lack of opioid tolerance, use of concomitant sedatives or hypnotics, increased intra-abdominal pressure (e.g., PNP), and severe OSAHS, which may precipitate massive pharyngeal collapse. *CSA/PCIA* with light general anesthesia has been used for gastroplastic surgery. It is technically easier to perform than TEAA/PCEA and produces a denser block with motor component, which

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is more predictable and controllable. *IT* opioids, with or without LAs, are technically easier to administer, and offer an excellent alternative for appropriate surgical procedures. Other methods of controlling postoperative pain in bariatric surgery include preemptive analgesia via LA wound infiltration before and after surgery, pre- and intraoperative nonopioid drug combination (ketorolac, clonidine, lidocaine, ketamine, magnesium sulfate, and methylprednisolone), and perioperative dexmedetomidine.

Some bariatric patients will develop esophageal spasm-like pain in the postoperative period, which may mimic myocardial ischemic pain. These usually respond to antacids and H_2-receptor antagonists.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010;(11):144-152.

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Sigurdson K, Ayas NT. The public health and safety consequences of sleep disorders. *Can J Physiol Pharmacol*. 2007;85(1):179-183.

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