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Miller's Anesthesia Review

Second Edition

Lorraine M. Sdrales
Ronald D. Miller

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MILLER'S ANESTHESIA REVIEW

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MILLER'S ANESTHESIA REVIEW

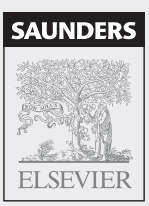
SECOND EDITION

Lorraine M. Sdrales, MD

Attending Anesthesiologist
Cedars-Sinai Medical Center
Los Angeles, California

Ronald D. Miller, MD

Professor of Anesthesia and Perioperative Care
Department of Anesthesia and Perioperative Care
University of California, San Francisco, School of Medicine
San Francisco, California



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CONTRIBUTORS

Meredith C.B. Adams, MD
Assistant Professor, Departments of Anesthesiology, Psychiatry, and Neurology, University of Florida; Section Chief, Pain Medicine, North Florida/South Georgia Veterans Health System, Gainesville, Florida

Dean B. Andropoulos, MD, MHCM
Chief of Anesthesiology, Department of Pediatric Anesthesiology, Texas Children's Hospital; Professor, Department of Anesthesiology and Pediatrics, Baylor College of Medicine, Houston, Texas

Sheila R. Barnett, MD
Associate Professor of Anesthesiology, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, Massachusetts

Luca M. Bigatello, MD
Director, Surgical Critical Care, Department of Anesthesiology and Pain Medicine, St. Elizabeth's Medical Center, Boston, Massachusetts

Thomas J.J. Blanck, MD, PhD
Professor and Chairman, Department of Anesthesiology, Professor of Physiology and Neuroscience, New York University Langone Medical Center, New York, New York

Lundy Campbell, MD
Associate Clinical Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Lydia Cassorla, MD
Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Daniel Cole, MD
Professor of Anesthesiology, College of Medicine Mayo Clinic; Chair, Department of Anesthesiology, Mayo Clinic Arizona, Phoenix, Arizona

Adam Collins, MD
Associate Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Anil de Silva, MD
Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Ken Drasner, MD
Professor of Clinical Anesthesia, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Helge Eilers, MD
Associate Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

John Feiner, MD
Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Alana Flexman, MD
Clinical Assistant Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Charles J. Fox, MD
Vice Chair for Academics, Department of Anesthesiology, Tulane University Medical Center, New Orleans, Louisiana

William R. Furman, MD
Professor of Anesthesiology and Surgery, Vice Chair for Clinical Affairs, Department of Anesthesiology, Vanderbilt University School of Medicine; Executive Medical Director, Perioperative Services, Vanderbilt University Hospital, Nashville, Tennessee

Steven Gayer, MD, MBA
Professor, Department of Anesthesiology and Ophthalmology, The Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida

David B. Glick, MD, MBA
Associate Professor, Department of Anesthesia and Critical Care, University of Chicago; Medical Director, Pre- and Post-Anesthesia Care Units, University of Chicago, Chicago, Illinois

Erin A. Gottlieb, MD
Assistant Professor, Department of Pediatrics and Anesthesiology, Baylor College of Medicine; Attending Anesthesiologist, Division of Pediatric Cardiovascular Anesthesiology, Texas Children's Hospital, Houston, Texas

Tula Gourdin, MBA
Analyst, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Michael A. Gropper, MD, PhD
Professor and Executive Vice Chairman, Department of Anesthesia and Perioperative Care, University of California, San Francisco; Director, Critical Care Medicine, University of California, San Francisco Medical Center, San Francisco, California

Jennifer E. Hofer, MD
Assistant Professor, Department of Anesthesia and Critical Care, The University of Chicago Medical Center, Chicago, Illinois

Robert W. Hurley, MD, PhD
Associate Professor, Departments of Anesthesiology, Neurology, Orthopaedics and Rehabilitation, and Psychiatry, University of Florida; Chief of Pain Medicine, College of Medicine, University of Florida; Medical Director, University of Florida Pain and Spine Center, Gainesville, Florida

Steve Hyman, MD, MM
Associate Professor of Clinical Anesthesiology, Department of Anesthesiology, Vanderbilt University School of Medicine, Nashville, Tennessee

Alan David Kaye, MD, PhD
Professor and Chairman, Department of Anesthesiology, Professor, Department of Pharmacology, Louisiana State University School of Medicine-New Orleans, New Orleans, Louisiana

Jae-Woo Lee, MD
Associate Professor in Residence, Department of Anesthesiology and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Eric Y. Lin, MD
Assistant Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Lawrence Litt, PhD, MD
Emeritus Professor, Departments of Anesthesia and Perioperative Care, and Radiology, University of California, San Francisco, School of Medicine, San Francisco, California

Henry Liu, MD
Associate Professor of Anesthesiology, Director of Cardiothoracic and Vascular Anesthesia, Tulane University Medical Center, New Orleans, Louisiana

Linda Liu, MD
Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Jennifer Lucero, MD
Assistant Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Anuj Malhotra, MD
Pain Management Fellow, Department of Anesthesia, Stanford University, Palo Alto, California

Vinod Malhotra, MD
Professor, Department of Anesthesiology and Urology, Vice Chair for Clinical Affairs, Clinical Director of the Operating Rooms, Weill Cornell Medical College and Medical Center, New York, New York

Rachel Eshima McKay, MD
Clinical Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Pankaj Mehta, MD
Faculty of Interventional Pain Medicine, Cleveland Clinic Foundation, Cleveland, Ohio

Douglas G. Merrill, MD, MBA
Professor of Anesthesiology, Dartmouth Medical School; Director, The Center for Perioperative Services; Medical Director, Outpatient Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire

Ronald D. Miller, MD
Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Theodora K. Nicholau, PhD, MD
Clinical Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Howard D. Palte, MBChB, FCA(SA)
Assistant Professor, Department of Anesthesiology, University of Miami, Miami, Florida

Anup Pamnani, MD
Assistant Professor, Department of Anesthesiology, Weill Cornell Medical College, New York, New York

Siamak Rahman, MD
Associate Clinical Professor, Department of Anesthesiology, University of California, Los Angeles, Los Angeles, California

James P. Rathmell, MD
Professor of Anesthesia, Harvard Medical School; Vice Chair and Chief, Division of Pain Medicine, Department of Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts

Mark Rollins, MD, PhD
Associate Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Andrew D. Rosenberg, MD
Chief, Department of Anesthesiology, New York University Hospital For Joint Diseases; Executive Vice-Chair, Department of Anesthesiology, New York University School of Medicine, New York, New York

Patricia Roth, MD
Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Isobel A. Russell, MD, PhD, FACC
Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine; Chief, Cardiac Anesthesia Services, University of California, San Francisco Medical Center, San Francisco, California

David Shimabukuro, MDCM
Associate Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Randolph H. Steadman, MD
Professor and Vice Chair, Department of Anesthesiology, David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, California

Greg Stratmann, MD, PhD
Associate Professor, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Bobbie Jean Sweitzer, MD
Professor, Departments of Anesthesiology and Critical Care and Medicine, University of Chicago; Director, Anesthesia Perioperative Medicine Clinic, University of Chicago Medical Center, Chicago, Illinois

Pekka Talke, MD
Professor, Chief of Neuroanesthesia, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine, San Francisco, California

Arthur W. Wallace, MD, PhD
Professor in Residence and Vice Chair, Department of Anesthesia and Perioperative Care, University of California, San Francisco, School of Medicine; Chief of Anesthesia, Veterans Affairs Medical Center, San Francisco, California

Jeffrey D. Wilkinson, MD
South County Anesthesia Associates; Chairman, Quality Committee of the Board, St. Anthony's Medical Center, St. Louis, Missouri

Victor W. Xia, MD
Associate Clinical Professor, Department of Anesthesiology, David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, California

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PREFACE

As with all medical disciplines, the practice of anesthesia requires a solid knowledge base as well as clinical competence. There are many textbooks that provide the student of anesthesiology with the information needed to practice anesthesia. What was lacking was a book that allowed students at every level to actively participate in their learning. This study guide lets the reader evaluate his or her own knowledge and formulate answers alone or in groups, and it provides an alternate means of study of the information.

The format of the book is question and answer. It is organized in a logical progression from basic anesthesia principles and concepts to more complex issues. These include the delivery of anesthesia in various settings and the administration of anesthesia to patients with organ system dysfunction and disease states. All the answers are current, fully formed, and self-explanatory, and the page number references provided at the end of each question refer the reader to the *Basics of Anesthesia*, Sixth Edition, text where further information on the given topic can be found.

There are several ways this study guide can be used. The first-year anesthesia resident may use it to solidify information read. Anesthesia residents at every level may use it to prepare for specific clinical applications that they may face on a subspecialty rotation or with given cases. Anesthesia residents can also use this study guide for group study in which they will be required to verbalize answers to questions on given topics. Similarly, faculty may use the study guide to quiz residents orally in a coherent, progressive manner in formal or informal settings. This question and answer book can be used for self-study for Board examinations, which may be particularly useful to the anesthesiologist who is in practice and is required to register with the ABA MOCA program for recertification every 10 years. Finally, anesthesiologists in practice may find the study guide useful to refresh their knowledge base and review old and new information that they may not have been taught during their residencies. The multiple uses of this study guide make it an appropriate choice for students, teachers, and clinicians of anesthesiology at every level.

Lorraine M. Sdrales
Ronald D. Miller

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Chapter

1 SCOPE OF ANESTHESIA PRACTICE

Ronald D. Miller, Tula Gourdin

INTRODUCTION

1. When did the specialty of anesthesiology become recognized?
2. Initially, how was anesthesia primarily used and how did it evolve?
3. Name the two medical organizations whose approval allowed anesthesia to be recognized as a medical specialty.

DEFINITION OF ANESTHESIOLOGY AS A SPECIALTY

4. Besides monitoring and maintenance of normal physiology during the perioperative period, what are some of the areas that define the practice of anesthesia?
5. Name some of the organizations that comprise the American system of anesthesiology.

EVOLUTION OF ANESTHESIA AS A MULTIDISCIPLINARY MEDICAL SPECIALTY

6. Name the four subspecialties of anesthesiology that require an additional certification process from the American Board of Anesthesiology (ABA).
7. In pain management, anesthesiologists are usually part of a multidisciplinary team. Name some of the other specialties that provide services that support pain management.
8. Describe an open versus a closed critical care unit.
9. Which other anesthesia subspecialties are evolving toward a separate certification process?
10. What factor dictates whether some institutions have subspecialized anesthesia teams? Give an example of two such teams.

PERIOPERATIVE PATIENT CARE

11. What services are included in perioperative care?
12. What was the impetus behind the creation of preoperative clinics and who generally manages these?
13. Describe the standard perioperative pathway.
14. What is throughput?

TRAINING AND CERTIFICATION IN ANESTHESIOLOGY

15. What subspecialties are studied in the clinical anesthesia postgraduate training years (years 1 to 3)?
16. Describe the fundamental steps that lead to being a "board-certified anesthesiologist."
17. What is the emphasis of the Maintenance of Certification in Anesthesiology (MOCA)?
18. What are other anesthesia specialties that the ABA certifies?
19. Name the three new professional performance concepts developed by the Accreditation Council for Graduate Medical Education and the American Board of Medical Specialties.

OTHER ANESTHETIC PROVIDERS

20. What are the training differences between a certified registered nurse anesthetist and an anesthesiologist assistant?

QUALITY OF CARE AND SAFETY IN ANESTHESIA

21. The Joint Commission provides quality improvement guidelines in anesthesia for health care organizations. What three fundamental areas do these guidelines address?
22. Continuous quality improvement (CQI) programs may focus on both critical incidents and sentinel events. Describe critical incidents versus sentinel events.
23. What are some of the key factors in preventing patient injuries related to anesthesia?
24. Provide two examples of Patient Safety Practices and the Suggested Penalties for Failure to Adhere to the Practice as published in the *New England Journal of Medicine*.

ORGANIZATIONS WITH EMPHASIS ON ANESTHESIA AND SAFETY

25. Anesthesia has the distinction of being the only specialty in medicine with a foundation dedicated to issues of safety in patient care. Name the foundation.
26. Which organization provides a retrospective database of patient and safety data that can be used to assess and improve patient care?
27. Which organization investigates legal cases as a vehicle for identifying patient and practice areas of risk?
28. Name the foundation that provides research support in anesthesia.

PROFESSIONAL LIABILITY

29. This chapter states that 93 claims were filed in the United Kingdom in the years 1995 to 2007. What two areas of patient care and safety did these claims emphasize?
30. What is the anesthesiologist's best protection against medicolegal action?
31. What actions should the anesthesiologist take in the event of an accident?

RISKS OF ANESTHESIA

32. What is the estimated mortality rate from anesthesia?
33. What are some of the factors that have contributed to the decrease in anesthesia-related deaths?
34. What is the anesthesiologist's greatest anesthesia patient safety issue?
35. Vigilance accounts for a large proportion of avoidance of adverse anesthesia events. What are some of the factors in the operating room environment that diminish the anesthesiologist's ability to perform the task of vigilance?

HAZARDS OF WORKING IN THE OPERATING ROOM

36. Name some of the most prevalent hazards encountered in the operating room?

SUMMARY AND FUTURE OUTLOOK

37. Anesthesiology is constantly evolving and changing. Describe some of the changes the specialty has undergone and the direction it is moving toward.

ANSWERS*

INTRODUCTION

1. In the early 19th century, the concept of providing analgesia and eventually anesthesia became increasingly possible. (11)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

2. The major emphasis was initially on surgical anesthesia, which evolved into airway management including endotracheal intubation, which led to the development of critical care medicine, regional anesthesia, and pain medicine. (11)

3. The two organizations whose approval allowed anesthesia to be recognized as a medical specialty are the American Medical Association and the American Board of Medical Specialties. (11)

DEFINITION OF ANESTHESIOLOGY AS A SPECIALTY

4. The American Board of Anesthesiology defines anesthesiology as a discipline within the practice of medicine that deals with:
   a. Assessment of, consultation for, and preparation of patients for anesthesia.
   b. Relief and prevention of pain during and following surgical, obstetric, therapeutic, and diagnostic procedures.
   c. Monitoring and maintenance of normal physiology during the perioperative period.
   d. Management of critically ill patients.
   e. Diagnosis and treatment of acute, chronic, and cancer-related pain.
   f. Clinical management and teaching of cardiac and pulmonary resuscitation.
   g. Evaluation of respiratory function and application of respiratory therapy.
   h. Conduct of clinical, translational, and basic science research.
   i. Supervision, teaching, and evaluation of performance of both medical and paramedical personnel involved in perioperative care.
   j. Administrative involvement in health care facilities and organizations, and medical schools necessary to implement these responsibilities. (11-12)

5. As with other medical specialties, anesthesiology is represented by professional societies (American Society of Anesthesiologists, International Anesthesia Research Society), scientific journals (*Anesthesiology*, *Anesthesia and Analgesia*), a residency review committee with delegated authority from the Accreditation Council for Graduate Medical Education to establish and ensure compliance of anesthesia residency training programs with published standards, and a medical specialty board, the American Board of Anesthesiology, which establishes criteria for becoming a certified specialist in anesthesiology. Other countries have comparable systems of training and certifying mechanisms. (12)

EVOLUTION OF ANESTHESIA AS A MULTIDISCIPLINARY MEDICAL SPECIALTY

6. In addition to board certification in anesthesiology, the American Board of Anesthesiology has an additional certification process for pain management, critical care medicine, hospice and palliative medicine, and sleep medicine. (12)

7. Many other supportive services are involved in the pain management specialty of anesthesia, including neurology, medicine, psychiatry, and physical therapy. (12)

8. Regarding critical care units, usually a "closed" system means that full-time critical care physicians take care of the patients. An "open" system means that the patient's attending physician continues to provide the care in the intensive care unit (ICU). (12)

9. The American Board of Pediatrics and the American Board of Anesthesiology have commenced a combined integrated training program in both pediatrics and anesthesiology that would take 5 years instead of the traditional 6. In addition, cardiac anesthesiologists who now serve both pediatric and adult cardiac patients may move toward a separate certification process. (12)

10. Institutional patient volume in a given specialty often dictates whether only subspecialized anesthesia teams can administer anesthesia to these patients. Two examples may be obstetric or neurosurgical anesthesia teams. (13)

PERIOPERATIVE PATIENT CARE

11. Preoperative care includes preoperative evaluation, preparation in the immediate preoperative period, intraoperative care, postanesthesia care unit (PACU), acute postoperative pain management, and possibly the ICU. (13)

12. Initially preoperative clinics were formed when patients were no longer admitted to the hospital the day before surgery. Also the increased complexity of patient medical risks and surgical procedures prompted the creation of preoperative clinics that allowed patients to be evaluated before the day of surgery. These clinics should be multidisciplinary and lead by anesthesia. (13)

13. The pathway includes preoperative evaluation, the accuracy of predicting length and complexity of surgical care, and patient flow in and out of PACUs. (13)

14. Throughput is the term used to describe the efficiency of each patient's perioperative experience. This can be influenced by such things as operating room availability, length of surgery scheduling times, availability of beds in the PACU, and many other issues. At some institutions perioperative or operating room directors are appointed to manage this perioperative process. (13)

TRAINING AND CERTIFICATION IN ANESTHESIOLOGY

15. All aspects of clinical anesthesia are covered in postgraduate training for anesthesia, including obstetric, pediatric, cardiothoracic, neuroanesthesia, anesthesia for outpatient surgery, recovery room care, regional anesthesia and pain management, as well as training in critical care medicine. (13)

16. To become a certified diplomate of the American Board of Anesthesiology, one must complete an accredited postgraduate training program, pass a written and oral examination, and meet licensure and credentialing requirements. (14)

17. MOCA emphasizes continuous self-improvement and evaluation of clinical skills and practice performance to ensure quality and public accountability. In 2000, board certification became a 10-year, time-limited certificate that emphasizes participation in MOCA. (14)

18. Pain Management, Critical Care Medicine, Hospice and Palliative Medicine, and Sleep Medicine are issued to diplomats who have completed 1 year of additional postgraduate training in the respective subspecialty, meet licensure and credentialing requirements, and pass a written examination. (14)

19. Evaluation of a clinician's professional performance now includes data regarding General Competences, Focused Professional Practice Evaluation, and Ongoing Professional Practice Evaluation. (14)

OTHER ANESTHETIC PROVIDERS

20. The certified registered nurse anesthetist (CRNA) must first be a registered nurse, spend 1 year as a critical care nurse, and then complete 2 to 3 years of didactic and clinical training in the techniques of administration of anesthetics in an approved nursing training program. The anesthesiologist assistant completes a graduate level 27-month program leading to a master of science degree in anesthesia. (14-15)

QUALITY OF CARE AND SAFETY IN ANESTHESIA

21. The Joint Commission guidelines evaluate quality of care based on the measurement and improvement of these areas:
    a. Structure (personnel and facilities used to provide care)
    b. Process (sequence and coordination of patient care activities such as performance and documentation of a preanesthetic evaluation, and continuous attendance to and monitoring of the patient during anesthesia)
    c. Outcome (15)

22. Critical incidents (e.g., ventilator disconnection) are events that cause or have the potential to cause injury if not noticed and corrected in a timely manner. Measurement of the occurrence rate of important critical incidents may serve as a substitute for rare outcomes in anesthesia and lead to improvement in patient safety. Sentinel events are isolated events that may indicate a systematic problem

(e.g., syringe swap because of poor labeling, drug administration error related to keeping unneeded medications on the anesthetic cart). (15)

23. Some key factors for the prevention of patient injury in anesthesia are vigilance, up-to-date knowledge, and adequate monitoring. (15)

24. The following examples of patient safety practices and suggested penalties are from Table 2-1, page 16. The Patient Safety Practice is listed first, followed by the suggested initial penalty.

    a. Practice hand hygiene.
        i. Initial penalty: Education and loss of patient care privileges for 1 week
    b. Following an institution's guidelines regarding provider-to-provider sign out at the end of a shift
        ii. Initial penalty: Education and loss of patient care privileges for 1 week
    c. Performing a "time-out" before surgery
        iii. Initial penalty: Education and loss of operating room privileges for 2 weeks
    d. Marking the surgical site to prevent wrong-site surgery.
        iv. Initial penalty: Education and loss of operating room privileges for 2 weeks
    e. Using the checklist when inserting central venous catheters
        v. Initial penalty: Counseling and review of evidence; loss of catheter insertion privileges for 2 weeks (16)

ORGANIZATIONS WITH EMPHASIS ON ANESTHESIA AND SAFETY

25. The Anesthesia Patient Safety Foundation (APSF) is dedicated to patient safety issues and has a quarterly newsletter that provides discussion on this topic. (15)

26. The Anesthesia Quality Institute (AQI) is the primary source of information for quality improvement in the practice of anesthesiology. AQI provides the National Anesthesia Clinical Outcomes Registry (NACOR) on its website. (16)

27. The American Society of Anesthesiology Closed Claims Project is a retrospective analysis of legal cases with adverse outcomes. Its investigations have helped identify patient and practice risk areas that tend to have difficulties and require added attention with regard to quality and safety. (16)

28. The Foundation for Anesthesia Education and Research (FAER) encourages research, education, and scientific innovation in anesthesiology, perioperative medicine, and pain management. (16)

PROFESSIONAL LIABILITY

29. The majority of the 93 claims in the United Kingdom from 1995-2007 involved drug administration errors with muscle relaxants being the most common issue. The second area involved being awake and paralyzed. (16)

30. Besides continuing medical education, the anesthesiologist should be thoroughly knowledgeable of the patient's condition and care. This includes preoperative and postoperative visits, as well as detailed records of the course of anesthesia. (17)

31. The anesthesiologist should promptly document the facts on the patient's medical record and immediately notify the appropriate agencies, particularly one's own medical center administration and legal office. In addition, the anesthesiologist should provide the hospital and the company that writes the physician's professional liability insurance with a complete account of the incident. (17)

RISKS OF ANESTHESIA

32. Currently, it is estimated that the mortality rate from anesthesia is approximately 1 in 250,000 patients. (17)

33. The increased safety of anesthesia is presumed to reflect the introduction of improved anesthesia drugs and monitoring, as well as the training of anesthesiologists. In addition, motivating patients to stop smoking, lose weight, avoid excess intake of alcohol, and achieve optimal medical control of essential

hypertension, diabetes mellitus, and asthma before undergoing elective surgery has led to a decrease in anesthesia-related deaths. (17)

34. Difficult airway management is perceived to be the greatest anesthesia patient safety issue. Other examples of possible adverse outcomes besides death include peripheral nerve damage, brain damage, airway trauma, intraoperative awareness, eye injury, fetal/newborn injury, and aspiration of gastric contents. (17)

35. Prominent among the factors are sleep loss and fatigue with known detrimental effects on work efficiency and cognitive tasks (monitoring, clinical decision making). (17)

HAZARDS OF WORKING IN THE OPERATING ROOM

36. Anesthesiologists are exposed to vapors from chemicals, ionizing radiation, and infectious agents. There is psychological stress from demands of the constant vigilance required for patients under anesthesia. In addition, interactions with members of the operating team may introduce varying levels of interpersonal stress. Other hazards include latex sensitivity from exposure to latex gloves, substance abuse, mental illness and suicide, and infection control. (18)

SUMMARY AND FUTURE OUTLOOK

37. Responsibilities of the anesthesiologist have grown in magnitude, scope, and depth. Anesthesia has become a leading specialty with regard to inpatient medicine, especially in the perioperative period including critical care and pain medicine. The specialty will become more valuable to medicine overall by attempting to anticipate future societal needs and continuing to dedicate its members to the pursuit of excellence. (18)

Chapter

2 BASIC PHARMACOLOGIC PRINCIPLES

Jeffrey D. Wilkinson

1. What is pharmacokinetics?
2. What is pharmacodynamics?

PHARMACOKINETICS

3. What factors govern drug absorption?
4. How is absorption via buccal mucosa significantly different from drug absorption via the stomach?
5. What aspects of absorption make transdermal drug delivery distinct from other modes of drug delivery? Name some examples of drugs for which a transdermal application is clinically important.
6. What is the mechanism for the offset of local anesthetic effects following nerve block?
7. What is "first order" transfer? How does doubling the dose of a drug affect the shape of a plot of drug absorbed versus time?
8. How does absorption rate from its delivery site affect peak plasma concentration of a drug? What does absorption rate mean regarding the relative safety of intercostal nerve blocks?
9. Define distribution. Define volume of distribution.
10. Distinguish central volume of distribution from peripheral volume of distribution.
11. What factors increase a peripheral volume of distribution for a drug?
12. What are two empiric models of peripheral volumes of distribution that are clinically useful?
13. Generally speaking, what is clearance of a drug? What is the difference between systemic clearance and "intercompartmental" clearance?
14. How are most anesthetic drugs removed from the body?
15. What processes are used in the liver to metabolize drugs?
16. What drugs are metabolized by cytochrome CYP 3A4?
17. What drugs or substances induce CYP 3A4? What drugs or substances inhibit CYP 3A4?
18. What function important to anesthesia does CYP 2D6 have? What drugs inhibit CYP 2D6, and what clinical implication does this have?
19. Why do remifentanil, succinylcholine, and esmolol generally vanish from the plasma so quickly after intravenous administration?
20. Why is the pharmacokinetics of succinylcholine less predictable than other drugs cleared by ester hydrolysis?
21. Define "linear" pharmacokinetics.
22. Describe the formula for rate of drug metabolism in terms of liver blood flow.
23. What is an extraction ratio? What is the formula for clearance in terms of hepatic blood flow? What are the units for clearance?

24. In the case of a drug exhibiting "linear" pharmacokinetics, what is significant about the constant relationship between metabolic rate and drug concentration?
25. What does it mean to say that a drug's metabolism is "flow limited"? Name a drug whose metabolism is "flow limited."
26. What does it mean to say that a drug's metabolism is "capacity limited"? What effect does an alteration of blood flow to the liver have on drugs whose metabolism is "capacity limited"?
27. How is the maximum metabolic rate (V_m) of the liver defined? What is K_m?
28. What factors may alter the maximum metabolic rate for a drug in the liver? How do changes in maximum metabolic rate for a drug alter the clearance of "flow limited" and "capacity limited" drugs?
29. What does it mean for a drug to have saturable pharmacokinetics?
30. What class of drugs significant to anesthesia practice are eliminated by the kidneys?
31. Why is a normal serum creatinine value in an elderly person not a reliable indicator of the individual's ability to clear drugs in the kidney?
32. Describe the clearance of propofol from the bloodstream following intravenous injection.
33. What is distribution clearance? What is the clinical significance of this phenomenon?
34. What is the capacity for plasma proteins to bind most anesthetic drugs? How does the number of protein binding sites for a drug in plasma influence the amount of a drug in the plasma bound to proteins?
35. What effect does a change in plasma protein concentrations have on the apparent potency of a drug?
36. Sketch a graph plotting time versus the amount of drug for a first order pharmacokinetic process. What does it mean to say that a first order pharmacokinetic process demonstrates exponential decay?
37. What do the rate constants between pharmacokinetic compartments relate?
38. For anesthetic drugs, which compartment model best reflects their pharmacokinetic behavior? What about anesthetic drug pharmacokinetics makes this model appropriate? What do the "compartments" correspond to?
39. Why is it impossible to achieve a steady-state drug concentration with a bolus of drug followed by a simple infusion when a drug is best described by a multiple compartment model?
40. What is the time course of drug effect? Why does this exist for anesthesia drugs, and what pharmacokinetic properties does this process exhibit?
41. Define context-sensitive half-time. What are its limitations? Why is context-sensitive half-time a more meaningful concept with regard to the offset of anesthetic drug effects than drug half-life?
42. Why is morphine not an appropriate choice for continuous infusion during anesthesia? Define context-sensitive effect site decrement time.

PHARMACODYNAMICS

43. When a drug's concentration is equal to its dissociation constant for the binding of a certain receptor, what may be said regarding occupation of those receptors? If a dissociation constant is relatively high, what does this mean regarding the nature of the binding between a receptor and a drug?
44. Define receptor full agonist. What is a partial agonist?
45. Define receptor antagonist. What is an inverse agonist?
46. Distinguish efficacy from affinity.
47. What is the difference between competitive and noncompetitive antagonism?
48. How does binding of a receptor by a drug result in drug effect?
49. What three types of receptors are of most significance to anesthesia? For each type of receptor, name several drugs important in anesthesia whose effects are mediated by that receptor type.

50. Sketch a graph plotting the dose of a drug (or measure of exposure) versus its response (drug effect). If a dose-response curve is "shifted to the left," what does this mean regarding drug (or exposure) potency?
51. Define ED_{50}, LD_{50}, and therapeutic index. Why is a drug with a higher therapeutic index safer?
52. Describe the interaction of hypnotics and opioids, specifically with regard to fentanyl and isoflurane MAC.
53. What is a response surface?
54. Define additive drug interactions, supraadditive interactions, and infraadditive interactions.

ANSWERS*

1. Pharmacokinetics is the process by which the body "disposes" of drugs via absorption, distribution, metabolism, and elimination. It can be thought of as "what the body does to the drug." (35)
2. Pharmacodynamics is the process by which drugs interact with specific receptors in the body to produce pharmacologic effects. It can be thought of as "what the drug does to the body." (35)

PHARMACOKINETICS

3. Drug absorption is governed by route of delivery, bioavailability of the drug, and possibly first-pass metabolism. (36)
4. Drug absorption via buccal mucosa differs from absorption from lower in the gastrointestinal tract because presence of food does not hinder delivery of drug to the mucosa. Also, venous outflow from the buccal mucosa returns directly to the systemic circulation, thereby avoiding the potential for the first-pass hepatic effect that is present for drugs absorbed in the stomach, which first enter the portal venous system. (36)
5. Transdermal drug delivery is distinct in that skin is designed to be a significant barrier to absorption. This means that drugs delivered transdermally will have a markedly delayed onset of action following administration. Also, the skin serves as a depot of the drug, resulting in prolonged drug effect following removal of the skin application. Examples of drugs delivered transdermally include clonidine, scopolamine, nitroglycerin, and fentanyl. (36)
6. Local anesthetics applied in nerve blocks have their pharmacologic effects ended by movement of the drug away from the site of action. The process by which the body absorbs this locally applied bolus of drug, thus ending its local effects, is the same by which the body absorbs drugs injected into tissues for the purpose of eliciting systemic drug effects that follow absorption. (36)
7. "First order" transfer is when the rate of drug absorption is proportional to the concentration gradient. Doubling the dose of a drug does not affect the shape of the curve (absorption over time) when a "first order" transfer is occurring. Concentrations will be exactly twice as high at all times, but peak absorption will occur at the same time and the shape of the curve will be identical. (36)
8. The absorption rate from drug delivery sites significantly affects peak plasma concentrations. The higher the absorption rate, the higher the peak plasma concentration that will result. Nerve blocks at sites with rapid absorption result

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

in higher peak plasma concentrations of the local anesthetic injected, providing a risk of toxicity relatively greater than nerve blocks at sites with slower absorption. Intercostal blocks are performed in areas of relatively high absorption. (36)

9. Distribution is the process by which an injected drug mixes with blood and body tissues after its administration. Measuring plasma concentration of a drug allows calculation of a mixing volume, or volume of distribution. Volume of distribution is thus a calculated number (dose of drug administered intravenously divided by plasma concentration) that reflects the apparent volume of body tissues that the drug is distributed across, assuming all the tissues it is distributed across are in equilibrium with plasma concentration. Higher levels of drug remaining in the plasma after drug administration lead to a smaller calculated volume of distribution. (36)

10. Central volume of distribution is the apparent volume immediately (within a minute) following intravenous drug injection. It anatomically consists of the heart, the great vessels, and the lungs. Peripheral volumes of distribution are those volumes of distribution that are calculated after the injected drug has had time to distribute to tissues to which distribution of drug is slower. These peripheral tissues include muscle, fat, and bone. While there is an anatomic correlation to central and peripheral volumes of distribution, volume of distribution is a calculated number that does not necessarily equate to an actual physical volume. (36)

11. The solubility of the drug in the tissue relative to the solubility in the blood or plasma determines the peripheral volume of distribution. If the drug is highly soluble in the tissue, then less of it will stay in the plasma. Sampling the plasma concentration of the drug will result in calculation of a higher volume of distribution than if plasma levels remained higher. Drug properties that lower free plasma levels include low levels of binding to plasma proteins, a lower degree of ionization, and higher lipid solubility. (36)

12. One clinically useful model to describe peripheral volumes of distribution divides the body into tissue beds: "vessel rich group" (brain, most organs), muscle group, fat group, and "vessel poor group" (skin, cartilage, ligaments). Another is to identify the number of compartments in the body needed to explain the pharmacokinetics of the drug in question. The pharmacokinetics of most anesthetic drugs can be explained by a three compartment model (one central volume of distribution, and two peripheral volumes of distribution). In spite of names given to different compartments in different models, such compartments are empiric, and do not necessarily correlate directly to underlying anatomic structures or physiologic processes. (36-37)

13. Clearance is the removal of drug from tissue. Systemic clearance is when the drug is permanently removed from the body. "Intercompartmental" clearance is when the drug leaves the body tissue in question but moves into a different body tissue. (37)

14. Most anesthetic drugs are removed from the body by hepatic metabolism. (37)

15. In the liver, drugs are metabolized through the processes of oxidation, reduction, conjugation, and hydrolysis. Oxidation and reduction occurs via the cytochrome P-450 system. (37)

16. Drugs important to anesthesia that are metabolized by CYP 3A4 include acetaminophen, alfentanil, dexamethasone, fentanyl, lidocaine, methadone, midazolam, and sufentanil. Also, propofol is partly oxidized by CYP 3A4. (37)

17. Rifampin, rifabutin, tamoxifen, glucocorticoids, carbamazepine, barbiturates, and St. John's wort induce CYP 3A4, increasing the metabolism of substrates of CYP 3A4 (hastening clearance). Inhibitors of CYP 3A4 include midazolam, propofol, grapefruit juice, antifungal drugs, protease inhibitors, "mycin" antibiotics, and

selective serotonin reuptake inhibitors (SSRIs). In the case of midazolam, this has been shown to prolong the effects of other drugs metabolized by CYP 3A4, such as alfentanil and fentanyl. (37)

18. CYP 2D6 is the cytochrome in the liver responsible for the conversion of codeine to morphine (the active metabolite of codeine). CYP 2D6 is inhibited by quinidine and SSRIs. The clinical implication of this is that codeine, oxycodone, and hydrocodone, which all rely on activity of CYP 2D6 for production of the active metabolite from which their clinically relevant pharmacologic effects are derived, are poor analgesic choices for patients receiving SSRIs. (37)

19. Remifentanil, succinylcholine, and esmolol are cleared in the plasma and tissue by ester hydrolysis. This occurs very quickly because these esterases are so abundant. (37)

20. The pharmacokinetics of succinylcholine are less reliable than that of other drugs cleared by plasma and tissue esterases because it is metabolized specifically by butylcholinesterase (formerly known as "pseudocholinesterase"). Defects in the gene for butylcholinesterase lead to a potentially significant slowing in the metabolism of succinylcholine. (37)

21. "Linear" pharmacokinetics are said to exist for a drug when the rate of the drug's metabolism is directly proportional to its concentration. This is a general characteristic of anesthetic drugs. (37)

22. Rate of metabolism equals liver blood flow times the difference in drug concentration between blood flowing into the liver and blood flowing out. (38)

23. The extraction ratio of a drug is the fraction of the drug that is removed from the plasma during passage through the liver. Clearance by the liver is equal to hepatic blood flow multiplied by the extraction ratio. (Therefore, units of clearance are liters per minute.) Hepatic extraction ratios are unchanging properties of specific drugs. More of a drug is metabolized by the liver when the drug is being delivered to the liver in increasing concentrations. This must be true for the extraction ratio to remain constant. (37-38)

24. For most anesthetic drugs, metabolic rate is proportional to drug concentration ("linear" pharmacokinetics). The proportionality constant that relates the drug concentration to the metabolic rate is another definition of clearance.

$$\text{Rate of metabolism (grams/minute)} = \text{proportionality constant (liters/minute)} \times \text{inflow concentration (grams/liter)}.$$

Extraction ratio and proportionality constant (clearance) are only constant if drugs exhibit "linear" pharmacokinetics, but this is generally true of anesthetic drugs. (38)

25. The clearance of a "flow limited" drug is limited only by the rate of blood flowing to the liver. Changes in hepatic blood flow result in a proportional change in drug clearance. Such drugs have extraction ratios near or equal to 1. The liver has a seemingly boundless ability to metabolize such drugs. One drug exhibiting "flow limited" clearance is propofol. (38)

26. The clearance of a "capacity limited" drug is limited by the liver's ability to metabolize the drug. Such drugs have low extraction ratios (much less than 1). Alterations of liver blood flow have no effect on clearance of "capacity limited" drugs because liver blood flow has no effect on clearance of such drugs. One drug exhibiting "capacity limited" clearance is alfentanil. (38)

27. The maximum metabolic rate of the liver for a given drug (V_m) is the theoretical rate of drug metabolism if every possible enzyme in the liver were being used for that function. K_m is the concentration of drug in the plasma associated with half of the maximum metabolic rate. (38)

28. Factors altering the maximum metabolic rate for a drug in the liver include enzyme inhibition, enzyme induction, and liver disease. Clearance of "flow limited" drugs is relatively insensitive to changes in maximum metabolic rate because there is such a reserve of metabolic capacity for these drugs. For clearance of such drugs to be affected by an alteration in metabolic rate requires such alteration to be massive. Clearance of "capacity limited" drugs is very sensitive to changes in the maximum metabolic rate, because the ability of the liver to metabolize the drug is so small. (38)

29. For a drug to have saturable pharmacokinetics means that the concentration of the drug in the plasma exceeds the concentration at which the metabolic rate of the drug is half its maximum (K_m). Clearance of such drugs is a function of drug concentration (at clinical plasma concentrations). On the other hand, drugs that do not have saturable pharmacokinetics (i.e., their concentration is well below K_m) are metabolized at a rate proportional to their concentration (most anesthetic drugs). Clearance of these drugs is a constant. (40)

30. Steroidal muscle relaxants, including pancuronium, vecuronium, and rocuronium are at least partially eliminated by the kidneys; 85% of pancuronium is eliminated by the kidneys, while 20% to 30% of vecuronium and 10% to 20% of rocuronium are eliminated. (40)

31. Clearance of drugs by the kidney is achieved by filtration of drug from the plasma at the glomerulus and direct transport to the tubules. Creatinine clearance is generally a good indicator of renal ability to clear drugs because it is a good measure of glomerular filtration. Increasing age is an independent factor in the establishment of a patient's creatinine clearance. Leaving serum creatinine unchanged and increasing a patient's age results in shrinking of the numerator in the formula for creatinine clearance. In this, it can be seen that creatinine clearance decreases with age even if serum creatinine never changes. Therefore, creatinine clearance may be decreased despite "normal" serum creatinine levels. In fact, this is inevitably true the older a person gets. Serum creatinine must eventually fall to below "normal" values for creatinine clearance to remain "normal" as very advanced age is reached. (40)

32. Propofol is primarily cleared by metabolism in the liver. Every bit of propofol that flows to the liver is cleared there, at all clinically significant doses and even in the presence of all but the most massive insults to the cellular processes responsible for its metabolism. Propofol's clearance is actually greater than hepatic blood flow. This is only possible if, in addition to the robust ability of the liver to metabolize this drug, there are extrahepatic sites of drug metabolism. About a quarter of administered propofol is eliminated by the kidneys. Propofol is eliminated virtually completely by metabolism (metabolism occurring in both liver and kidney), with only a minute fraction (less than 1%) excreted in the urine unchanged. Renal elimination of propofol is not a function of filtration, but is a function of renal blood flow since the kidneys remove every molecule of the drug that enters them. (37-38, 40)

33. Distribution clearance is the transfer of a drug out of the plasma into peripheral tissues. The drug remains in active form and may be sequestered in tissues for an extended period, serving as a reservoir for recurrent or prolonged pharmacologic effects of drug administration. (40)

34. The capacity of plasma proteins to bind most anesthetic drugs is very large. That is, the number of sites on proteins available to bind drug is far greater than the number of molecules of an anesthetic drug administered at clinical levels. This does not necessarily mean that a lot of the drug will become bound to plasma proteins upon arrival in the bloodstream. Such binding is dependent on the rate constants for binding and dissociation of each specific drug has for plasma proteins. The effect of an excess of protein binding sites is that the amount of drug bound to plasma proteins is purely a function of the concentration of the plasma protein. Whether this function allocates a large or small amount of drug to a protein-bound form is governed by the rate constants for binding and dissociation. (40)

35. If plasma protein levels decrease due to aging or some disease process, then the free fraction of drug will increase. This will increase the apparent potency of the drug—with a couple of caveats. First, the increase in potency will be greater for drugs that are highly protein bound. A decrease in plasma protein levels has much more effect on drugs highly bound to plasma proteins. Potency of the drug will only appear to increase if the drug in question is more than 90% protein bound (free fraction $<10\%$). Second, any noted increase in potency will only exist directly after intravenous bolus injection, while the volume of distribution is that of the central compartment, and protein binding of a drug is only to proteins in the plasma. Once drug concentration in the plasma equilibrates with peripheral tissues, then tissue proteins also participate in drug binding. The amount of drug binding by plasma proteins once the total body concentration of the drug is in equilibrium is trivial when compared to the amount bound by proteins in the tissue. For this reason, variations in plasma protein levels are significant to drug potency only immediately after administration, but have no significant effect on drug potency once drug concentration has equilibrated with the peripheral tissues. (40)

36. First order pharmacokinetic processes demonstrate exponential decay, which is to say that the rate of decrease in drug amount slows as the amount of the drug decreases. (Conversely, rate of decrease in the drug amount speeds up if the amount of drug increases.) (41, Figure 5-4)

37. Rate constants between compartments in pharmacokinetic compartment models relate flow of drug between compartments to the amount of drug in the driving compartment. (41)

38. For most anesthetic drugs, three distinct phases of pharmacokinetics following bolus injection can be distinguished, which is the defining characteristic of a three compartment pharmacokinetic model. These three phases correspond to rapid distribution, slow distribution, and the terminal phase. The distribution phases reflect the peripheral volumes initially filling with the drug, and the terminal phase reflects the drug being discharged back into the plasma. These three processes are definitive of a pharmacokinetic three compartment model, but do not discreetly correspond to the "three compartments" themselves. The three compartments themselves represent one central volume of distribution (central compartment) and two peripheral volumes of distribution (peripheral compartments). (41)

39. To achieve a steady-state drug concentration for a drug best described by a multiple compartment model, the initial bolus of the drug must be followed by an infusion of drug that changes over time. The initial rate of infusion must be high enough to compensate for the drug leaving the central compartment for the peripheral compartment(s). After the peripheral compartment(s) have come to equilibrium with the plasma concentration, then the infusion must be decreased to a rate that exactly matches the rate of clearance of the drug. (42-43)

40. Time course of the drug effect is the delay between introduction of the drug into the plasma and the onset of measurable drug effect. This exists for anesthetic drugs because most of them produce their desired clinical effects via actions occurring outside the plasma. The drug must be delivered and diffuse into its target tissue before it produces effects, and this takes a certain amount of time. The site of the drug effect is connected to the plasma by a first order pharmacokinetic process, which means that the higher the drug concentration in the plasma, the faster the drug levels will rise in the target tissue site. The factor that relates the plasma concentration to the target tissue concentration is the equilibration rate constant. (43-44)

41. Context-sensitive half-time is the time necessary for a drug's plasma concentration to decrease 50% after discontinuation of a continuous intravenous infusion of specific duration. The limitation of this value is that it fails to take into account equilibration delay, which is to say it does not factor in the time lag between changes in plasma drug concentration and concentration at target tissue

sites. Context-sensitive half-time has much more clinical utility for anesthesia practice than drug half-life. Half-life is indicative of the time it takes to eliminate a drug from the body. Context-sensitive half-time is indicative of the time it takes plasma levels of drug to fall. Termination of the clinical effect of an anesthetic drug (i.e., awakening) is dependent on its plasma level (and by extension, corresponding target tissue concentration) of the drug and not the drug's overall presence in the body. (44)

42. Morphine is not an appropriate choice for continuous infusion during anesthesia, because it has a very slow plasma-effect site equilibration. Although morphine has rapid plasma pharmacokinetics (a short context-sensitive half-time), it has very slow blood-brain equilibration (a long context-sensitive effect site decrement time). Context-sensitive effect site decrement time relates the time course of effect site concentration with the duration of drug delivery. Drugs such as morphine, which do not equilibrate quickly between their plasma concentrations and target tissue concentrations, do not have their clinical effects well represented by context-sensitive half-time values. (44)

PHARMACODYNAMICS

43. When a drug's concentration is equal to its dissociation constant for the binding of a certain receptor, then 50% of those receptors are bound by the drug. A high dissociation constant means that the receptor has low affinity for the drug (weak binding). A low dissociation constant means that the receptor has high affinity for the ligand drug (tight binding). (45)

44. A full agonist is a drug that activates a receptor to its maximum capacity. A partial agonist is a drug that binds a receptor and produces a less effective response than a full agonist, even at high concentrations. (45)

45. An antagonist is a drug that blocks access to a receptor by agonists, but itself produces no activation of the receptor. An inverse agonist is a drug that binds a receptor and produces a pharmacologic response that is below the baseline response measured in the absence of the drug. This is usually thought to result from the inverse agonist acting to block access to the receptor by endogenous agonist(s). (45)

46. Efficacy of a drug is the level of activation of receptors that results when the drug interacts with the receptors. Affinity refers to how much of a drug binds to receptors at any given drug concentration. These are completely independent properties; therefore, drugs may have identical affinities for a receptor type, but have very different efficacies. The difference between, for example, full agonists and antagonists is not a function of their relative affinities for the receptor in question. By definition, it is a function of their relative efficacies. (45)

47. Competitive antagonism is when an antagonist competes with an agonist for receptor binding, causing the total number of receptors bound by the agonist to decrease. The competitive antagonist displaces an agonist, without blocking it, and can therefore be displaced from the receptor by an increased dose of agonist. A noncompetitive antagonist alters the conformation of the receptor by irreversibly binding to the receptor complex. (45)

48. Binding of a receptor by a drug causes the receptor to favor, and spend more time in, one of its conformations more than it did before being bound by the drug. The particular conformation favored by receptor-drug interaction facilitates the particular biochemical cascade that results in the drug effect. (45)

49. G-protein-coupled receptors mediate the action of opioids, serotonin, all vasoactive amines, prostaglandins, and histamine. Ligand-gated ion channels mediate the action of propofol, midazolam, thiopental, ketamine, and muscle relaxants. Voltage-gated ion channels are the target of local anesthetic action. (46)

50. Shifting of a dose-response curve "to the left" means that a lower dose of drug is necessary to provide an effect. This means that a shift in the curve "to the left" represents an increase in drug potency. Conversely, shifting the curve "to the right" represents a decrease in drug potency. (46, Figure 5-11)

51. ED_{50} is the dose of drug required to produce a specific effect in 50% of individuals. LD_{50} is the dose required to produce death in 50% of individuals. Therapeutic index is the ratio between LD_{50} and ED_{50}. The higher the therapeutic index, the further the lethal dose of the drug is from the therapeutic dose. This makes administering the drug safer because giving a dose greater than that needed for a therapeutic response is less likely to climb to the level that constitutes a lethal dose. (46)

52. Fentanyl administration in conjunction with isoflurane administration results in an effective decrease in the MAC of the volatile anesthetic. This decrease in MAC is proportional to fentanyl dose, but it levels off and never reaches zero because fentanyl alone cannot ensure nonresponsiveness. (46-47)

53. A response surface is a three-dimensional surface that shows the effect of the combination of any two drugs. (46-47)

54. If drugs have additive effects, their concomitant administration results in pharmacologic effects equivalent to the sum of the effects each would have produced if administered alone. If drugs have supraadditive (synergistic) effects, their concomitant administration produces pharmacologic effects in excess of the sum of each drug's individual effects. If drugs have infraadditive effects, their concomitant administration produces pharmacologic effects more than what either would produce if administered alone, but less than if the individual effects of each drug were added to one another. (47-48)

Chapter

3 CLINICAL CARDIAC AND PULMONARY PHYSIOLOGY

John Feiner

HEMODYNAMICS

ARTERIAL BLOOD PRESSURE

1. What is mean arterial pressure (MAP)?
2. What is the relationship of MAP to cardiac output and systemic vascular resistance?
3. What is the "pulse pressure"?
4. What factors affect pulse pressure?

SYSTEMIC VASCULAR RESISTANCE

5. What pathologic factors may decrease systemic vascular resistance?
6. How is systemic vascular resistance calculated?
7. Where is most of the resistance in the vascular system?
8. How is resistance related to the radius of the blood vessel?

CARDIAC OUTPUT

9. Which monitors allow calculation of cardiac output?
10. How is stroke volume calculated?
11. What is the cardiac index?
12. How might changes in heart rate affect stroke volume?
13. What is the definition of ejection fraction and what is a normal value?

PRELOAD

14. How can "preload" be measured clinically?
15. When will central venous pressure (CVP) poorly reflect filling pressures in the left heart?
16. What is the Frank-Starling mechanism?
17. What are common causes of low preload?
18. What is systolic pressure variation and how might it be useful in analyzing hypotension?

CONTRACTILITY

19. What is "contractility"?
20. What are some important clinical causes of low contractility?

AFTERLOAD

21. What does low systemic vascular resistance (SVR) or afterload do to ejection fraction?
22. What does low SVR or afterload do to cardiac filling pressures?
23. What does low SVR or afterload do to end-systolic volume and how might this best be detected by monitoring?

CARDIAC REFLEXES

Autonomic Nervous System

24. What are the physiologic effects of the sympathetic and parasympathetic nerves on the cardiovascular system?

RECEPTOR SYSTEMS

25. What are the baroreceptors and where are they located?
26. What is the Bainbridge reflex?
27. What effects do anesthetic agents have on cardiac reflexes?

CORONARY BLOOD FLOW

28. What is the usual myocardial oxygen extraction and how does this compare to the body as a whole?
29. When is the subendocardium perfused?

PULMONARY CIRCULATION

PULMONARY ARTERY PRESSURE

30. What are normal pulmonary artery (PA) pressures?

Pulmonary Vascular Resistance

31. How does pulmonary vascular resistance (PVR) respond to increased cardiac output?
32. How does lung volume affect PVR?
33. What drugs modify PVR?
34. What is the effect of hypoxia on PVR?
35. What are some pathologic causes of elevated PVR?

ZONES OF THE LUNG

36. How does gravity affect pulmonary blood flow?

Pulmonary Edema

37. What are the two types of pulmonary edema?

PULMONARY GAS EXCHANGE

OXYGEN

38. How is blood oxygen measured?
39. What is the "P50"? What is a normal value?
40. What are common clinical factors that shift the oxyhemoglobin dissociation curve left and right?
41. What are the benefits of a rightward shift in the oxyhemoglobin dissociation curve?
42. What is the equation describing the effect of ventilation on oxygenation?
43. How does increased F_{IO_2} improve oxygenation during hypercapnia?
44. Is it possible to deliver hypoxic gas mixtures with a modern anesthesia machine?
45. What does an A-a gradient mean with respect to a problem in oxygenation?
46. What is intrapulmonary shunt?
47. What is the shunt equation?
48. Is diffusion limitation a significant clinical cause of hypoxemia?

49. Which causes of hypoxemia are very responsive to supplemental oxygen and therefore easily treated with higher F_{IO_2}?
50. How does low mixed venous oxygen saturation affect arterial oxygenation?

CARBON DIOXIDE

51. What are the three forms in which carbon dioxide is carried in the blood?
52. Why is hypercapnia a problem clinically?
53. What are the four physiologic causes of hypercapnia?
54. What are significant causes of increased CO_2 production under anesthesia?
55. What are the various types of dead space?
56. What pathologic conditions may increase dead space?
57. What is a normal value for physiologic dead space?
58. What is the Bohr equation?
59. How quickly can apnea increase P_{aCO_2}?

PULMONARY MECHANICS

60. What are pulmonary mechanics?

Static Properties

61. What factors contribute to the static pressure in the lung?
62. How is surface tension reduced in the lungs?
63. What is the definition of static compliance?
64. What is functional residual capacity (FRC) with respect to the static mechanical properties of the lung and chest wall?

Dynamic Properties and Airway Resistance

65. What determines airway resistance?
66. How can one distinguish clinically between elevated airway pressure produced from resistance or static compliance?
67. What are important clinical causes of elevated airway resistance?

CONTROL OF BREATHING

Central Chemoreceptors

68. Where are the central chemoreceptors located?
69. What is the main stimulus for the central chemoreceptors?
70. How would the central chemoreceptors respond to lactic acidosis?

Peripheral Chemoreceptors

71. What are the primary peripheral chemoreceptors?
72. What factors stimulate the peripheral chemoreceptors?
73. Why do peripheral chemoreceptors effectively sense arterial, not venous, blood values?

Hypercapnic Ventilatory Response

74. How is the hypercapnic ventilatory response measured?
75. What receptors drive the hypercapnic response?
76. What is an "apneic threshold"?
77. How quickly does a CO_2 response develop?

Hypoxic Ventilatory Response

78. How is hypoxic ventilatory drive measured?
79. What receptors are responsible for hypoxic stimulation of ventilation?
80. How does hypoxia depress ventilation?
81. How quickly does the hypoxic response develop?
82. What is the effect of higher P_{CO_2} on hypoxic drive?

EFFECTS OF ANESTHESIA

83. Do opioids depress hypercapnic ventilatory drive, hypoxic ventilatory drive, or both?

Disorders of Ventilatory Control

84. What ventilatory problems are premature infants of low postconceptual age at risk for?
85. What is Ondine curse?
86. When is periodic breathing most likely to occur?

INTEGRATION OF THE HEART AND LUNGS

87. What is the Fick equation?

Oxygen Delivery

88. What is oxygen delivery?

Oxygen Extraction

89. Why is examining oxygen extraction clinically useful?
90. What is normal mixed venous oxygen saturation?
91. How would the arterial to venous oxygen content difference change with higher F_{IO_2}?
92. Why is the oxygen extraction ratio useful?
93. How can the body respond physiologically to anemia or increased metabolic demand (oxygen consumption)?

ANSWERS*

HEMODYNAMICS

ARTERIAL BLOOD PRESSURE

1. Mean arterial pressure (MAP) is the average blood pressure. On modern monitors, MAP is calculated from integrating the arterial waveform over time. MAP can often be estimated by adding one third of the pulse pressure to the diastolic blood pressure. (50)
2. MAP is the product of cardiac output (CO) and SVR, or MAP = CO × SVR. This is similar to electricity where voltage = current × resistance. (If we were to be exactly correct, we would use the pressure drop across the systemic vascular system, or MAP – CVP.) (50)
3. Pulse pressure is the difference between systolic and diastolic blood pressure. (50)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

4. Pulse pressure is produced from the stroke volume being pushed into the aorta. The compliance features of the aorta therefore have a very significant effect on pulse pressure so that a stiff aorta results in a higher pulse pressure, a common feature of aging. A lower diastolic pressure can reduce pulse pressure by moving to a more compliant part of the aortic compliance curve. A higher stroke volume generally increases pulse pressure. Lower SVR can decrease pulse pressure because part of the stroke volume "runs off" rapidly during ejection. Aortic insufficiency can increase pulse pressure as the diastolic pressure drops significantly during backward flow into the left ventricle. (50-51)

SYSTEMIC VASCULAR RESISTANCE

5. Classic pathologic causes of low SVR include sepsis, anaphylactic and anaphylactoid reactions, and reperfusion of ischemic organs. Many anesthetic drugs and neuraxial anesthesia also lower SVR.
6. $SVR = 80 \times \frac{(MAP - CVP)}{CO}$, where MAP is mean arterial pressure, SVR is systemic vascular resistant, CVP is central venous pressure, and CO is cardiac output. The factor "80" converts the SVR to the proper units. (51)
7. Most of the resistance in the vascular system is in the arterioles. Despite having smaller diameters, there are large numbers of capillaries in parallel, resulting in overall lower resistance at this level of the vascular tree. (51)
8. Resistance is inversely proportional to the fourth power of the radius of the vessel. (51)

CARDIAC OUTPUT

9. Cardiac output can be determined by thermodilution with a PA catheter. In addition, transesophageal echocardiography (TEE) may be used to estimate cardiac output. A variety of other noninvasive monitors are available and being developed that estimate cardiac output, including Doppler of the ascending aorta and arterial pressure waveform analysis. Thermodilution is still the dominant technique. The Fick equation can also be used to calculate cardiac output from the oxygen consumption, and arterial and mixed venous oxygen content. (51)
10. Stroke volume is the cardiac output divided by heart rate. It is important to calculate stroke volume, because a high heart rate may make cardiac output appear normal despite inadequate stroke volume. (51)
11. Because the appropriate cardiac output changes with body size, the cardiac "index" is used to normalize for body size by dividing cardiac output by body surface area. (51)
12. An excessively rapid heart rate might not leave sufficient time to fill the ventricle. Loss of a "p" wave with certain rhythms will also lead to inadequate ventricular filling from loss of atrial contraction. (51)
13. Ejection fraction is the percentage of ventricular blood volume that is pumped during a single contraction or SV/end-diastolic volume. Unlike stroke volume, ejection fraction does not change with body size. A normal ejection fraction is 60% to 70%. (51, Figure 6-3)

PRELOAD

14. The volume of the heart at end-diastole can be directly measured by transesophageal echocardiography (TEE). Ventricular filling pressures can be measured on the right side of the heart with central venous pressure and on the left side of the heart by pulmonary capillary wedge pressure. A complete picture of preload would still require both pressure and volume information to more fully understand the compliance of the heart. Systolic pressure variation may also be an important indicator of low preload. (51-52, Figure 6-1)
15. CVP will poorly reflect filling of the left ventricle in a number of pathologic conditions. With pulmonary disease and elevated PVR, right heart failure may

develop with elevated CVP despite poor filling of the left ventricle. With left ventricular failure, CVP may be normal despite elevated left heart filling pressures as long as right ventricular function is preserved. (51)

16. The Frank-Starling mechanism describes how the heart responds to increased filling by increasing contraction and stroke volume. This can be described by the cardiac function curves in Figure 6-2. (51)

17. "Hypovolemia" or low circulating blood volume is a key cause of low preload. Blood loss and fluid loss from other sources are commonly faced during surgery. Low preload can also occur with venodilation from an anesthetic agent and neuraxial anesthesia. Pathologic problems such as pericardial tamponade and tension pneumothorax may result in low preload (inadequate filling of the heart) despite normal blood volume and high CVP. (52)

18. Systolic pressure variation describes the regular changes in systolic pressure that occur with ventilation. During mechanical ventilation, significant systolic pressure variation reflects low preload. Systolic pressure variation may be more useful than other monitors in determining which patients will appropriately respond to fluid administration. In cases of hypotension, SPV may indicate low preload. Extreme SPV may indicate other important causes of hypotension, such as pericardial tamponade or tension pneumothorax. Pulse pressure variation, which is closely related, requires a computer to evaluate; systolic pressure variation can be measured with a standard arterial line and monitor. (52)

CONTRACTILITY

19. Contractility, or inotropic state, describes the force of contraction independent of preload and afterload. It is reflected in the rate of rise of pressure over time. Graphically, it is reflected in the systolic pressure volume relationship. (52, Figure 6-3)

20. Important causes of poor contractility that may be associated with hypotension include myocardial ischemia, previous myocardial infarction, cardiomyopathy, and myocardial depression from a number of different drugs. In addition, when considering a differential diagnosis of hypotension, valvular heart disease would be considered as low contractility. (52, Table 6-1)

AFTERLOAD

21. Low SVR or afterload increases ejection fraction, which can approach 75% or even 80% in low SVR states. This is a classic feature of low SVR conditions such as liver failure. (52-53, Figure 6-4)

22. Low SVR or afterload lowers cardiac filling pressure (central venous pressure or pulmonary capillary wedge pressure) via the Frank-Starling mechanism. Vasodilation can therefore cause relative hypovolemia and a volume-responsive condition. Likewise high SVR or afterload increases cardiac filling pressure. (52-53, Figure 6-4)

23. Low SVR or afterload leads to low end-systolic left ventricular volume. This is a pathognomonic sign of low SVR on TEE. (52-53, Figure 6-4)

CARDIAC REFLEXES

Autonomic Nervous System

24. The parasympathetic nervous system primarily affects the cardiovascular system by decreasing heart rate through vagal innervation of the sinoatrial node. Mild negative effects on contractility are probably less important. The sympathetic nervous system can increase heart rate and contractility, but it also causes peripheral vasoconstriction. (54)

RECEPTOR SYSTEMS

25. Baroreceptors are present in the carotid sinus and aortic arch. Increased blood pressure will stimulate baroreceptors, leading to parasympathetic stimulation and a decrease in sympathetic stimulation. (54)

26. The Bainbridge reflex describes the increase in heart rate from atrial stretch. This helps increase cardiac output in response to increased venous return. (54)

27. Anesthetic agents decrease cardiac reflex responsiveness. This increases the likelihood of hypotension under anesthesia. (54)

CORONARY BLOOD FLOW

28. The myocardium extracts a higher percentage of oxygen than other tissues in the body, up to 60% to 70%. Normal whole body oxygen extraction is approximately 25%. (54)

29. Intramural pressure of the myocardium during systole stops blood flow to the subendocardium. Therefore, blood flow to the subendocardium occurs predominantly during diastole. (54)

PULMONARY CIRCULATION

PULMONARY ARTERY PRESSURE

30. The pulmonary circulation has much lower pressures than the system circulation. This is due to lower PVR compared to the systemic vascular resistance, since both systems accept the entire cardiac output. Since these pressures can be measured clinically with a PA catheter, the anesthesiologist should be familiar with normal and pathologic values, which are shown in Table 6-2. (54-55, Table 6-2)

Pulmonary Vascular Resistance

31. Pulmonary artery pressure stays remarkably constant over a wide range of cardiac output. PVR accommodates to increased cardiac output by *distention* and *recruitment* of capillaries, so that resistance decreases as cardiac output increases. (55)

32. Both high and low lung volumes increase PVR. At high lung volumes, intraalveolar vessels are compressed. At low lung volumes, extraalveolar vessels are compressed. Increased PVR at low lung volumes may be physiologically helpful in diverting blood flow from a collapsed lung. (55)

33. Elevated PVR can be very difficult to treat. Inhaled nitric oxide, prostaglandins, and phosphodiesterase inhibitors may lower PVR, but cannot always completely reverse elevated PA pressure. (55)

34. Hypoxia increases PVR through "hypoxic pulmonary vasoconstriction" (HPV). This process may significantly improve gas exchange by lowering blood flow to areas of poor ventilation. However, global hypoxia, such as occurs at high altitude, can result in increased PA pressure through HPV. (55)

35. Pathologic elevation in PVR may occur with pulmonary emboli. In addition, arteriolar hyperplasia may occur with certain congenital cardiac diseases (Eisenmenger syndrome), idiopathically (primary pulmonary hypertension), and associated with cirrhosis (portopulmonary hypertension). Intrinsic lung disease from a variety of causes can also increase PVR. (55)

ZONES OF THE LUNG

36. Because the hydrostatic changes due to gravity are of a similar order of magnitude as PA pressure, gravity can have significant effects on pulmonary blood flow. Notable effects are in zone 1, where airway pressure is higher than pulmonary artery pressure, leading to no perfusion and therefore dead space. If areas of poor gas

exchange are in an elevated position, lower perfusion can result, improving gas exchange. In lung surgery, the lower PA pressure in the nondependent collapsed lung helps gas exchange. (55)

Pulmonary Edema

37. Hydrostatic leak can occur in the lung when pulmonary capillary pressure is elevated. Pulmonary edema (hydrostatic) results when lymphatic system removal of fluid is overwhelmed. The risk of pulmonary edema increases as pulmonary capillary wedge pressure exceeds 20 mm Hg. Capillary leak can also occur with pulmonary injury from a variety of causes, such as aspiration or sepsis. The adult respiratory distress syndrome (ARDS) represents very significant lung injury with a high risk of mortality. (56)

PULMONARY GAS EXCHANGE

OXYGEN

38. Three measurements of blood oxygen are used clinically: partial pressure (in mm Hg), oxygen saturation (in %), and oxygen content (in mL O_2/dL). The oxyhemoglobin dissociation curve (Figure 6-5) relates oxygen partial pressure and saturation. "Content," really a concentration, is the sum of the amount of oxygen in hemoglobin (1.39 mL O_2/dL/g hemoglobin) and in the dissolved (0.003 mL O_2/mm Hg). (56)

39. The "P50" is the partial pressure at which hemoglobin is 50% saturated, normally 26.8 mm Hg. Sigmoidal curves are usually defined by such midpoints. This is shown graphically in Figure 6-5. (56, Figure 6-5)

40. The most important factors shifting the oxyhemoglobin dissociation curve to the right are metabolic acidosis and hypercapnia. Metabolic alkalosis and hypocapnia shift the curve to the left. Lower 2-3 DPG in stored blood leads to a significant left shift. (56, Table 6-3)

41. Right shifts of the oxyhemoglobin dissociation curve improve unloading of oxygen in the tissues. For the same tissue P_{O_2} more oxygen will be unloaded because of a right shift. Because of the sigmoidal shape of the curve, little change in loading of oxygen in the lungs will occur because of the rightward shift. (56)

42. The "alveolar gas equation" is used most to determine the effect of ventilation on oxygenation. The equation describes the transfer of oxygen from the environment to the alveoli, and therefore contains all the determinants of alveolar oxygen: barometric pressure, F_{IO_2}, and ventilation. (57)

43. F_{IO_2} is another determinant of alveolar oxygen, and it can overcome the effect of higher CO_2 on alveolar oxygen. The effect of hypoventilation with and without supplemental oxygen is shown in Figure 6-8. (57-58)

44. Modern anesthesia machines can effectively prevent delivery of hypoxic gas mixtures. Multiple features are necessary, including pin indexing of tanks and gas hoses, shut-off valves for nitrous oxide, and use of oxygen to drive the bellows. These safety mechanisms might be overcome if a gas other than oxygen were delivered through the oxygen piping, which has occurred because of construction mishaps. A monitor measuring F_{IO_2} is therefore still critical. Hypoxemia still occurs because of unintentional delivery of room air in patients requiring supplemental oxygen. (58)

45. Calculation of an A-a gradient divides the potential causes of hypoxemia into two groups of causes. Figure 6-7 illustrates this division. The first group of causes includes all the factors that determine alveolar oxygen: F_{IO_2}, barometric pressure (altitude), and ventilation. A normal A-a gradient would indicate that this first group is the

problem. An abnormal A-a gradient indicates a gas exchange issue, usually $\dot{V}/\dot{Q}$ mismatch or shunt. (58)

46. Shunt describes the passage of mixed venous blood through the lung, unexposed to alveolar gas. This commonly occurs because alveoli are collapsed, or filled with fluid such as in pneumonia or pulmonary edema. Mixed venous blood combines with blood passing through normal lung, lowering the Pa_{O_2}, which is the end result of the mixture. (58-59, Figure 6-9)

47. The shunt equation quantitatively describes the physiologic effect of shunt on oxygenation. Since $\dot{V}/\dot{Q}$ mismatch may also be present, the shunt equation really describes a simple two-compartment model analyzing oxygenation as if it were all pure shunt. (59)

48. Diffusion impairment or limitation is not a major clinical cause of hypoxemia. However, diffusion limitation is often misunderstood. If an alveolus is filled with fluid, such that no diffusion of oxygen occurs, this is *shunt*, not diffusion limitation. Diffusion limitation occurs when a partial pressure gradient still exists between the alveolus and the capillary blood after the blood has passed through. Sufficient time for diffusion usually occurs, such that equilibration occurs early in the process. Even alveolar thickening, which may slow diffusion, does not usually result in diffusion limitation because equilibration of P_{O_2} between the alveolus and capillary blood does occur. Diffusion limitation may be a clinically significant physiologic problem at extreme altitude during exercise. (59)

49. Hypoventilation, diffusion impairment, and $\dot{V}/\dot{Q}$ mismatch are all very responsive to supplemental oxygen. High F_{IO_2} can effectively eliminate hypoxemia from these causes. Shunt is much more resistant to supplemental oxygen. At shunt fractions over 30%, hypoxemia may remain despite administration of 100% oxygen. Higher F_{IO_2} does improve oxygenation with pure shunt, although there is an incorrect impression that this impact is minimal. The effect of F_{IO_2} is difficult to calculate and is not linear, so it is best graphically illustrated as in Figure 6-9. (59)

50. Low mixed venous oxygen levels may affect Pa_{O_2}, but only in the presence of intrapulmonary shunt. For the same shunt, lower mixed venous oxygen results in a lower Pa_{O_2}. (59)

CARBON DIOXIDE

51. In the blood, CO_2 is carried as dissolved gas, as bicarbonate, and bound to hemoglobin as carbaminohemoglobin. The greatest total quantity of CO_2 is as bicarbonate, which is in fairly rapid equilibrium with CO_2 through carbonic acid. Despite being the smallest total, the CO_2 from carbaminohemoglobin represents about one third of the arterial to venous CO_2 movement. (59)

52. Hypercapnia can be well tolerated, although at higher levels, probably approaching 80 mm Hg or greater, hypercapnia can cause CO_2 narcosis. The most significant problem is what hypercapnia represents. A major cause of hypercapnia is oversedation or narcotization. This could progress to apnea and anoxia. Hypercapnia may also represent impending respiratory failure from a variety of causes. (59-60)

53. Physiologically, hypercapnia can be caused by (1) rebreathing (elevated inspired CO_2), (2) hypoventilation, (3) elevated CO_2 production, and (4) elevated dead space. (60-61)

54. The most concerning cause of significant CO_2 production under general anesthesia is malignant hyperthermia (MH). While fever alone will increase CO_2 production, the increase is not dramatic. MH may increase CO_2 production several fold. Thyroid storm may increase CO_2 production. Absorption of CO_2 introduced during laparoscopy may be quite significant for certain procedures, particularly if

subcutaneous CO_2 emphysema develops. The CO_2 removed through the lungs appears as if it is CO_2 production. (60, Table 6-4)

55. Dead space is described as anatomic, alveolar, or physiologic (total). Anatomic dead space consists of the conducting airways, which are not involved in gas exchange, plus the larynx and pharynx. Alveolar dead space consists of alveoli that are not involved in gas exchange, usually from lack of blood flow. Physiologic or total dead space consists of all dead space, and is the easiest to measure. "Equipment" dead space may be produced by the addition of tubing beyond the *y*-connector of the anesthesia circuit. (60-61)

56. Many forms of end-stage lung disease, such as emphysema, are characterized by elevated dead space. Pulmonary emboli of any source increase dead space. Hypovolemic shock increases dead space, since very low PA pressures result in more zone 1 of the lung, where alveoli are not perfused and therefore represent dead space. (60-61)

57. Normal dead space is 25% to 30% and consists almost entirely of anatomic dead space. (60-61)

58. The Bohr equation is used to calculate dead space, Vd/Vt. It requires measuring $Paco_2$ and mixed-expired CO_2 by collecting exhaled gas. The gradient from $Paco_2$ to end-tidal $Paco_2$ is a reflection of alveolar dead space and is a simple semiquantitative way of evaluating dead space under general anesthesia. (61)

59. CO_2 jumps up fairly rapidly during the first 30 seconds to one minute of apnea. This jump is due to rapid transition to mixed venous CO_2 levels, which usually means an increase of about 6 mm Hg. This occurs because the lungs do not continue to store CO_2, so once equilibration of CO_2 occurs across the alveoli, $Paco_2$ will jump to mixed venous levels. Thereafter, CO_2 increases due to metabolism at a slower rate of about 2 to 3 mm Hg/min. (61)

PULMONARY MECHANICS

60. Pulmonary mechanics describes the pressure, volume, and flow relationships of gas within the lungs and the tracheobronchial tree. (61)

Static Properties

61. The lung itself has elastic properties. It requires pressure to expand. The chest wall and abdominal cavity produce a pressure effect on the lung. Surface tension, which exists at any air-fluid interface, also contributes. (61)

62. Without surfactant, surface tension would make the lungs much stiffer. Additionally, alveoli would be less stable and would tend to collapse. (61-62)

63. Static compliance is the change in volume divided by the change in pressure. By static, this means that the pressure and volume measurements are made at a point of no gas flow, which would contribute a resistive pressure component. Low or poor compliance would indicate that more pressure is needed to inflate the lungs. (62-63, Figures 6-12 and 6-13)

64. The FRC is simply the balance point between the lungs collapsing and the chest wall expanding. Stiffer lungs will produce a lower FRC, because this balance point will occur at a lower lung volume. On the other hand a disease such as emphysema, with loss of elastic recoil, results in a higher FRC. (62)

Dynamic Properties and Airway Resistance

65. Similar to the vascular system, resistance is largely determined by airway diameter. However, turbulent gas flow can add a significant resistance component, which can happen at airway narrowing. (62)

66. Pressure from resistance only occurs during gas flow. By ceasing gas flow with an inspiratory pause, one can determine the static or plateau pressure. (62, Figure 6-12)

67. High airway resistance can be caused by a number of common clinical conditions. A useful differential might trace the potential resistance anatomically, starting with airway equipment, including the endotracheal tube. Cause of resistance in the upper airways can include compression, foreign bodies, and secretions. In the lower airway, bronchoconstriction becomes the dominant cause. (62-63, Table 6-5)

CONTROL OF BREATHING

Central Chemoreceptors

68. The central chemoreceptors are located on the ventral surface of the brainstem. (62)

69. Carbon dioxide is the main stimulus for the central chemoreceptors. While the signal transduction may be through protons, the mechanisms are not completely understood. Because CO_2 crosses the blood-brain barrier, for clinical purposes, we consider that CO_2 is the primary stimulus. (62-63)

70. The central chemoreceptors are protected from metabolic acid by the blood-brain barrier. Cerebrospinal fluid pH will change in response to peripheral blood pH changes, but this may take days. An acute lactic acidosis will therefore have no effect on central chemoreceptors, except due to decreases in $Paco_2$ that may occur from the ventilatory response to the peripheral acidosis. (63)

Peripheral Chemoreceptors

71. The carotid bodies are the primary peripheral chemoreceptors in humans. Aortic bodies do not appear to have a significant clinical effect (which was studied in humans who had aortic body denervation). (63)

72. The peripheral chemoreceptors are stimulated by low pH, high $Paco_2$, and low Pao_2. Unlike the central chemoreceptors, the peripheral chemoreceptors are not protected from an acute metabolic acidosis, which will cause stimulation and hyperventilation (the lower $Paco_2$ from this hyperventilation will affect the central chemoreceptors). (63)

73. High blood flow relative to metabolic rate creates a tissue with hardly any arterial to venous Po_2 difference. This allows the carotid bodies to effectively sense arterial values. (63)

Hypercapnic Ventilatory Response

74. While a variety of techniques are used to obtain ventilatory data, the slope of CO_2 versus minute ventilation is the primary measure of hypercapnic ventilatory responsiveness. The slope is the change in minute ventilation divided by the change in CO_2 (usually end-tidal Pco_2 since a noninvasive measurement can be preferable). (63-64, Figure 6-14)

75. The central chemoreceptors are the major receptor system responsible for hypercapnic drive. However, in room air, approximately one third of the CO_2 response is from peripheral chemoreceptor drive. Usually hypercapnic drive is measured at higher Fio_2 where the majority of the response will then be from central chemoreceptors. (63-64)

76. Below a certain value of $Paco_2$, ventilation usually ceases. In an awake person, this can be difficult to measure due to an awake drive to breath. Under general

anesthesia, this phenomenon is easy to observe. With mechanical ventilation, if a patient is hyperventilating, spontaneous ventilatory efforts cease at a P_{CO_2} about approximately 5 mm Hg lower than the set point. As CO_2 is allowed to build up again, ventilation begins slowly and will stabilize again at the set point. (63-64)

77. CO_2 ventilatory drive is a slow response, with a time constant of approximately 2 minutes. This is rarely appreciated, although it is easy to observe that ventilation takes noticeable time to stabilize as CO_2 rises to a patient's set point. (64)

Hypoxic Ventilatory Response

78. Hypoxic ventilatory drive can be measured from a plot of P_{O_2} versus minute ventilation or Sa_{O_2} versus minute ventilation. Because the relationship of P_{O_2} to minute ventilation is nonlinear, more complex parameters would be needed to describe the relationship, which then are not very clinically useful. A plot of Sa_{O_2} (Sp_{O_2} is conveniently and noninvasively measured by pulse oximetry) versus minute ventilation is quite linear. Hypoxic responsiveness can then be measured by a simple slope (which will be negative), the change in minute ventilation divided by the change in Sp_{O_2}. (64, Figure 6-15)

79. Hypoxic ventilatory stimulation is from the carotid bodies. (64)

80. Central nervous effects of hypoxia lead to a slower development of ventilatory depression known as hypoxic ventilatory decline. The carotid bodies initially lead to increased minute ventilation, but if hypoxia is prolonged, ventilation drops to a level lower than peak ventilation, but still above baseline. This central response is a regulated response probably involving several inhibitory neurotransmitters. (64)

81. Hypoxic drive from the peripheral chemoreceptors develops extremely rapidly. The time constant is 10 to 20 seconds. Peak ventilation will therefore usually occur within 1 minute. The response is rapid enough that carotid body output will actually vary in response to the small oscillations of P_{O_2} and P_{CO_2} that occur with tidal breathing. (64)

82. The hypoxic drive is significantly higher with a higher P_{CO_2}. This synergistic response between P_{O_2} and P_{CO_2} will be most noticeable during apnea. (64)

EFFECTS OF ANESTHESIA

83. Opioids and most ventilatory depressants work on neurons in the integratory area of the brainstem. They do not affect detection of hypoxia or hypercapnia per se. The clinically observed respiratory depression therefore affects both hypercapnic and hypoxic ventilatory drive equally. (64)

Disorders of Ventilatory Control

84. Premature infants less than 60 weeks of postconceptual age can be at risk of apnea following general anesthesia. (64)

85. Originally described following surgery near the high cervical spinal cord, Ondine curse describes patients with a nearly absent drive to breath. While awake, they may breathe fairly normally. But asleep, or under general anesthesia, breathing can be significantly depressed. This is due to abnormalities in the central integratory system that seem to blunt the hypoxic and hypercapnic ventilatory responses. Idiopathic forms of Ondine curse, which can be seen in children, are usually referred to as primary central alveolar hypoventilation syndrome. (64)

86. Periodic breathing, most commonly Cheyne-Stokes breathing, occurs frequently when some degree of hypoxia is present. The stimulation of the carotid bodies can lead to overshoots and undershoots of ventilation. Periodic breathing can often be observed on sedated patients with some degree of hypoxia during sleep. This is

a major cause of sleep disturbance at high altitudes. Some patients with central sleep apnea have problems primarily with periodic breathing. Periodic breathing will not usually be observed in patients who are awake. (64)

INTEGRATION OF THE HEART AND LUNGS

87. The Fick equation describes the relationship between cardiac output, oxygen consumption, and oxygen about (arterial to venous content difference). (64)

Oxygen Delivery

88. Oxygen delivery (DO_2) is defined as the product of cardiac output (CO) and arterial oxygen content (Cao_2), $DO_2 = CO \bullet Cao_2$. (65)

Oxygen Extraction

89. Examining oxygen extraction provides a better global indication of whether cardiac output is matched to the body's oxygen needs. Oxygen extraction may provide clinically and diagnostically useful clues as to disease state. In cardiogenic shock, oxygen extraction is high because cardiac output is insufficient. In sepsis and liver failure, oxygen extraction may be very low. (65)

90. Normal whole body mixed venous oxygen saturation is about 75%. Individual organs and tissues can differ significantly. (65)

91. Arterial to venous oxygen content difference ($Cao_2 - Cvo_2$) is independent of Fio_2, whereas the mixed venous oxygen saturation (Svo_2) can increase significantly with higher Pao_2. (65)

92. Oxygen extraction ratio is probably the most reliable index. It is the oxygen extraction value most independent of Fio_2 and hemoglobin level. (65)

93. The two major compensatory mechanisms for increased demand or less availability of oxygen is (1) increased cardiac output and (2) increased extraction. This is readily apparent by examining the Fick equation. In anemia without general anesthesia, the primary compensation is increased cardiac output. Increased extraction occurs with more severe anemia. Under anesthesia, the cardiac output compensation may be blunted, and oxygen extraction is more important. In exercise, both increased cardiac output and increased extraction are utilized. (65)

Chapter

4 AUTONOMIC NERVOUS SYSTEM

David B. Glick

1. What are the two principal branches of the autonomic nervous system (ANS), and what is the primary function of each?

THE SYMPATHETIC NERVOUS SYSTEM

2. Where do the preganglionic fibers of the sympathetic nervous system (SNS) originate?
3. Where are the ganglia of the SNS located?
4. How are sympathetic signals amplified to broaden the sympathetic response?
5. What neurotransmitter and receptor are involved in the autonomic ganglia?
6. What is the most common neurotransmitter released by the postganglionic sympathetic neurons when they synapse with their target organs?
7. What are the other neurotransmitters of the SNS?
8. What are some of the common cotransmitters released at the terminal of the postganglionic sympathetic fibers, and what do they do?
9. What receptor types do the various classic sympathetic neurotransmitters bind to at the target organ?
10. Where are α_2 receptors located, and what happens when they are stimulated?
11. What are the chemical intermediates in the synthesis of norepinephrine from tyrosine substrate, and where does this process occur?
12. What is the rate limiting step in the synthesis of norepinephrine, and what enzyme catalyzes this step?
13. Where is epinephrine synthesized?
14. What percent of the norepinephrine reserve stored in vesicles at the sympathetic nerve terminal is released with each depolarization of the postganglionic nerve?
15. How is the action of norepinephrine at the synapse terminated?

THE PARASYMPATHETIC NERVOUS SYSTEM

16. Where do the preganglionic fibers of the parasympathetic nervous system (PNS) originate?
17. Where are the ganglia of the PNS located?
18. How are the postganglionic neurons of the PNS different from the postganglionic neurons of the SNS?
19. What happens to ACh after it is released into the synaptic cleft?

ADRENERGIC PHARMACOLOGY

20. Which adrenergic effect of norepinephrine predominates, the α or the β? What are the usual clinical responses seen to administration of norepinephrine?
21. What risks are associated with the administration of norepinephrine?
22. What receptors does epinephrine stimulate?
23. What life-threatening events are treated with epinephrine?
24. Name two ways that the local vasoconstrictive effects of epinephrine are used clinically.

25. What are the therapeutic effects of intravenous epinephrine?
26. Which response, sympathetic or parasympathetic, predominates in the following organs? The heart, the vasculature, the bronchial tree, the uterus, the gastrointestinal tract, and the pancreas.
27. What are the usual infusion rates for the catecholamines dopamine, norepinephrine, epinephrine, and dobutamine?
28. What are the primary endocrine and metabolic effects of epinephrine administration?
29. In what circumstances is an intravenous bolus of 1.0 mg of epinephrine appropriate?
30. What are epinephrine's primary effects at low, medium, and high infusion rates?
31. What are the mechanisms of action of epinephrine for the treatment of bronchospasm? How is the epinephrine administered? What is the dosing?
32. What is the concern when giving epinephrine to a patient during a halothane-based anesthetic?
33. What receptors bind dopamine?
34. In what two ways does dopamine exert its sympathomimetic effects?
35. Which vascular beds are uniquely dilated by dopamine?
36. How is dopamine metabolized?
37. How does the dose of dopamine administered affect its clinical response?
38. How does dopamine affect renal function in shocklike states?

SYNTHETIC CATECHOLAMINES

39. What receptors are stimulated by isoproterenol?
40. Why has isoproterenol fallen into disuse?
41. Which adrenergic receptors are stimulated by dobutamine?
42. What patients are most likely to benefit from treatment with dobutamine?
43. What is the problem with prolonged administration of dobutamine?
44. Which receptors are stimulated by fenoldopam?
45. What are the pharmacologic effects of fenoldopam?
46. What are the clinical uses of fenoldopam?

NONCATECHOLAMINE SYMPATHOMIMETIC AMINES

47. Through what two mechanisms do most noncatecholamine sympathomimetic amines exert their effects?
48. Name three noncatecholamine sympathomimetic amines.
49. What are the advantages and disadvantages of using ephedrine to treat hypotension in pregnancy?
50. What is the cause of tachyphylaxis after repeat doses of ephedrine?
51. Should ephedrine be used to treat life-threatening events?

α_1 AGONISTS

52. What is the primary effect of phenylephrine and when is its use common?
53. What is the usual dosing for intravenous phenylephrine?
54. Besides its effects on the cardiovascular system, what other pharmacologic actions does phenylephrine have?

α_2-ADRENERGIC AGONISTS

55. What is the mechanism of action of the α_2-adrenergic agonists?
56. What are the clinical effects of administering α_2 agonists?
57. What is "clonidine withdrawal"?
58. What drug is commonly used to treat clonidine withdrawal?
59. How does the administration of an α_2 agonist affect a patient's anesthetic requirements?
60. What effect do the α_2 agonists have on perioperative mortality?
61. How is clonidine used in the treatment of chronic pain syndromes?
62. What is the context-specific half-life of dexmedetomidine?
63. What is the dosing for a dexmedetomidine infusion?
64. What makes dexmedetomidine an attractive agent for use in awake intubations?
65. What makes dexmedetomidine an attractive agent for use in patients with sleep apnea?

β_2 AGONISTS

66. What are two common uses for β_2-adrenergic agonist drugs?

α-ADRENERGIC RECEPTOR ANTAGONISTS

67. What side effects are commonly associated with the use of α_1 antagonists as antihypertensive therapies?
68. What must happen before there is complete recovery from α_1-blockade with phenoxybenzamine?
69. What are the primary clinical effects of treatment with phenoxybenzamine?
70. Phenoxybenzamine is most often used to treat what disease?
71. What is the treatment for phenoxybenzamine overdose?
72. What effect does prazosin have on serum lipid levels?

β-ADRENERGIC ANTAGONISTS

73. What are some of the clinic indications for β-blocker therapy?
74. What benefit has been demonstrated for the use of perioperative β-blockers in patients at risk for coronary artery disease?
75. What are the risks of giving perioperative β-blockers?
76. What are the current recommendations for initiating β-blockade perioperatively?
77. What are the significant characteristics that differentiate the intravenous β-blockers commonly used in anesthetic practice?
78. What are the primary effects of the cardioselective (β_1 selective) β-blockers?
79. What are the cardiac side effects of β-blockade?
80. What are the risks of treating diabetics with β-blockers?
81. Can β-blockers be used in patients who have pheochromocytomas?
82. How should a β-blocker overdose be treated?
83. Which drug-drug interactions are particularly concerning when a patient is on β-blockers?
84. How is propranolol metabolized?
85. What effect does propranolol have on the oxyhemoglobin dissociation curve?
86. What is the intravenous dosing for the cardioselective β-blocker metoprolol?
87. What adrenergic receptors are antagonized by labetalol?
88. What is the dosing for labetalol?
89. Why is labetalol used to treat hypertension during pregnancy?
90. What accounts for the short half-life of esmolol?
91. When is esmolol an especially good choice for β-blockade?

CHOLINERGIC PHARMACOLOGY

92. What are the pharmacologic effects of the muscarinic antagonists?
93. How does the quaternary structure of glycopyrrolate affect its clinical actions?
94. In what kinds of cases are muscarinic antagonists still commonly given as premedications?
95. Why is glycopyrrolate given when neuromuscular blockade is reversed with the anticholinesterase drugs?
96. What are the common uses and side effects of a scopolamine patch?
97. What is the central anticholinergic syndrome and how is it treated?
98. What is the mechanism of action of the cholinesterase inhibitors (anticholinesterases)?
99. What is the clinical use for the cholinesterase inhibitors in the perioperative period?
100. What is the anesthetic risk for patients who use echothiophate eye drops?

ANSWERS*

1. The two principal branches of the ANS are the sympathetic and parasympathetic nervous systems. The sympathetic nervous system (SNS) is responsible for increasing cardiac output and shunting blood to the skeletal muscles to enable the

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

"fight or flight" response necessary when an organism is threatened. The parasympathetic nervous system (PNS), on the other hand, is responsible for the body's maintenance functions such as digestion and genitourinary function. (66)

THE SYMPATHETIC NERVOUS SYSTEM

2. The preganglionic neurons of the SNS originate from the thoracic and lumbar regions of the spinal cord. (66)
3. Most of the ganglia of the SNS are distributed along the paired sympathetic chains that are immediately lateral to the left and right borders of the vertebral column. Other sympathetic fibers extend to ganglia along the midline in the celiac or mesenteric plexuses. (66)
4. The initial sympathetic signal is amplified as the preganglionic fibers do not synapse at the ganglion of the level of their origin alone; rather they course up and down the sympathetic chain activating ganglia of the adjacent spinal levels thereby widening the body's response to the sympathetic signal. (66-68)
5. The neurotransmitter released at both sympathetic and parasympathetic ganglia is acetylcholine (ACh) and the postganglionic receptors that bind the ACh in both the SNS and the PNS are nicotinic receptors. (68)
6. While preganglionic sympathetic fibers are short (traveling only from the spinal column to the adjacent sympathetic chains before they synapse at the sympathetic ganglia), the postganglionic sympathetic neurons are relatively long as they must travel from the sympathetic chain to the target organ. The neurotransmitter released at the terminal end of the postganglionic sympathetic fiber at the synapse with its target organ is usually norepinephrine. (68)
7. Besides norepinephrine, the other classic neurotransmitters of the SNS are epinephrine and dopamine. (68)
8. Identified sympathetic cotransmitters include adenosine triphosphate (ATP) and neuropeptide Y. These molecules are released into the sympathetic synapse with the target organ and modulate the sympathetic activity. (68)
9. Norepinephrine and epinephrine bind to adrenergic receptors located postsynaptically on the target organ. These receptors include α_1, β_1, β_2, and β_3 receptors. Dopamine binds postsynaptically to dopamine-1 (D-1) receptors. (68)
10. α_2 Receptors are located presynaptically on the terminal end of the postganglionic nerve fiber. When norepinephrine binds to the α_2 receptor, subsequent norepinephrine release is decreased (negative feedback). (68)
11. Tyrosine is converted to dihydroxyphenylalanine (DOPA), DOPA is converted to dopamine, and dopamine is converted to norepinephrine. These transformations occur in the postganglionic sympathetic nerve ending. (69)
12. The rate limiting step in the synthesis of norepinephrine is the conversion of tyrosine to DOPA. The enzyme that catalyzes this reaction is tyrosine hydroxylase. (69)
13. Norepinephrine is converted to epinephrine in the adrenal medulla. The enzyme that catalyzes the methylation of norepinephrine to epinephrine is phenylethanolamine *N*-methyltransferase. (69)
14. Approximately 1% of the stored norepinephrine is released with each depolarization, so there is a tremendous functional reserve of norepinephrine at the nerve ending. (69)
15. After being released from the adrenergic receptor(s), most of the norepinephrine in the synaptic cleft is actively taken up at the presynaptic nerve terminal and transported to vesicles for reuse. Norepinephrine that escapes reuptake and makes its way into the bloodstream is metabolized by either the monoamine oxidase (MAO) or catechol-*O*-methyltransferase enzyme in the blood, liver, or kidney. (69)

THE PARASYMPATHETIC NERVOUS SYSTEM

16. The preganglionic fibers of the PNS arise from cranial nerves III, VII, IX, and X and from sacral nerve roots. (69)
17. Unlike the ganglia of the SNS that are located in ganglionic chains on either side of the vertebral column, the ganglia of the PNS are located close to or within their target organs. (70)
18. The postganglionic neurons of the PNS are short (since the PNS ganglia are close to or within the target organs), and they release acetylcholine (ACh) from their terminal end when the postganglionic neuron depolarizes. (70)
19. ACh released from the parasympathetic neuron binds to postsynaptic muscarinic receptors on the target cell. Upon release from these receptors, ACh is rapidly metabolized within the synapse by the cholinesterase enzyme. (70)

ADRENERGIC PHARMACOLOGY

20. Norepinephrine's stimulatory effects on α_1-adrenergic receptors predominate. This leads to an increase in peripheral vascular resistance and a resultant increase in diastolic, systolic, and mean arterial pressure. The increase in systemic vascular resistance can also lead to a reflex bradycardia. (70)
21. Besides the acute risks associated with severe hypertension that can occur with the administration of norepinephrine, the vasoconstriction caused by norepinephrine can decrease the blood flow to the pulmonary, renal, and mesenteric circulations so infusions must be carefully monitored to decrease the risk of injury to these vital organs. Additionally, prolonged norepinephrine infusions can cause ischemia of the fingers because of the marked peripheral vasoconstriction. (70)
22. Epinephrine binds to α- and β-adrenergic receptors. (70)
23. Exogenous epinephrine is given intravenously to treat cardiac arrest, circulatory collapse, and anaphylaxis. (70)
24. Epinephrine is commonly added to local anesthetics to decrease the spread of the local anesthetic. It can also be injected locally to decrease surgical blood loss from the soft tissue (as in tumescent anesthesia for liposuction). (70)
25. Among the therapeutic effects of intravenous epinephrine are: positive inotropy, chronotropy, and enhanced conduction through the heart (β_1 mediated); smooth muscle relaxation in the vasculature and bronchial tree (β_2 mediated); and vasoconstriction (α_1 mediated). The predominant effect depends on the dose of epinephrine administered. (70)
26. Most organs receive dual innervation from the SNS and PNS. When an organ receives these dual inputs one or the other normally predominates. In the heart, the rate and force of the contraction are mainly determined by the cholinergic (PNS) response. Vascular tone is determined solely by adrenergic (SNS) inputs. The tone of the smooth muscle of the bronchial tree is predominantly controlled by PNS inputs. Uterine tone is primarily controlled by adrenergic inputs. The gastrointestinal tract's primary inputs are from the PNS. The pancreas' insulin release is controlled exclusively by the SNS. (70-72)
27. All the exogenous catecholamines have short half-lives so they are administered as continuous infusions. The usual dose for dopamine is 2 to 20 μg/kg/min. The usual dose of norepinephrine is 0.01 to 0.1 μg/kg/min. The usual dose of epinephrine is 0.03 to 0.15 μg/kg/min. The usual dose of dobutamine is 2 to 20 μg/kg/min. (72)
28. Epinephrine's endocrine and metabolic effects result in increased blood glucose (via decreased insulin release), increased lactate, and increased free fatty acids. (72)

29. An intravenous dose of 1.0 mg of epinephrine is given for cardiovascular collapse, asystole, ventricular fibrillation, electromechanical dissociation, or anaphylactic shock. This dose of epinephrine is chosen because it constricts the peripheral vasculature while maintaining myocardial and cerebral perfusion. (72)

30. At low infusion rates (1 to 2 μg/min), epinephrine's primary action is a β_2-mediated decrease in airway resistance and vascular tone. At medium doses (2 to 10 μg/min) of epinephrine one usually sees an increase in heart rate, an increase in myocardial contractility, and increased conduction through the AV node. At high doses (> 10 μg/min), the α_1 effects predominate and there is a generalized vasoconstriction with a reflex bradycardic response. (72)

31. Epinephrine is effective therapy for bronchospasm both because of its direct effect as a bronchodilator (via relaxation of the bronchial smooth muscle) and because it decreases antigen-induced release of bronchospastic substances (as may occur during anaphylaxis) by stabilizing the mast cells that release these substances. When using epinephrine to treat bronchospasm, it can be given subcutaneously. The usual SQ dose is 300 μg every 20 minutes with a maximum of three doses. (72)

32. Epinephrine decreases the myocardial refractory period, so giving epinephrine during a halothane-based anesthetic increases the risk of cardiac arrhythmias associated with the administration of halothane. This risk seems to be lower in pediatric cases (the population in which halothane is still used) and the arrhythmic risk increases with hypocapnia. (72)

33. Dopamine is bound by α, β, and dopaminergic receptors. (72)

34. Dopamine binds to the adrenergic receptors on target cells to cause a *direct* adrenergic effect. Dopamine also causes the release of endogenous norepinephrine from storage vesicles. This is referred to as dopamine's *indirect* sympathomimetic effect. (72)

35. Dopamine is unique in its ability to selectively improve blood flow through the renal and mesenteric beds in shocklike states by binding to postjunctional dopamine-1 receptors. (72)

36. Dopamine, like the other endogenous catecholamines, is rapidly metabolized by MAO and COMT. The rapid metabolism by these enzymes results in dopamine's half-life of 1 minute. (72)

37. At doses between 0.5 to 2 μg/kg/min the dopamine-1 receptors are stimulated resulting in renal and mesenteric vascular dilation. At doses between 2 to 10 μg/kg/min, the β_1 effects predominate with increases in cardiac contractility and cardiac output. At doses greater than 10 μg/kg/min, the α_1 effects predominate, and there is generalized vasoconstriction negating any benefit to renal perfusion. (72)

38. Whereas previous literature suggested that low-dose dopamine infusions protected the kidneys and aided in diuresis, recent studies have shown no renal protection when dopamine is administered during periods of global hypoperfusion, and the use of dopamine under these circumstances has been called into question. (72)

SYNTHETIC CATECHOLAMINES

39. Isoproterenol is bound by the β_1- and β_2-adrenergic receptors, with its β_1 effects predominating. Because it is not taken up into the adrenergic nerve ending like the endogenous catecholamines, its half-life is longer than the endogenous catecholamines. (72)

40. Administration of isoproterenol is associated with marked tachycardia and arrhythmias. As a result, it has been removed from the ACLS resuscitation protocols. Its one remaining use is as a chronotropic agent after cardiac transplantation. (72)

41. Dobutamine stimulates β_1-adrenergic receptors without significant effects on β_2, α, or dopaminergic receptors. (72)

42. Dobutamine is particularly useful in patients with congestive heart failure (CHF) or myocardial infarction complicated by low cardiac output. Doses lower than 20 μg/kg/min usually do not cause tachycardia. Because dobutamine has no indirect adrenergic action, it is effective even in catecholamine-depleted states such as chronic CHF. While dobutamine treatments have improved exercise tolerance in chronic CHF, they have not been shown to improve survival. (72)

43. Prolonged treatment with dobutamine causes down-regulation of β receptors, and tolerance to its hemodynamic effects is significant after 3 days. To avoid the problem of tachyphylaxis, intermittent infusions of dobutamine have been used in the long-term treatment of heart failure. (72)

44. Fenoldopam is a selective dopamine-1 agonist. (72)

45. Fenoldopam is a potent vasodilator that increases renal blood flow and diuresis. It is usually administered as a continuous infusion at 0.1 to 0.8 μg/kg/min. (72)

46. Because of unconvincing data from clinical trials, fenoldopam is no longer used to treat CHF or chronic hypertension. It is still used as an alternative to sodium nitroprusside to treat severe acute hypertension. Its peak effects occur in 15 minutes. (72)

NONCATECHOLAMINE SYMPATHOMIMETIC AMINES

47. Noncatecholamine sympathomimetic amines exert their effects on the α and β receptors via both *direct* and *indirect* actions. The direct effects result from the binding of these compounds to the adrenergic receptors like other sympathomimetic agents. The indirect effects result from the release of endogenous norepinephrine stores that these compounds induce. (73)

48. Mephentermine, metaraminol, and ephedrine. (73)

49. Animal models suggest that ephedrine does not decrease uterine blood flow significantly and, as a result, it has been the drug of choice for treating hypotension in the parturient for many years. Recent studies, however, suggest that phenylephrine causes less fetal acidosis than ephedrine and so the use of phenylephrine to treat hypotension in these laboring patients is on the rise. (73)

50. The response to the indirect sympathomimetic effects of ephedrine wanes as the body's stores of norepinephrine available for release become depleted. (73)

51. While ephedrine is widely used as a first-line drug to treat intraoperative hypotension, data from the closed-claims database suggest that relying on ephedrine in situations where there is life-threatening hypotension rather than switching early on to epinephrine leads to an increase in morbidity from these events. (73)

α_1 AGONISTS

52. The primary effect of the α_1 agonists is to cause vasoconstriction. The rise in blood pressure that results leads to a reflex slowing of the heart rate. These agents are used when blood pressure is low and cardiac output is adequate (e.g., to treat the hypotension that can accompany the delivery of a spinal anesthetic). Phenylephrine is also used when a decrease in afterload compromises coronary perfusion in the context of aortic stenosis. (73)

53. Phenylephrine has a rapid onset of action and a short duration of action (5 to 10 minutes). It can be given as a bolus of 40 to 100 μg or as an infusion starting at 10 to 20 μg/min. (73)

54. Phenylephrine is also a mydriatic and nasal decongestant. It can be applied topically to the nostril to prepare the nose for nasotracheal intubation. (73)

α_2-ADRENERGIC AGONISTS

55. The α_2 agonists bind the presynaptic α_2 receptor on the postganglionic sympathetic neuron and decrease the release of norepinephrine. This results in a decrease in the overall sympathetic tone of the patient. (73)

56. Besides the decrease in blood pressure, the α_2 agonists have sedative, anxiolytic, and analgesic effects. (73)

57. Acute stoppage of chronic clonidine therapy can lead to a rebound hypertensive crisis, so clonidine should be continued throughout the perioperative period. If a patient is unable to take clonidine orally, administration can be topical via a transdermal patch. (73)

58. Labetalol is commonly used to treat clonidine withdrawal syndrome. (73)

59. α_2 Agonists reduce the requirements for other intravenous or inhaled anesthetics as part of a general or regional anesthetic technique. (73)

60. Like the β-blockers, the α_2 agonists decrease the incidence of myocardial infarction and perioperative mortality in patients undergoing vascular surgeries. (73)

61. Clonidine is used to treat patients with reflex sympathetic dystrophy and other neuropathic pain syndromes. Epidural clonidine has orphan drug approval from the U.S. Food and Drug Administration (FDA) for the treatment of intractable pain. (73)

62. The distribution half-life of dexmedetomidine is less than 5 minutes, making its clinical effect quite short. (73)

63. Because of its short clinical effect dexmedetomidine is run as a continuous infusion of 0.3 to 0.7 μg/kg/hr either with or without a 1 μg/kg loading dose given over 10 minutes. (73)

64. The relatively minor impact of α_2 induced sedation on respiratory function combined with its short duration of action has made dexmedetomidine a popular sedative agent for awake fiber-optic intubations. (73)

65. Infusions of dexmedetomidine in the perioperative period in obese patients with sleep apnea minimize the need for narcotics while providing adequate analgesia. (73)

β_2 AGONISTS

66. β_2 agonists (metaproterenol and albuterol) are used to treat reactive airway disease. Ritodrine (another β_2 agonist) is used to interrupt premature labor. All of these agents lose their β_2 selectivity when given at higher doses which leads to β_1 associated adverse events. (74)

α-ADRENERGIC RECEPTOR ANTAGONISTS

67. The common side effects of α_1-blockers are orthostatic hypotension, fluid retention, and nasal stuffiness. (74)

68. Because phenoxybenzamine irreversibly binds α_1 receptors, new receptors must synthesized before complete recovery can occur. (74)

69. The primary clinical effects of phenoxybenzamine are decreased blood pressure and increased cardiac output (both are the result of decreased peripheral vascular resistance). (74)

70. Phenoxybenzamine is most often used to create a "chemical sympathectomy" ahead of resection of a pheochromocytoma (a catecholamine secreting tumor). Effective α-adrenergic blockade in these patients makes arterial pressure less labile intraoperatively and has decreased surgical mortality dramatically. (74)

71. When exogenous sympathomimetic drugs are given following α-blockade, their effects are inhibited. Nevertheless, a phenoxybenzamine overdose is treated with an infusion of norepinephrine. Presumably, this is effective because some of the α receptors remain free of the phenoxybenzamine. (74)

72. Prazosin lowers low-density lipid levels and raises high-density lipid levels. (74)

β-ADRENERGIC ANTAGONISTS

73. β-blockers are used in ischemic heart disease, postinfarction management, arrhythmias, hypertrophic cardiomyopathy, hypertension, heart failure, migraine prophylaxis, thyrotoxicosis, and glaucoma. (74)

74. In the 1990s, the Perioperative Ischemia Research Group showed that patients going for surgery who were at risk for coronary artery disease and who were given perioperative β-blockers had a decrease in all cause mortality up to 2 years after surgery. (74)

75. The POBBLE and DIPOM studies showed no survival benefit to initiating β-blockers in patients undergoing vascular surgery or patients with diabetes (two of the "at-risk" groups for coronary artery disease). Furthermore, a large retrospective study showed an increased risk of morbidity in patients started on β-blockers who did not have clear-cut evidence of coronary artery disease. (74)

76. At this point, the only strong indication for initiating β-blockade perioperatively is for patients who need vascular surgery and have evidence of coronary ischemia on preoperative testing. While these are the only indications for initiating β-blockade immediately ahead of surgery, it is important to remember that patients on chronic β-blocker therapy for angina, arrhythmias, or hypertension should continue their β-blockers because acute β-blocker withdrawal can lead to life-threatening events. (74)

77. The β-blockers commonly used during anesthesia are propranolol, metoprolol, labetalol, and esmolol. These intravenous agents are differentiated based on their duration of action and cardioselectivity. (74)

78. With β_1 selective blockade, velocity of atrioventricular conduction, heart rate, and cardiac contractility all decrease. Renin release and lipolysis also decrease with β_1-blockade. At higher doses, the cardioselectivity of the β_1-blockers is lost and β_2 receptors are also blocked, which can lead to bronchoconstriction, vasoconstriction, and decreased glycogenolysis. (74)

79. Life-threatening bradycardia or asystole may occur with β-blockade. In addition, β-blockade can precipitate heart failure in patients with compromised cardiac contractility. (75)

80. Diabetes mellitus is a relative contraindication to the long-term use of β-blockers because warning signs of hypoglycemia (tachycardia and tremor) can be masked and because compensatory glycogenolysis is inhibited. (75)

81. To avoid worsening the hypertension in patients with pheochromocytomas, β-blockers should only be given after the patient is fully α blocked. (75)

82. A β-blocker overdose may be treated with atropine. Isoproterenol, dobutamine, glucagon, or cardiac pacing may also be necessary depending on the patient's symptoms and response to initial therapy. (75)

83. The combination of a β-blocker with either verapamil or digoxin can lead to life-threatening effects on heart rate (verapamil or digoxin) and contractility (verapamil) or conduction (digoxin). (75)

84. Propranolol is highly lipid soluble and extensively metabolized in the liver, so changes in liver function or hepatic blood flow can profoundly affect propranolol's clinical response and duration of action. (75)

85. Propranolol shifts the oxyhemoglobin dissociation curve to the right. (75)

86. Intravenous dosing for metoprolol is 2.5 to 5 mg every 2 to 5 minutes up to a total dose of 15 mg. The doses are titrated to the patient's heart rate and blood pressure. (75)

87. Labetalol is a competitive antagonist of the α_1- and β-adrenergic receptors. (75)

88. Five to 10 mg of labetalol can be given intravenously every 5 minutes. Because, like propranolol, it is metabolized in the liver, changes in hepatic blood flow affect its clearance. (75)

89. Labetalol is used acutely and chronically to treat hypertension during pregnancy because uterine blood flow is not affected by labetalol therapy, even with significant reductions in blood pressure. (75)

90. Esmolol is hydrolyzed by blood-borne esterases, resulting in a half-life for the drug of only 9 to 10 minutes. (75)

91. Because of its short half-life, esmolol is particularly useful when the duration of β-blockade desired is short or in critically ill patients in whom the adverse effects of bradycardia, heart failure, or hypotension may require rapid discontinuation of the drug. (75)

CHOLINERGIC PHARMACOLOGY

92. The muscarinic antagonists cause an increase in heart rate, sedation, and dry mouth. (75)

93. The quaternary structure of glycopyrrolate (as opposed to the tertiary structure of atropine and scopolamine) makes it impossible for this larger compound to cross the blood-brain barrier. As a result, glycopyrrolate has fewer CNS effects than the other two muscarinic antagonists. (75-76)

94. Preoperative use of muscarinic antagonists continues in some pediatric and otorhinolaryngologic cases or when planning fiber-optic intubation to dry the oral secretions. (76)

95. Glycopyrrolate is given along with the reversal agent to block the adverse effects (bradycardia) of the anticholinesterase. Glycopyrrolate is used because it has a longer duration of action than atropine and because unlike atropine or scopolamine it does not cross the blood-brain barrier, so there are fewer CNS side effects (sedation or delirium). (76)

96. A scopolamine patch is used prophylactically to protect against postoperative nausea and vomiting. It can be associated with adverse eye, bladder, skin, and psychological effects. (76)

97. The distortion of mentation (delusions and/or delirium) that can result from atropine or scopolamine's effects on the CNS has been labeled the "central anticholinergic syndrome." It is treated with physostigmine, a cholinesterase inhibitor that has a tertiary structure that allows it to cross the blood-brain barrier. (76)

98. The cholinesterase inhibitors inhibit the cholinesterase enzyme that normally catalyzes the inactivation of acetylcholine at the nicotinic and muscarinic receptors. As a result, these drugs sustain cholinergic agonism at the cholinergic receptors. (76)

99. The cholinesterase inhibitors are used clinically in the reversal of muscle relaxation produced by nondepolarizing neuromuscular blocking drugs. The accumulation of acetylcholine that results from the administration of the anticholinesterases allows acetylcholine to more effectively compete with

nondepolarizing neuromuscular blocking drugs for sites on the nicotinic receptor, thereby overcoming the effects of the paralytic agents. (76)

100. Echothiophate iodine irreversibly binds the cholinesterase enzyme and can interfere with the metabolism of succinylcholine (as the anticholinesterases impair the function of the pseudocholinesterase enzyme as well) leading to a marked prolongation of succinylcholine's paralytic effects. (76)

Chapter

5 INHALED ANESTHETICS

Rachel Eshima McKay

MECHANISM OF ACTION

1. What characterizes the anesthetic state?
2. Which characteristics of the anesthetic state are achieved by the administration of inhaled volatile anesthetics?
3. Which characteristics of the anesthetic state are achieved by the administration of nitrous oxide?

PHYSICAL PROPERTIES

4. Why are vaporizers required for the inhaled administration of volatile anesthetics?
5. Describe how a vaporizer for volatile anesthetics works.
6. What are the characteristics of desflurane that preclude its delivery in the conventional variable-bypass vaporizer?
7. What considerations must be taken into account when administering inhaled anesthetics at high altitude?
8. What are two potentially toxic compounds that can be produced as a result of the degradation or metabolism of volatile anesthetics?
9. What is a potentially toxic compound that can be produced as a result of the interaction between sevoflurane and the carbon dioxide absorbent? What factors may increase this risk?
10. What is the potential risk of human exposure to compound A? How can this risk be minimized?
11. What is a potentially toxic compound that can be produced as a result of the interaction between desflurane and the carbon dioxide absorbent? What factors may increase this risk?
12. What is the potential risk of carbon monoxide production from the carbon dioxide absorbent?

RELATIVE POTENCY OF INHALED ANESTHETICS

13. How are relative inhaled anesthetic potencies compared?
14. What are MAC values for isoflurane, sevoflurane, desflurane, and nitrous oxide in a 30- to 55-year-old?
15. What concentration of anesthetic is sufficient to provide amnesia in volunteers? How does this value relate to surgical patients?
16. What factors increase MAC?
17. What factors decrease MAC?

PHARMACOKINETICS OF INHALED ANESTHETICS

18. Describe the process by which induction of anesthesia is achieved by an inhaled anesthetic.
19. What six factors determine the alveolar partial pressure of anesthetic?

20. Describe a strategy that allows maintenance of stable anesthetic partial pressure in the brain after the induction of anesthesia.
21. How does a shunt affect the induction of an inhalation anesthetic?
22. How is anesthetic solubility expressed?
23. How does anesthetic solubility influence speed of induction?
24. What is the "second gas effect"?
25. How does nitrous oxide affect the enzyme methionine synthase? How might this relationship affect patients receiving nitrous oxide?
26. How does nitrous oxide affect closed air-filled spaces in the body? What is the clinical relevance of this?
27. What are some differences between the induction of inhaled anesthesia and recovery from anesthesia?
28. How are volatile anesthetics metabolized?
29. What is diffusion hypoxia?

CIRCULATORY EFFECTS

30. Why might an individual patient's responses vary in the circulatory effects of equipotent doses of a given inhaled volatile anesthetic?
31. How do inhaled volatile anesthetics affect arterial blood pressure? What is the mechanism by which this effect occurs?
32. How does the substitution of nitrous oxide for an equipotent portion of volatile anesthetic affect arterial blood pressure at a given anesthetic dose?
33. How do inhaled volatile anesthetics affect heart rate? What is the mechanism by which this occurs?
34. How do inhaled volatile anesthetics affect cardiac output?
35. How do inhaled volatile anesthetics affect myocardial rhythm?
36. How do inhaled volatile anesthetics affect myocardial conduction?
37. How do inhaled volatile anesthetics affect coronary artery blood flow? What is coronary artery steal syndrome? What is its clinical relevance?

EFFECTS ON VENTILATION

38. How is the rate of breathing affected by inhaled volatile anesthetics?
39. How is the tidal volume affected by inhaled volatile anesthetics?
40. How is the minute ventilation affected by inhaled volatile anesthetics? How is the overall pattern of ventilation affected by inhaled volatile anesthetics?
41. How is the ventilatory drive affected by inhaled volatile anesthetics?
42. How does the addition of nitrous oxide to a volatile anesthetic affect the ventilatory drive and the resultant $Paco_2$?
43. How do inhaled volatile anesthetics affect hypoxic pulmonary vasoconstriction?
44. How do inhaled volatile anesthetics affect bronchial tone?
45. How do inhaled anesthetics differ in their capacity to cause airway irritation? How do these differences affect their use in various clinical situations?

OTHER ORGAN SYSTEM EFFECTS

46. How does nitrous oxide affect cerebral blood flow and intracranial pressure?
47. How do inhaled volatile anesthetics affect cerebral blood flow and intracranial pressure?
48. How do inhaled volatile anesthetics affect cerebral metabolic oxygen requirements?
49. How do inhaled volatile anesthetics affect evoked potentials?
50. What electroencephalographic (EEG) changes occur with increasing concentration of inhaled volatile anesthetics?
51. How do inhaled volatile anesthetics affect neuromuscular function?
52. Which inhaled anesthetics have the potential to trigger malignant hyperthermia?
53. How do inhaled volatile anesthetics affect the liver?

ANSWERS*

MECHANISM OF ACTION

1. Characteristics of the anesthetic state include immobility, amnesia, analgesia, and skeletal muscle relaxation. (81)

2. Characteristics of the anesthetic state that are achieved by inhaled volatile anesthetics include immobility, amnesia, and skeletal muscle relaxation. Analgesia is difficult to define in an amnestic, immobile patient, but surrogate measures of perception of painful stimuli (i.e., increases in heart rate or blood pressure at the time of incision or intubation) suggest that inhaled anesthetics do not possess analgesic characteristics at concentrations typically used in clinical practice. (81)

3. Nitrous oxide contributes to immobility, but is not reliable in doing so when administered alone. It has amnestic effects at higher concentration (although these are difficult to assure), and in contrast to potent inhaled anesthetics, does not contribute to skeletal muscle relaxation. (81)

PHYSICAL PROPERTIES

4. Volatile anesthetics exist as liquids at room temperature and at atmospheric pressure. The inhaled delivery of these anesthetics requires that the anesthetics be vaporized. Vaporizers allow not only the vaporization of liquid anesthetics, but they also reliably and accurately deliver the specified concentration of anesthetic to the common gas outlet and ultimately to the patient. Nitrous oxide exists as a gas at room temperature and therefore does not require a vaporizer for inhaled delivery to a patient. (81)

5. Conventional volatile anesthetic vaporizers are classified as agent-specific, variable-bypass, flow-over, temperature-compensated, out-of-circuit vaporizers. After passing through the flowmeters, gases mix in the common manifold, then enter the vaporizers. Once in the vaporizer there are different streams of flow that the gases can take. The gases may be diverted by a temperature-compensating bypass valve to the bypass chamber, or they may enter the vaporizing chamber.

   The temperature-compensating bypass valve adjusts the amount of gas that enters each of the other two chambers. When the temperature of the vapor is warm, more gas is directed to the vaporizer outlet via the bypass chamber than when the temperature is relatively cooler. The opposite occurs when the temperature of the vapor is relatively cooler. That is, more of the gas is directed toward the vaporizing chamber. The temperature-compensating valve allows the vaporizer to compensate for changes in temperature, so the desired concentration of volatile anesthetic is maintained.

   Typically about 20% of the gas flows through the vaporizing chamber. A higher dialed concentration will result in more gas going to the vaporizing chamber than otherwise. In the vaporizing chamber, there are a series of wicks that have been saturated with the liquid anesthetic. (Vaporizers are designed for a specific gas as the quantity of anesthetic in the gas phase is dependent on the vapor pressure of the anesthetic gas, a physical property that is unique to each anesthetic.) As the gas passes over the series of wicks, the gas becomes saturated with the anesthetic vapor. The gas, now saturated with anesthetic vapor, enters the mixing bypass chamber. In the mixing bypass chamber, the saturated gas mixes with the unsaturated gas that has been diverted there. Together the gases pass through the vaporizer outlet toward the common gas outlet at the desired concentration of volatile anesthetic. (82-83)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

6. The two characteristics of desflurane that preclude its delivery in a conventional variable-bypass vaporizer are its volatility and its potency. At 20 °C, the vapor pressure of desflurane is 669 mm Hg, whereas those of isoflurane and sevoflurane are 238 mm Hg and 157 mm Hg, respectively. In addition, the boiling point of desflurane is near room temperature. Because of its volatility, erratic and dangerously high concentrations of desflurane would be delivered if a conventional variable-bypass vaporizer were to be used. The Tec-6 heated vaporizer was developed to address this problem. Desflurane's potency is substantially lower than that of other volatile anesthetics—roughly three times less than that of sevoflurane and almost five times less than that of isoflurane. Thus, the large number of molecules converted from liquid to gas phase would create a large cooling effect (from the heat of vaporization) and it would not be possible to compensate without externally heating the anesthetic. Thus, desflurane vaporization requires a vaporizer that is electrically heated and pressurized for these reasons. (83 and Table 8-1)

7. Although vaporizer output is conventionally expressed in volumes percent, the pharmacologically relevant measure is anesthetic partial pressure. Administration of anesthesia at high altitude will result in higher volumes percent vaporizer output when a variable bypass vaporizer is used. However, the increase in anesthetic partial pressure will be minimized by the overall decrease in ambient pressure, and the clinical effect will be very small. On the other hand, the Tec 6 vaporizer behaves differently, since it is a blender of two gases and maintains constant volumes percent output. Therefore, at high altitude, although the volumes percent output will be unaffected, the delivered partial pressure will be substantially smaller and an adjustment must be made to avoid unintentional delivery of partial pressures below those clinically needed. The anesthesiologist should select the desired anesthetic vaporizer setting that would be appropriate at sea level, and multiply by this value by the ratio of sea level divided by the local barometric pressures. (82-83)

8. Two potentially toxic compounds that can be produced as a result of the degradation or metabolism of volatile anesthetics include compound A and carbon monoxide. (83)

9. A potentially toxic compound that can be produced as a result of the interaction between sevoflurane and the carbon dioxide absorbent is compound A. This can occur with either soda lime or baralyme, but the risk appears to be higher with baralyme. Other factors that may increase the risk of compound A production include the low inflow of fresh gases, high concentrations of sevoflurane, higher absorbent temperatures, and fresh absorbent. (83, Table 8-1)

10. The concern with exposure to compound A is for nephrotoxicity. Compound A has been shown to be nephrotoxic in animals. Indeed, in humans prolonged exposure to sevoflurane at low fresh gas flows (1 L/min) has been shown to result in transient proteinuria, enzymuria, and glycosuria. There has been no evidence for increased serum creatinine levels or prolonged deleterious effects, however. This is evidenced by the millions of anesthetics that have been administered with sevoflurane without harm. Regardless, the recommendation is that when sevoflurane is administered fresh gas flows should be greater than 1 L/min for the first 2 hours, then 2 L/min thereafter. (83)

11. A potentially toxic compound that can be produced as a result of the interaction between desflurane and the carbon dioxide absorbent is carbon monoxide. Carboxyhemoglobin concentrations can reach as high as 30%. This can occur with either soda lime or baralyme, but the production of carbon monoxide appears to be greater with baralyme. Other factors that appear to increase the production of carbon monoxide include the higher anesthetic concentrations, an increased

temperature, and greater dryness of the absorbent. The majority of cases of carbon monoxide toxicity occurred after 2 days of disuse of the absorbent, particularly with continued airflow through the circle system. (83, Table 8-1)

12. The production of carbon monoxide from the interaction between desflurane and carbon dioxide absorbent can result in the inhaled delivery of carbon monoxide to the patient. The diagnosis of carbon monoxide poisoning under these conditions can be difficult because the toxicity may be masked by the anesthesia itself and the pulse oximetry readings are likely to be unchanged. (83)

RELATIVE POTENCY OF INHALED ANESTHETICS

13. Relative potency between inhaled anesthetics is most commonly described by the dose required to suppress movement in 50% of patients in response to surgical incision, known as MAC (minimum alveolar concentration). Since this dose has a standard deviation of approximately 10%, 95% of patients should not move in response to incision at 1.2 MAC, and 99% should not move at 1.3 MAC. (83-84 and Table 8-1)

14. In a 30- to 55-year-old, MAC of isoflurane is 1.15%, sevoflurane 1.85%, desflurane 6%, and nitrous oxide 104%. MAC values are additive. For example, 0.5 MAC of nitrous oxide administered with 0.5 MAC isoflurane has the same effect as 1 MAC of any inhaled anesthetic in preventing movement in response to incision. (83-84, Table 8-1)

15. The expired concentration of isoflurane that prevented recall of events in 50% of volunteers was 0.20 MAC, and the concentration preventing recall in 95% of volunteers was 0.40 MAC. Assuming a standard normal distribution in dose-response, and a standard deviation of 0.10 MAC, the calculated highest anesthetic concentration required by 1 in 100,000 subjects with the highest requirement would be 4.27 standard deviations above the mean, or 0.627 MAC or more. Extrapolation of this value to the context of surgery must be made with caution, however, because (1) the dose required to prevent recall of painful as opposed to verbal stimulation may be considerably larger; and (2) the ratio of concentration necessary to prevent recall versus MAC differs substantially between potent inhaled anesthetics and nitrous oxide (recall occurs with as much as 0.6 MAC of nitrous oxide). (84)

16. Age has a large influence on MAC, being highest at 6 months of age. After 6 months of age, MAC declines, increases again during adolescence, and thereafter declines until the end of life. Other factors that increase MAC include acute amphetamine use, cocaine, ephedrine, and chronic alcohol use. Hyperthermia, hypernatremia, and red hair color also increase MAC. (Table 8-2)

17. Older age decreases MAC. Hyponatremia, anemia, hypothermia, hypoxia, and pregnancy all decrease MAC, as does acute alcohol ingestion and chronic amphetamine use. The concomitant administration of certain drugs such as propofol, etomidate, barbiturates, ketamine, opioids, local anesthetics, benzodiazepines, α_2-agonists, lithium, and verapamil all decrease MAC. (Table 8-2)

PHARMACOKINETICS OF INHALED ANESTHETICS

18. The induction of anesthesia relies on delivery of inhaled anesthetic from the alveoli to the brain via the arterial blood. By controlling the inspired partial pressure, a gradient is created between the machine, the alveoli, the arterial blood, and the brain. Higher inspired anesthetic partial pressure is needed during inhaled induction to offset the impact of anesthetic uptake into the blood and tissues. This is termed the concentration effect. The delivery of higher fresh gas flow allows the avoidance of rebreathing anesthetic-depleted gases. Anesthetic present in the alveoli is taken up by the blood and carried to the tissues, including the brain; initially the uptake of anesthetic in the blood limits the rate at which the

partial pressure in the brain can rise. As the gradient diminishes, alveolar partial pressure approaches equilibrium with blood and vessel rich tissue and the partial pressure in the alveoli begins to reflect partial pressure in the brain. The primary objective of inhalation anesthesia is to establish equilibrium between the alveoli and the brain, such that there is a constant, optimal partial pressure of anesthetic in the brain. This can be reflected in the partial pressure of anesthetic in the alveoli, or end-tidal anesthetic value. (84)

19. The alveolar partial pressure is determined by input of anesthetic into the alveoli minus the uptake of anesthetic into the pulmonary arterial blood. The input of anesthetic into the alveoli is determined by the inspired partial pressure of anesthetic, alveolar ventilation, and the characteristics of the breathing circuit. The uptake of anesthetic from the alveoli is determined by the anesthetic solubility in blood and tissues, cardiac output, and the alveolar to venous partial pressure difference. For a high partial pressure in the alveoli, and thus a rapid induction of anesthesia, the following should occur: a high inspired partial pressure of anesthetic, a high minute ventilation, a low volume breathing circuit, high fresh gas flows, a low solubility of anesthetic in the tissues, a low cardiac output, and a small alveolar to venous partial pressure difference. (84-85 and Table 8-3)

20. A higher inspired anesthetic partial pressure is needed during an inhaled induction to offset the impact of anesthetic uptake into the blood and tissues and higher fresh gas flow allows for the avoidance of rebreathing. Uptake diminishes as the anesthetic partial pressure in blood and tissues approaches that in the alveoli. The speed at which this equilibration takes place is expressed as a time constant. The time constant related to a tissue group is correlated to the amount of anesthetic that can be dissolved in that tissue divided by the blood flow received by the tissues. The vessel-rich tissue group (i.e., brain, heart, kidneys, and liver) accounts for less than 10% of the body mass but it receives 75% of cardiac output. One time constant reflects about 67% equilibration between blood and tissue, and complete equilibration is achieved in three time constants. After three time constants (6 to 12 minutes), 75% of returning venous blood has the same anesthetic partial pressure as the alveolus, resulting in narrowing of the alveolar-venous difference, reduced uptake, and if inspired anesthetic concentration is maintained, a rapid increase in brain concentration. The brain time constant for isoflurane is 3 to 4 minutes, whereas those of sevoflurane and desflurane are about 2 minutes. Therefore, complete equilibration between alveoli and the brain may be achieved as quickly as 6 to 10 minutes. Delivered anesthetic concentration must therefore be decreased after 5 to 10 minutes to avoid a subsequent rapid rise in brain concentration after equilibration with the vessel-rich tissues has taken place. The decrease in delivered anesthetic may be achieved by decreasing vaporizer concentration, fresh gas flows, or both. (84-85, Table 8-4 and Figure 8-4)

21. A right-to-left shunt slows the rate of the induction of an inhalation anesthetic through the dilutional effect of shunted blood without the mixing of anesthetic with blood that is being delivered to the tissues from ventilated alveoli. The clinical impact of this is probably negligible, however. (87)

22. Anesthetic solubility in blood and tissues is denoted by partition coefficients. A partition coefficient can be viewed as the affinity of anesthetic for one particular tissue, and indicates the quantitative ratio of anesthetic distributed between two phases when partial pressures are equal. For example, a blood gas partition coefficient of 0.65 means that the concentration of sevoflurane in the alveolus is 1 and 0.65 in blood at equilibrium. Partition coefficients are dependent upon temperature and, unless otherwise stated, are given for 37° C. (85-86 and Table 8-1)

23. When an anesthetic has a high solubility in blood, it means that a large amount of inhaled anesthetic must be dissolved in the blood before equilibration with the gas phase is reached. The blood can be considered a pharmacologically inactive reservoir, and the size of this reservoir is directly related to the solubility of the anesthetic in blood. Therefore greater inhaled anesthetic solubility slows induction. (86 and Figure 8-5)

24. The second gas effect describes the influence of one gas, administered at high volume, on the uptake of a companion gas. The process occurs when a large volume of "first" gas (e.g., nitrous oxide) is taken up during induction, and this uptake effectively concentrates the "second" gas (oxygen or potent inhaled anesthetic) into a smaller alveolar volume. Pharmacokinetic models have proven the second gas effect, but its clinical importance is doubtful. (85)

25. Nitrous oxide inactivates methionine synthase, the enzyme that regulates vitamin B_{12} and folate metabolism. While this inactivation may not usually produce clinically evident change, patients with an underlying critical illness, exposure to chemotherapy, or preexisting vitamin B_{12} deficiency may suffer neurologic or hematologic sequelae. Another consequence of methionine synthase inactivation is increased serum homocysteine concentration since the enzyme is needed to convert cysteine to methionine. Elevated homocysteine levels and increased frequency of ischemic episodes have been concurrently demonstrated in patients undergoing carotid endarterectomy while receiving nitrous oxide. (86-87)

26. Nitrous oxide is 34 times more soluble than nitrogen in blood, as reflected by their respective blood gas partition coefficients of 0.46 versus 0.014. As a result, nitrous oxide can more readily diffuse out of the circulation and occupy an air-filled compartment than the air in the compartment can diffuse from the compartment into the circulation. The result of this imbalance is an increase in the gas contents of a closed air-filled space. The space and volume of gas will expand if the walls of the space are compliant (e.g., intestinal gas, pneumothorax, air embolism), or the pressure in the space will increase if the walls of the space are noncompliant (e.g., middle ear, eye, cerebral ventricles, supratentorial subdural space). The magnitude of volume or pressure increase in the air-filled space will be influenced by the alveolar partial pressure of nitrous oxide, blood flow to the compartment, and the duration of nitrous oxide administration. Presence of a closed pneumothorax is a contraindication to nitrous oxide administration. Difficulty with ventilation encountered in the setting of chest trauma may reflect nitrous oxide expansion of a previously unrecognized pneumothorax. Air bubbles associated with venous air embolism expand rapidly when exposed to nitrous oxide. (87)

27. The recovery from anesthesia differs from the induction of anesthesia in several ways. First, there cannot be a concentration effect to accelerate recovery. For example, the inhaled pressure of anesthetic cannot be less than zero to augment the partial pressure of anesthetic gradient from the brain to the alveoli. Second, there are variable concentrations of anesthetic in the tissues at the start of recovery, and there are thus multiple reservoirs of anesthetic throughout the body. These reservoirs are of variable influence, and their significance is dependent on the duration of the anesthetic as well as the solubility characteristic of the anesthetic itself. And finally, the metabolism of anesthetic may impact the rate of recovery. The clinical significance of the metabolism of anesthetics on the rate of recovery of anesthetics is minimal for the less lipid-soluble anesthetics such as isoflurane, desflurane, and sevoflurane. The metabolism of halothane may play a role in the rate of recovery of anesthesia. (88, Figures 8-6, 8-7)

28. All volatile anesthetics are biotransformed to a variable extent in the liver. Halothane, isoflurane, and desflurane all undergo oxidative metabolism (15% to 40%, 0.2%, and 0.02%, respectively) by cytochrome P-450 enzymes to produce

trifluoroacetate. Sevoflurane is metabolized (5% to 8%) to hexafluoroisopropanol. (Table 8-1, 89, 96)

29. Diffusion hypoxia is a term used to describe the dilution of oxygen in the alveoli due to the presence of another gas. This can occur at the conclusion of a nitrous oxide anesthetic when there is an initial high volume output of nitrous oxide diffusing from the blood to the alveoli and filling the alveoli. If the patient is breathing room air at the time, the partial pressure of oxygen in the alveoli can be diluted to the extent that hypoxia results. Diffusion hypoxia at the conclusion of a nitrous oxide anesthetic can be avoided through the inhaled delivery of 100% oxygen. (90)

CIRCULATORY EFFECTS

30. The circulatory effect of an inhaled anesthetic for a given patient is influenced by multiple factors. These can include the effects of age, surgical stimulation, coexisting diseases such as myocardial dysfunction and stenotic valve lesions, intravascular fluid volume status, and concurrent drug administration. (90)

31. The volatile anesthetics all produce a dose-dependent decrease in mean arterial blood pressure, although the mechanism by which they exert their effects varies. Halothane primarily acts to decrease blood pressure by decreasing myocardial contractility and cardiac output. Isoflurane, desflurane, and sevoflurane primarily decrease blood pressure through their effects of peripheral vasodilation and an associated decrease in systemic vascular resistance. Nitrous oxide, when administered alone, causes minimal if any alteration in blood pressure. (90 and Figures 8-8 and 8-9, Table 8-6)

32. Nitrous oxide, when administered alone, causes little if any alteration of blood pressure. The substitution of nitrous oxide for an equipotent dose of a volatile anesthetic therefore results in a smaller decrease in arterial blood pressure than would have otherwise occurred if the volatile anesthetic were administered alone. This is in part the basis for the administration of nitrous oxide in combination with a volatile anesthetic. The combination of nitrous oxide with a volatile anesthetic allows for an increase in the MAC of anesthesia delivered with less circulatory depression than would occur if an equivalent dose of anesthetic composed of a volatile agent alone were to be used. (92-93 and Figure 8-11)

33. Halothane has minimal effect on heart rate. Isoflurane, sevoflurane, and desflurane all tend to increase heart rate, but each behaves in a somewhat different manner. At concentrations as low as 0.25 MAC, isoflurane induces a linear, dose-dependent heart rate increase. Heart rate shows minimal increase with desflurane below 1 MAC, but above 1 MAC a steep dose-dependent increase in heart rate and blood pressure may be observed. In contrast to desflurane and isoflurane, heart rate in the presence of sevoflurane does not increase until the concentration exceeds 1.5 MAC. The tendency for desflurane to stimulate the circulation (i.e., increase MAP and heart rate) is attenuated with the administration of β-adrenergic blocker (esmolol), opioid (fentanyl), and the passage of time (10 to 15 minutes). The transient increase in heart rate that occurs above 1 MAC of desflurane results from sympathetic nervous system stimulation, rather than baroreceptor reflex response to decreased MAP. (90-91 and Figure 8-12)

34. Halothane produces a dose-dependent decrease in the cardiac index that parallels the decrease in blood pressure that is seen with its administration. In contrast, cardiac index is minimally influenced by administration of isoflurane, sevoflurane, and desflurane over a wide range of concentrations in young healthy adults. (92 and Figure 8-10)

35. The only inhaled volatile anesthetic that has any effect on myocardial rhythm is halothane. The administration of halothane may be accompanied by a junctional rhythm, and halothane sensitizes the myocardium to premature ventricular extrasystoles, especially in the presence of catecholamines. Sensitization of the myocardium to ventricular extrasystoles is exaggerated in the presence of hypercarbia. In contrast, isoflurane, sevoflurane, and desflurane do not affect myocardial rhythm. (93)

36. Inhaled volatile anesthetics all prolong the QT interval on the electrocardiogram, particularly halothane and sevoflurane. Although malignant arrhythmias have been reported in patients receiving halothane who were subsequently found to have congenital long QT syndrome, the clinical significance of sevoflurane's QT interval prolongation is unclear. Regardless, sevoflurane should be avoided in patients with known congenital long QT syndrome. (93)

37. Isoflurane has been shown to selectively dilate small coronary arterioles in animal models. If coronary arterioles undergo vasodilation and blood flow is diverted from narrowed arterioles that are already maximally dilated to healthy arterioles with less resistance, this theoretically could result in ischemia in the areas supplied by the narrowed arterioles, and this process is known as "coronary steal." However these concerns turned out not to be valid. Isoflurane, sevoflurane, and desflurane all appear to exert a protective effect on the heart, limiting the area of myocardial injury and preserving function after exposure to ischemic insult. (93)

EFFECTS ON VENTILATION

38. Inhaled volatile anesthetics produced a dose-dependent increase in the rate of breathing. Although the exact mechanism for this is unclear, it is believed to result from central nervous system stimulation by the anesthetic. (93)

39. Inhaled volatile anesthetics decrease the tidal volume of patients breathing the anesthetic, leading to an increase in dead space ventilation in a dose-dependent manner. (93)

40. Inhaled anesthetics increase breathing frequency and decrease tidal volume in a dose-dependent manner. The pattern of breathing is regular, rapid, and shallow. The decrease in tidal volume is not sufficiently compensated by the increase in respiratory rate, however. This results in a decrease in the minute ventilation of individuals breathing an inhaled anesthetic. The resting $Paco_2$ of these patients is increased as a result. The resting $Paco_2$ is used as an index to evaluate the degree of respiratory depression that is produced by inhaled anesthetics. (93)

41. Inhaled anesthetics produce a dose-dependent depression of the ventilatory drive. The mechanism by which this occurs is thought to be due to direct depression of the medullary ventilatory centers along with a lesser contribution from depressant effects on chest wall mechanics. Normally, minute ventilation should increase by 1 to 3 L/m for every 1 mm Hg increase in carbon dioxide, but in anesthetized patients there is a blunting of carbon dioxide responsiveness. This effect of inhaled anesthetics results in a progressive increase in carbon dioxide as anesthetic concentration rises. Indeed, at 1 MAC, carbon dioxide responsiveness is two to four times less than baseline values. At 1.7 MAC of desflurane in 100% oxygen, volunteer subjects become apneic. Volatile anesthetics all blunt or abolish the ventilatory stimulation evoked by arterial hypoxemia, even at a partial pressure below that where patients are awake. This is of great clinical importance during early recovery, when the concomitant effects of opioid and unresolved neuromuscular weakness may interact to compound ventilatory depression. (93-94 and Figures 8-14, 8-15, and 8-16)

42. The administration of nitrous oxide to patients does not change their $Paco_2$ levels from awake levels. Although there is an increase in the anesthetic depth when

nitrous oxide is added to a volatile anesthetic, the patient's $Paco_2$ does not change with the addition of nitrous oxide to the volatile anesthetic. Similarly, the substitution of nitrous oxide for an equivalent dose of volatile anesthetic results in less of an increase in the $Paco_2$ than that which would have otherwise occurred with the volatile anesthetic alone. (94, Figures 8-14 and 9-15)

43. Hypoxic pulmonary vasoconstriction is a reflex response of pulmonary arterioles to vasoconstrict in areas of low alveolar Pao_2 in an attempt to decrease perfusion to underventilated alveoli, as in atelectasis. Although inhaled volatile anesthetics alter pulmonary blood flow, inhibition of hypoxic pulmonary vasoconstriction is minimal. (94-95)

44. All volatile inhaled anesthetics have been shown to be bronchodilators and exert some attenuation of bronchospasm with their administration. The bronchodilating effects of inhaled volatile anesthetics may be due to decreased efferent vagal tone from the central nervous system and through direct relaxation of bronchial smooth muscle. In the absence of bronchoconstriction, the bronchodilating effects of the inhaled volatile anesthetics are small. (95)

45. Sevoflurane, halothane, and nitrous oxide are all nonpungent, causing minimal or no irritation over a broad range of concentrations. For this reason, sevoflurane and halothane, usually with nitrous oxide, are selected most frequently for inhaled induction of anesthesia, since very high concentrations can be introduced to overcome the initial uptake of anesthesia into the blood. Both desflurane and isoflurane are pungent, and can irritate the airway at concentrations above 1 MAC when given without opioids or propofol. However, isoflurane and desflurane may be administered via laryngeal mask airway (LMA) after propofol induction without greater incidence of coughing, breath holding, laryngospasm, or desaturation compared with sevoflurane or propofol, probably because anesthetic maintenance usually does not require concentrations in excess of 1 MAC, and small doses of opiate (1 μg/kg of fentanyl) attenuate or abolish the irritating effects. Because of their pungency, isoflurane and desflurane are not practical for inhaled induction of anesthesia. (95)

OTHER ORGAN SYSTEM EFFECTS

46. Nitrous oxide increases cerebral blood flow through cerebral vasodilation. The effect of nitrous oxide appears to be blunted in the presence of intravenous anesthetics. Nitrous oxide has less of an effect on cerebral blood flow than volatile anesthetics. Limitation of the inspired concentration of nitrous oxide to less than 0.7 MAC minimizes its effect of cerebral vasodilation. (95)

47. Inhaled volatile anesthetics at concentrations above 0.6 MAC increase cerebral blood flow in a dose-dependent manner, most likely through the direct relaxation of vascular smooth muscle leading to vasodilation. Cerebral blood flow increase is greater with equipotent doses of halothane compared with isoflurane, sevoflurane, or desflurane. Intracranial pressure increases with all inhaled anesthetics above 1 MAC. Inhaled anesthetics do not abolish the cerebral vascular responsiveness to changes in $Paco_2$. (95-96)

48. Inhaled volatile anesthetics decrease the cerebral metabolic oxygen requirement. Volatile anesthetics also increase cerebral blood flow. Normally, cerebral blood flow parallels the cerebral metabolic oxygen requirement, such that as the cerebral metabolic oxygen requirement increases, so does cerebral blood flow. Given that volatile anesthetics increase cerebral blood flow and decrease cerebral metabolic oxygen requirements, it has been said the volatile anesthetics uncouple these two physiologic characteristics. (95-96)

49. All volatile anesthetics and nitrous oxide depress the amplitude and increase the latency of somatosensory evoked potentials in a dose-dependent manner, and

the somatosensory evoked potentials may be abolished at 1 MAC. Motor evoked potentials become unreliable at concentrations as low as 0.2 to 0.3 MAC. (96)

50. Increasing depth of anesthesia with inhaled volatile anesthetics is characterized by increased amplitude and synchrony of electroencephalogram (EEG) waveforms. Periods of electrical silence begin to occupy a greater proportion of time as depth increases (i.e., burst suppression), predominantly at 1.5 to 2.0 MAC. Sevoflurane and enflurane have been associated with appearance of epileptiform EEG activity at high concentrations, although the clinical implications of these observations are not clear. (96)

51. All the inhaled volatile anesthetics produce mild, dose-related skeletal muscle relaxation (desflurane > sevoflurane and isoflurane), and their administration may be helpful in achieving optimum surgical conditions. Use of inhaled volatile anesthetic will likewise potentiate the effect of neuromuscular blocking drugs. The clinician may minimize or avoid the use of neuromuscular blocking drugs by virtue of the inhaled anesthetic's effects on skeletal muscle tone. At the conclusion of surgery, the presence of inhaled volatile anesthetic will delay the recovery of neuromuscular function when the effects of muscle relaxants are no longer desired. Nitrous oxide does not provide skeletal muscle relaxation. (96)

52. All of the inhaled volatile anesthetics have the potential to trigger malignant hyperthermia in susceptible patients. Studies in animals suggest that this risk may be greater with the use of halothane than with the use of isoflurane, sevoflurane, or desflurane. Nitrous oxide is not a trigger for malignant hyperthermia. (96)

53. All inhaled volatile anesthetics have the potential to cause severe hepatic injury, leading to death or the requirement for liver transplantation. The mechanism for this injury is immunologic, requiring previous exposure to a volatile anesthetic. Trifluoroacetate, produced by metabolism of halothane, isoflurane, and desflurane, binds covalently to hepatocyte proteins and acts as a hapten. Hexafluoroisopropanol, produced by sevoflurane metabolism, does not appear to have the same antigenic behavior as trifluoroacetate. Exposure to halothane may result in a clinically milder form of liver injury characterized by elevation of transaminases, and may be mediated by reductive metabolism and related to conditions where hepatic blood flow is compromised. (96)

Chapter

6 INTRAVENOUS ANESTHETICS

Helge Eilers

1. Name some examples of intravenous anesthetics. What are the potential clinical uses of intravenous anesthetics?

PROPOFOL

2. What type of chemical structure is propofol?
3. What is the mechanism of action of propofol?
4. How is propofol cleared from the plasma?
5. What degree of metabolism does propofol undergo? How should the dose of propofol be altered when administered to patients with liver dysfunction?
6. What is the context-sensitive half-time of propofol relative to other intravenous anesthetics? What is the effect-site equilibration time of propofol relative to other intravenous anesthetics?
7. How does the emergence from a propofol anesthetic or propofol induction differ from the emergence seen with the other induction agents?
8. How does propofol affect the cardiovascular system?
9. How does propofol affect ventilation?
10. How does propofol affect the central nervous system?
11. How does propofol affect the seizure threshold?
12. What is the relationship between propofol and nausea and vomiting?
13. How is propofol administered for sedation?
14. How is propofol administered for maintenance anesthesia?
15. How can the pain associated with the intravenous injection of propofol be attenuated?
16. Why is asepsis important when handling propofol?
17. Which patients may be at risk for a life-threatening allergic reaction to propofol?

FOSPROPOFOL

18. What type of drug is fospropofol?
19. How are the structure, function, and physicochemical properties of fospropofol different from propofol?
20. What are the clinical uses of fospropofol?

BARBITURATES

21. Name some of the barbiturates. From what chemical compound are they derived?
22. What is the mechanism of action of barbiturates?
23. How are barbiturates cleared from the plasma?
24. What degree of metabolism do barbiturates undergo?
25. What is the context-sensitive half-time of barbiturates relative to other intravenous anesthetics? What is the effect-site equilibration time of barbiturates relative to other intravenous anesthetics?

26. How do methohexital and thiopental compare with regard to induction doses, duration of action, and clinical utility?
27. How do barbiturates affect the arterial blood pressure?
28. How do barbiturates affect the heart rate?
29. How do barbiturates affect ventilation?
30. How do barbiturates affect laryngeal and cough reflexes?
31. How do barbiturates affect the central nervous system? How do barbiturates affect an electroencephalogram?
32. How should thiopental be administered and dosed for cerebral protection in patients with persistently elevated intracranial pressures?
33. What are the various routes and methods for the administration of barbiturates in clinical anesthesia practice?
34. What are some potential adverse complications of the injection of thiopental?
35. What is the risk of a life-threatening allergic reaction to barbiturates?

BENZODIAZEPINES

36. Name some of the commonly used benzodiazepines. What are some of the clinical effects and properties of benzodiazepines that make them useful in anesthesia practice?
37. What is the mechanism of action of benzodiazepines?
38. Where are benzodiazepine receptors located?
39. How does midazolam compare with diazepam with regard to its affinity for the benzodiazepine receptor?
40. How does water-soluble midazolam cross the blood-brain barrier to gain access to the central nervous system?
41. What is the effect-site equilibration time of benzodiazepines relative to other intravenous anesthetics? How do the context-sensitive half-times of the benzodiazepines compare?
42. How do benzodiazepines affect the cardiovascular system?
43. How do benzodiazepines affect ventilation?
44. How do benzodiazepines affect the central nervous system?
45. What are some clinical uses of benzodiazepines in anesthesia practice?
46. How do midazolam and diazepam compare with regard to time of onset and degree of amnesia when administered for sedation?
47. What are some advantages and disadvantages of benzodiazepines for use as induction agents?
48. How can the effects of benzodiazepines be reversed?
49. What organic solvent is used to dissolve diazepam into solution? What are some of the effects of this solvent?
50. How common are allergic reactions to benzodiazepines?

KETAMINE

51. What chemical compound is ketamine a derivative of? What is its mechanism of action?
52. How do patients appear clinically after an induction dose of ketamine?
53. What is the mechanism by which the effects of ketamine are terminated?
54. What are the induction doses for intravenous and intramuscular routes of administration of ketamine? What is the time of onset for the effect of ketamine subsequent to its administration?
55. How does ketamine affect the cardiovascular system?
56. How does ketamine affect ventilation?
57. How does ketamine affect skeletal muscle tone? How does this affect the upper airway?
58. How does ketamine affect the central nervous system?
59. What does the emergence delirium associated with ketamine refer to? What is the incidence? How can it be prevented?
60. What are some common clinical uses of ketamine?

61. What can the repeated administration of ketamine lead to? How is it manifest clinically?
62. How common are allergic reactions to ketamine?

ETOMIDATE

63. What type of structure is etomidate? What is its mechanism of action?
64. How is etomidate cleared from the plasma?
65. What degree of metabolism does etomidate undergo?
66. What is the context-sensitive half-time of etomidate relative to other intravenous anesthetics? What is the effect-site equilibration time of etomidate relative to other intravenous anesthetics?
67. How does etomidate affect the cardiovascular system?
68. How does etomidate affect ventilation?
69. How does etomidate affect the central nervous system?
70. How does etomidate affect the seizure threshold?
71. What are the endocrine effects of etomidate?
72. What are some potential negative effects associated with the administration of etomidate?

DEXMEDETOMIDINE

73. What type of structure is dexmedetomidine?
74. What is the mechanism of action for dexmedetomidine?
75. What are some common clinical uses for dexmedetomidine?
76. What are the typical doses for dexmedetomidine when used as infusion in the operating room?
77. How does dexmedetomidine affect the cardiovascular system?
78. How does dexmedetomidine affect the respiratory system?
79. What are the effects of dexmedetomidine on cerebral blood flow?

ANSWERS*

1. Examples of intravenous anesthetics include the barbiturates, benzodiazepines, opioids, etomidate, propofol, ketamine, and dexmedetomidine. These drugs can be used as induction agents or, in combination with other anesthetics, for the maintenance of anesthesia. (100)

PROPOFOL

2. Propofol is a lipid-soluble isopropyl phenol formulated as an emulsion. The current formulation consists of 1% propofol, soybean oil, glycerol, and purified egg phosphatide. (100, Figure 9-1)
3. The mechanism by which propofol exerts its effects is not fully understood, but it appears to be in part via the gamma-aminobutyric acid (GABA) activated chloride ion channel. Evidence suggests that propofol may interact with the GABA receptor and maintain it in an activated state for a prolonged period, thereby resulting in greater inhibitory effects on synaptic transmission. Propofol also inhibits the NMDA subtype of the glutamate receptor, which may contribute to its CNS effects. (101)
4. Propofol is cleared rapidly from the plasma through both redistribution to inactive tissue sites and rapid metabolism by the liver. (100-101)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

5. Propofol is extensively metabolized by the liver to inactive, water-soluble metabolites, which are then excreted in the urine. Less than 1% of propofol administered is excreted unchanged in the urine. The metabolism of propofol is extremely rapid. Patients with liver dysfunction appear to rapidly metabolize propofol as well, lending some proof that extrahepatic sites of metabolism exist. This has been further supported by evidence of metabolism during the anhepatic phase of liver transplantation. (100)

6. The context-sensitive half-time refers to the time required to pass for the concentration of a particular drug to reach 50% of its peak plasma concentration after the discontinuation of its administration as a continuous intravenous infusion for a given duration. The context-sensitive half-time of a drug depends mostly on the drug's lipid solubility and clearance mechanisms. The continuous infusion of propofol rarely results in cumulative drug effects. After the continuous administration of propofol for several days for sedation in the intensive care unit the discontinuation of the infusion resulted in the rapid recovery to consciousness. The lack of cumulative effects of propofol illustrates that the context-sensitive half-time of propofol is short. The effect-site equilibration time refers to the interval of time required between the time that a specific plasma concentration of the drug is achieved and a specific effect of the drug can be measured. The effect-site equilibration time reflects the time necessary for the circulation to deliver the drug to its site of action, such as the brain. The rapid administration of an induction dose of propofol results in unconsciousness in less than 30 seconds, illustrating its rapid effect-site equilibration time. (100-101, Figure 9-3)

7. After the administration of propofol, patients experience a rapid return to consciousness with minimal residual central nervous system effects. Patients who are to undergo brief procedures or outpatient surgical patients may especially benefit from the rapid wake-up associated with propofol anesthesia. Propofol also tends to result in the patient awakening with a general state of well-being and mild euphoria. Patient excitement has also been observed. Hallucinations and sexual fantasies have been reported to have occurred in association with the administration of propofol. (101)

8. The administration of an induction dose of propofol results in a profound decrease in systolic blood pressure greater than any other induction agent. This effect of propofol appears to be primarily due to vasodilation, which is dose dependent. Unlike the barbiturates, the heart rate is usually unchanged with the administration of propofol. Propofol may selectively decrease sympathetic nervous system activity more than parasympathetic nervous system activity. In fact, propofol inhibits the normal baroreceptor reflex such that profound bradycardia and asystole have occurred in healthy adults after its administration. (102)

9. The administration of an induction dose of propofol (1.5 to 2.5 mg/kg) almost always results in apnea through a dose-dependent depression of ventilation in a manner similar to, but more prolonged than, that of thiopental. The apnea that results appears to last for 30 seconds or greater and is followed by a return of ventilation that is characterized by rapid, shallow breathing such that the minute ventilation is significantly decreased for up to 4 minutes. Propofol causes a greater reduction in airway reflexes than any other induction agent, making it a better choice as the sole agent for instrumentation of the airway. (102)

10. The administration of propofol results in decreases in intracranial pressure, cerebral blood flow, and cerebral metabolic oxygen requirements in a dose-dependent manner. In patients with an elevated intracranial pressure, the administration of propofol, however, may be accompanied by undesirable decreases in the cerebral perfusion pressure. (101-102)

11. The effects of propofol on the seizure threshold are controversial. The administration of propofol has resulted in seizures and opisthotonos and has been used to facilitate

the mapping of seizure foci. Propofol has also been used to treat seizures. High doses of propofol can result in burst suppression on the electroencephalogram. Excitatory effects that cause muscle twitching are not uncommon, but do not indicate seizure activity. (102)

12. Propofol appears to have a significant antiemetic effect, given the low incidence of nausea and vomiting in patients who have received a propofol anesthetic. In addition, propofol administered in subhypnotic doses of 10 to 15 mg has successfully treated both postoperative nausea and vomiting and nausea in patients receiving chemotherapy. (102)

13. Propofol may be administered for sedation through a continuous intravenous infusion at a rate of 25 to 75 μg/kg/min. At these doses, propofol will provide sedation and amnesia without hypnosis. Because of the pronounced respiratory depressant effect, propofol, even for sedation, should only be administered by individuals trained in airway management. (102)

14. Propofol may be administered for maintenance anesthesia through a continuous intravenous infusion at a rate of 100 to 200 μg/kg/min. The clinician may use signs of light anesthesia such as hypertension, tachycardia, diaphoresis, or skeletal muscle movement as indicators for the need to increase the infusion rate of propofol. For procedures lasting more than 2 hours, the use of propofol for maintenance anesthesia may not be cost effective. (102)

15. The injection of propofol intravenously can cause pain in awake patients. The pain can be attenuated by using large veins for its administration, or with the prior administration of lidocaine at the injection site. Alternatively, lidocaine may be mixed with the propofol for simultaneous infusion. (102)

16. Asepsis is important when handling propofol because the solvent for propofol, a lipid emulsion containing soybean oil, glycerol, and lecithin, provides for a favorable culture medium for bacterial growth. Ethylenediaminetetraacetic acid, metabisulfate, or benzyl alcohol is added to the propofol formulation in an attempt to suppress bacterial growth. (100)

17. Patients at risk for a life-threatening allergic reaction to propofol are those with a history of atopy or allergy to other drugs that also contain a phenyl nucleus or isopropyl group. Anaphylactoid reactions to the propofol itself and separate from the lipid emulsion have been reported. (100)

FOSPROPOFOL

18. Fospropofol is a water-soluble phosphate ester prodrug of propofol. It is metabolized by alkaline phosphatase in a reaction that produces propofol and also phosphate and formaldehyde, which is then further metabolized. (103, Figure 9-4)

19. Fospropofol is water-soluble and comes in an aqueous, sterile preparation. It can be injected without the need for a lipid emulsion, thereby reducing the risk for contamination. (103)

20. In the United States, fospropofol is currently approved for sedation during monitored anesthesia care. (103)

BARBITURATES

21. Thiopental is the most commonly used barbiturate in the practice of anesthesia. Other barbiturates include pentobarbital, thiamylal, and methohexital. The barbiturate compounds are a derivative of barbituric acid. Structural alterations of two of the carbon atoms of barbituric acid result in the barbiturates used in clinical practice. Historically, the barbiturates had been classified as short-acting or long-acting agents. This method of classification is no longer used because of the erroneous implication that the duration of action is predictable for a given agent. (103, Figure 9-5)

22. The mechanism of action of barbiturates is based on their ability to enhance and mimic the action of the neurotransmitter gamma-aminobutyric acid (GABA) in the central nervous system. GABA is the main inhibitory neurotransmitter in the central nervous system. Barbiturates bind to the GABA receptor and increase the duration of activity of the GABA receptor, such that the chloride ion influx into the cells is prolonged. The chloride ion hyperpolarizes the cell and inhibits postsynaptic neurons. At higher concentrations, the chloride ion channel may be stimulated by the barbiturate alone even in the absence of GABA. (104)

23. Barbiturates are cleared from the plasma primarily through its rapid redistribution to inactive tissue sites after its administration as a bolus. (103-104, Figure 9-6)

24. Barbiturates are eliminated from the body through hepatic metabolism. Less than 1% of the drug is excreted unchanged by the kidneys. (103-104)

25. Barbiturates are most often used for the intravenous induction of general anesthesia. Maximal brain uptake and onset of effect takes place within 30 seconds after the rapid intravenous injection of a barbiturate. Rapid awakening follows the administration of an induction dose of a barbiturate secondary to the rapid redistribution of these drugs. This accounts for the short effect-site equilibration time for these agents. The duration of action of a barbiturate after its intravenous injection is dictated by its redistribution from the plasma to inactive sites. Large or repeated doses of the lipid-soluble barbiturates can result in saturation of the inactive sites. This may lead to the accumulation of a drug and to prolonged effects of the usually short-acting drugs. The context-sensitive half-time of barbiturates is thus prolonged. (103-104, Figure 9-3)

26. The induction dose of methohexital is 1 to 1.5 mg/kg intravenously, whereas the induction dose of thiopental is 3 to 5 mg/kg IV. Methohexital undergoes greater hepatic metabolism than thiopental, resulting in a shorter duration of action and more rapid awakening. Based on the shorter duration of action of methohexital, it is sometimes chosen over thiopental for the induction of anesthesia for patients undergoing outpatient procedures when rapid awakening is desired. An example of a procedure in which methohexital is frequently chosen for the induction of anesthesia is electroconvulsive shock therapy. This is not only due to the short duration of action of methohexital, but also to its epileptogenic property. (105-106)

27. The administration of barbiturates typically results in a decrease in arterial blood pressure by 10 to 20 mm Hg. This decrease in blood pressure primarily results from peripheral vasodilation. The vasodilation that accompanies the administration of barbiturates is due to a combination of depression of the vasomotor center in the medulla and a decrease in sympathetic nervous system outflow from the central nervous system. Exaggerated blood pressure decreases may be seen in patients who are hypertensive, whether or not they are being treated by antihypertensives. The administration of barbiturates should also be undertaken with caution in patients who are dependent on the preload to the heart to maintain cardiac output, as in patients with ischemic heart disease, pericardial tamponade, congestive heart failure, heart block, or hypovolemia. (105)

28. The administration of barbiturates results in an increase in heart rate. This increase in heart rate is thought to be due to a baroreceptor-mediated reflex response to the decrease in blood pressure caused by the administration of the barbiturate. The increase in heart rate may increase myocardial oxygen requirements during a time when significant decreases in blood pressure may decrease coronary artery blood flow as well. Given this, the administration of a barbiturate to patients with ischemic heart disease must be done with extreme caution. Although the administration of barbiturates typically results in an increase in heart rate, the cardiac output may be decreased. This is in part due to the direct myocardial contractile depression that results from the administration of barbiturates. The effect of a decrease in cardiac output by barbiturates is not of such significance that it is frequently seen clinically, however. (105)

29. Barbiturates depress ventilation centrally by depressing the medullary ventilatory centers. This is manifest clinically as a decreased responsiveness to the ventilatory stimulatory effects of carbon dioxide. Depending on the dose administered, the patient will have a slow breathing rate and small tidal volumes to the extent that apnea follows. Typically, after an induction dose of barbiturate transient apnea will result and require controlled ventilation of the lungs. When spontaneous ventilation is resumed, it is again characterized by a slow breathing rate and small tidal volumes. (105)

30. Induction doses of thiopental alone do not reliably depress laryngeal and cough reflexes. Stimulation of the upper airway, as with the placement of an oral airway or an endotracheal tube, can result in laryngospasm or bronchospasm. It is therefore recommended that adequate suppression of these reflexes be obtained before instrumenting the airway. This can be accomplished with increased doses of a barbiturate, by the administration of a neuromuscular blocking drug, or by the addition of another preoperative medicine, such as opioids, to augment the anesthetic effects of thiopental during stimulation of the upper airway. (105)

31. Barbiturates are potent cerebral vasoconstrictors. This results in a decrease in cerebral blood flow, a decrease in cerebral blood volume, a decrease in intracranial pressure, and a decrease in cerebral metabolic oxygen requirements. Barbiturates are also thought to depress the reticular activating system, which is believed to be important in maintaining wakefulness. Thiopental produces a dose-dependent depression of the electroencephalogram. A flat electroencephalogram may be maintained with a continuous infusion of thiopental. Methohexital is the only barbiturate that does not decrease electrical activity on an electroencephalogram. In fact, methohexital activates epileptic foci and is often used intraoperatively to identify epileptic foci during the surgical ablation of these foci. The effects of barbiturates on the central nervous system indicate that barbiturates are useful for patients in whom elevated intracranial pressures are a concern. Examples of patients who may benefit from the administration of a barbiturate as an induction agent or as maintenance anesthesia include patients with intracranial space-occupying lesions or patients who have suffered head trauma. (105)

32. In patients with persistently elevated intracranial pressures, barbiturates may be administered intravenously in high doses to decrease the intracranial pressure. Care must be taken to avoid decreases in mean arterial pressure that would compromise the cerebral perfusion pressure under these conditions. To ascertain the optimal dose of barbiturate administered for these patients, an electroencephalogram can be obtained. The dose of barbiturate can be titrated to a flat-line electroencephalogram. When the electroencephalogram is isoelectric there is no further depression of cerebral metabolism or of cerebral metabolic oxygen requirements with increasing doses of barbiturate. This allows the clinician to administer the dose of barbiturate that provides the maximal benefit with minimal adverse effects. Barbiturates may offer some cerebral protection for patients with regional cerebral ischemia. Patients with global cerebral ischemia, such as from cardiac arrest, are not thought to derive any protection from the administration of barbiturates. (105-106)

33. There are various routes and methods for the administration of barbiturates in clinical anesthesia practice. For instance, the rapid intravenous administration of a bolus of barbiturate is indicated for a rapid sequence induction of anesthesia. The bolus of barbiturate should be immediately followed by the administration of succinylcholine or a nondepolarizing neuromuscular blocking drug to produce skeletal muscle paralysis and facilitate tracheal intubation under these conditions. Alternatively, small doses of intravenous thiopental, in the range of 0.5 to 1 mg/kg, may be administered to adult patients who have difficulty accepting the application of an anesthesia mask and/or the inhalation of a volatile anesthetic. The rectal

administration of the barbiturate methohexital can be used to facilitate the induction of anesthesia in young or uncooperative patients. (106)

34. Potential adverse complications of the injection of thiopental may result from accidental intraarterial, subcutaneous, and even appropriate venous administration of thiopental. The accidental intraarterial injection of barbiturates results in excruciating pain and intense vasoconstriction that can last for hours. It is believed that barbiturate crystal formation in the blood causes the occlusion of distant small diameter arteries and arterioles. There are several treatment modalities for this potential problem, including the intraarterial injection of papaverine and/or lidocaine, sympathetic nervous system blockade by stellate ganglion block of the involved upper extremity, and the administration of heparin to prevent thrombosis. Despite aggressive therapy, gangrene of the extremity often results. The accidental subcutaneous injection of barbiturates results in local tissue irritation. The irritation may proceed to pain, edema, erythema, or even tissue necrosis, depending on the volume and concentration injected. It has been recommended that 5 to 10 ml of 0.5% lidocaine be injected locally when the subcutaneous injection of thiopental occurs in an attempt to dilute the barbiturate. Venous thrombosis has been seen after the intravenous administration of thiopental. It is presumed that the thrombosis results from the deposition of barbiturate crystals in the vein. The crystallization of barbiturates is more likely to occur when the pH of the blood is too low to keep the alkaline barbiturate in solution. (105)

35. Life-threatening allergic reactions to barbiturates are rare. The risk has been estimated to be 1 in 30,000. (105)

BENZODIAZEPINES

36. Benzodiazepines that are commonly used in the perioperative period include midazolam, diazepam, and lorazepam. The most common effects of benzodiazepines are their anxiolytic and sedative effects. When administered at higher doses, benzodiazepines may also produce unconsciousness. Other properties of benzodiazepines include anterograde amnesia, a lack of retrograde amnesia, minimal cardiopulmonary depression, anticonvulsant activity, and relative safety when taken in overdose. Clinical uses of benzodiazepines include their use for preoperative medication, for intravenous sedation, for the intravenous induction of anesthesia, and for the suppression of seizure activity. In addition to the intravenous route of administration, benzodiazepines can be administered via intramuscular, intranasal, and sublingual routes. (106, Figure 9-7)

37. Benzodiazepines exert their effects through their actions on the gamma-aminobutyric acid (GABA) receptor. When GABA receptors are stimulated by the inhibitory neurotransmitter GABA, a chloride ion channel opens, allowing chloride ions to flow into the cell. This results in hyperpolarization of the neuron and a resistance of the neuron to subsequent depolarization. Benzodiazepines enhance the effect of GABA by binding to subunits of the GABA receptor and maintaining the chloride channel open for a longer period of time. (107, Figure 9-8)

38. Benzodiazepine receptors are located primarily on postsynaptic nerve endings in the central nervous system. The greatest density of benzodiazepine receptors is in the cerebral cortex. The distribution of benzodiazepine receptors is consistent with the minimal cardiopulmonary effects of these drugs. (107)

39. Midazolam has almost two times the affinity for benzodiazepine receptors than does diazepam, which is consistent with its greater potency. (107)

40. Midazolam is a hydrophilic drug. When midazolam is exposed to the pH of the blood it undergoes a change in its structure and becomes highly lipid soluble. This change in structure allows it to cross the blood-brain barrier and gain access to the central nervous system. (106-107)

41. Benzodiazepines are highly lipid-soluble drugs. This allows them to gain rapid entrance into the central nervous system by crossing the blood-brain barrier, where they are able to exert their effects. Thus the effect-site equilibration time of benzodiazepines is short, although it is slower than propofol or thiopental. The duration of action of benzodiazepines is dependent on the redistribution of the drug from the brain to inactive tissue sites. A continuous infusion or repeated boluses can result in saturation of the inactive tissue sites and a prolongation of the drug effect, particularly for the benzodiazepines that have active metabolites. For instance, diazepam undergoes hepatic metabolism to active metabolites, whereas midazolam has no active metabolites. The context-sensitive half-times for diazepam and lorazepam are prolonged when compared with that of midazolam. (107)

42. Induction doses of midazolam may lead to decreases in systemic blood pressure that are greater than those seen with the induction dose of diazepam. This effect of midazolam may be particularly pronounced in patients who are hypovolemic. The decrease in systemic blood pressure is believed to be due to decreases in systemic vascular resistance. (67, 107-108)

43. In general, benzodiazepines alone produce dose-dependent ventilatory depressant effects. Transient apnea may occur with the rapid administration of induction doses of midazolam, particularly if an opioid has been used for premedication. (108)

44. Benzodiazepines decrease cerebral blood flow and cerebral metabolic oxygen requirements in a dose-dependent manner, but there is a ceiling to this effect. This makes benzodiazepines safe for use in patients with intracranial space-occupying lesions, although the administration of benzodiazepines to patients with intracerebral pathologic processes may make subsequent neurologic evaluation of the patient difficult secondary to the potentially prolonged effects of these drugs. Benzodiazepines also have anticonvulsant effects that are thought to occur through the enhancement of the inhibitory effects of the neurotransmitter GABA acid in the central nervous system. Benzodiazepines have been shown to increase the seizure threshold or treat seizures due to local anesthetic toxicity, alcohol withdrawal, and epilepsy. The dose of diazepam used to treat seizures is 0.1 mg/kg intravenously. An isoelectric electroencephalogram is not able to be achieved with the administration of benzodiazepines. (107-108)

45. Clinical uses of benzodiazepines in anesthesia practice include preoperative medication, intravenous sedation, the intravenous induction of anesthesia, and the suppression of seizure activity. (109)

46. When administered for sedation, midazolam has a more rapid onset and produces a greater degree of amnesia than diazepam. The slow onset and greater duration of action of lorazepam limits its usefulness as a preoperative medication. All benzodiazepines may have prolonged and more pronounced sedative effects in the elderly. (109)

47. The intravenous induction doses of midazolam and diazepam are 0.1 to 0.2 mg/kg and 0.2 to 0.3 mg/kg, respectively. The time of onset of midazolam is anywhere between 30 and 80 seconds, depending on the dose and premedication. The time of onset of midazolam is more rapid than the time of onset of diazepam, making it the benzodiazepine of choice for the induction of anesthesia. The speed of onset of both these agents can be facilitated by the prior administration of opioids. Benzodiazepines are advantageous over barbiturates for the induction of anesthesia only because of their potentially lesser circulatory effects and greater reliability for the production of amnesia. A disadvantage of benzodiazepines for the induction of anesthesia is their lack of analgesic properties. Additional medicines would need to be administered to blunt the cardiovascular and laryngeal responses to direct laryngoscopy. The major disadvantage of benzodiazepines for the induction of anesthesia is delayed awakening, which limits the usefulness of benzodiazepines for

this purpose. Midazolam is the shortest-acting of the benzodiazepines and therefore the most appropriate choice of benzodiazepine for the induction of anesthesia. Even so, awakening after a single induction dose of midazolam in healthy volunteers takes more than 15 minutes. Diazepam and lorazepam require even greater periods of time before awakening after an induction dose, precluding their use as anesthesia induction agents. (108-109)

48. The effects of benzodiazepines can be reversed by a specific antagonist drug, flumazenil. Flumazenil is a competitive antagonist that binds to the benzodiazepine receptor but has little intrinsic activity. Flumazenil should be titrated to effect by administering 0.2 mg intravenously every 60 seconds up to a total dose of 1 to 3 mg. Flumazenil binds tightly to the benzodiazepine receptor but is cleared rapidly from the plasma. This results in a short duration of action of only about 20 minutes. The short duration of action of flumazenil requires that the patient be closely monitored for resedation after a dose of flumazenil is administered to reverse the effects of a benzodiazepine. Alternatively, an infusion of flumazenil may be started and titrated to the desired effect to maintain a constant plasma level of this reversal agent. (109)

49. Propylene glycol is an organic solvent used to dissolve lipid soluble diazepam into solution. Propylene glycol is likely responsible for the unpredictable absorption of diazepam when administered intramuscularly. It is also responsible for the pain and possible subsequent thrombophlebitis experienced by patients on the intravenous injection of diazepam. (109)

50. Allergic reactions to benzodiazepines are extremely rare. (109)

KETAMINE

51. Ketamine is a derivative of phencyclidine. The administration of ketamine produces unconsciousness and analgesia that is dose related. The exact mechanism by which ketamine exerts its effects is unknown. Ketamine occupies some μ-opioid receptors in the brain and spinal cord, which may partially explain its analgesic effects. Ketamine also binds to the NMDA receptor, which is believed to mediate the general anesthetic actions of ketamine. Other receptors that ketamine interacts with include monoaminergic receptors, muscarinic receptors, and calcium ion channels. Functionally, ketamine is believed to cause selective depression of the projections from the thalamus to the limbic system and cortex. The anesthesia derived from the administration of ketamine has thus been termed a *dissociative anesthesia*. There have not been any drugs isolated that are able to antagonize the effects of ketamine. (109-110, Figure 9-9)

52. After an induction dose of ketamine the patient appears to be in a cataleptic state. The appearance of the patient may be characterized as eyes remaining open with a slow nystagmic gaze; the maintenance of cough, swallow, and corneal reflexes; moderate dilation of the pupils; lacrimation; salivation; and an increase in skeletal muscle tone, with apparently coordinated but purposeless movements of the extremities. Induction doses of ketamine provide an intense analgesia and amnesia in patients despite the patient appearing as if he or she may be awake. (109)

53. The redistribution of highly lipid-soluble ketamine to inactive tissue sites allows for rapid awakening after the administration of a bolus of ketamine. Ketamine undergoes extensive hepatic metabolism to norketamine for its elimination. Norketamine has between 20% and 30% of the potency of ketamine and may contribute to some of the delayed effects of ketamine when administered as a continuous infusion. (110)

54. For the induction of anesthesia, the intravenous dose of ketamine is 1 to 2 mg/kg, whereas the intramuscular dose is 5 to 10 mg/kg. The induction of anesthesia after intravenous administration is achieved within 60 seconds. The induction of anesthesia after intramuscular administration is achieved within 2 to 4 minutes.

Return of consciousness after an intravenous induction dose of ketamine usually requires 10 to 20 minutes, whereas full orientation may take 60 to 90 minutes. Ketamine may also be administered orally or rectally. (110-111)

55. The administration of ketamine results in an increase in systemic blood pressure, pulmonary artery blood pressure, heart rate, and cardiac output. The systemic blood pressure may increase by 20 to 40 mm Hg over the first 5 minutes after induction doses of ketamine are administered. The rise in blood pressure is often sustained for over 10 minutes. The degree of hemodynamic change elicited by the administration of ketamine is not influenced by the dose of ketamine that is administered, but it can be blunted by the prior administration of barbiturates, benzodiazepines, or opioids. These cardiovascular effects of ketamine are most likely mediated centrally through the activation of the sympathetic nervous system and the direct stimulation of sympathetic nervous system outflow. Endogenous norepinephrine release has been found to accompany the administration of ketamine. This property of ketamine may make it useful as an induction agent in hypovolemic patients in whom hemodynamic support is beneficial. Conversely, patients with a history of myocardial ischemia may be adversely affected by the increases in myocardial oxygen demand induced by the administration of ketamine, making ketamine a poor choice for an induction agent in this patient population. Of note, the cardiovascular stimulatory effects of ketamine may not be as pronounced and may even be absent in patients who are catecholamine depleted. In catecholamine-depleted patients, such as the trauma patient, the administration of ketamine may actually lead to myocardial depression and a decrease in systemic blood pressure. (110)

56. The administration of ketamine can result in a transient depression of ventilation, even apnea with large doses, but the resting $Paco_2$ is typically unaltered in these patients. Ketamine relaxes bronchial smooth muscle, resulting in bronchodilation. This effect of ketamine is most likely mediated by its sympathomimetic effects and may make it useful as an induction agent in patients with bronchial asthma. The administration of ketamine also induces an increase in airway secretions. When ketamine is used as an induction agent, the administration of an antisialagogue preoperatively may be useful in decreasing the amount of airway secretions. (110)

57. Ketamine preserves and may even increase skeletal muscle tone. Patients have varying degrees of purposeful skeletal muscle movement and hypertonus after an induction dose of ketamine. The preservation of skeletal muscle tone results in maintenance of a patent upper airway and the preservation of cough and swallow reflexes. Despite this, airway protection by these reflexes against regurgitation or vomiting cannot be assumed. (110)

58. Ketamine has excitatory effects on the central nervous system such that there are increases in cerebral metabolism, cerebral blood flow, intracranial pressure, and cerebral metabolic oxygen requirements associated with its administration. These excitatory effects of ketamine are reflected by the development of theta wave activity on the electroencephalogram when ketamine is administered. Because of the central nervous system excitatory effects of ketamine, it is not recommended as an induction agent in patients with space-occupying intracranial lesions or after head trauma in whom increases in the intracranial pressure can be detrimental. (110)

59. The emergence after the administration of ketamine has been associated with a delirium, often referred to as an emergence delirium. The severity of the emergence delirium varies. The emergence of delirium manifests as vivid dreaming, visual and auditory illusions, and a sense of floating outside the body. These sensations are often associated with confusion, excitement, and fear, and are unpleasant to the patient. The emergence of delirium typically occurs in the first hour after emergence and persists for 1 to 3 hours. The incidence of emergence delirium with ketamine administration has been estimated to be up to 30%, and it is more likely

to occur when ketamine is used as the sole anesthetic agent. The risk of emergence delirium can be decreased with the preoperative or postinduction administration of benzodiazepines. (110)

60. Some common clinical uses of ketamine include its administration for the induction of anesthesia in hypovolemic patients, its intramuscular injection for the induction of anesthesia in children or in developmentally disabled patients who are difficult to manage, and for dressing changes and debridement procedures in burn patients. Small doses of ketamine may be titrated for its analgesic effects. (110-111)

61. The repeated administration of ketamine may result in the development of a tolerance to the analgesic effects of ketamine. Clinically, this would manifest as an increase in the dose of ketamine required with each subsequent anesthetic to provide sufficient analgesic effects. An example in which this situation may arise is in burn patients who are being administered ketamine while undergoing recurrent dressing changes. (110)

62. Allergic reactions to ketamine are uncommon. (110)

ETOMIDATE

63. Etomidate is an imidazole derivative. The mechanism by which etomidate exerts its effects is not completely understood. It appears that etomidate acts in part through agonist effects at the GABA receptor. (111, Figure 9-10)

64. The induction dose of etomidate is 0.3 mg/kg. The administration of etomidate in induction doses results in unconsciousness in less than 30 seconds. The duration of action of etomidate after an induction dose is very short, owing to its rapid clearance from the plasma through redistribution to inactive tissue sites. (111)

65. Etomidate rapidly undergoes nearly complete ester hydrolysis to pharmacologically inactive metabolites by the liver, with less than 3% of the drug being excreted in the urine unchanged. (111)

66. Like thiopental and propofol, etomidate is highly lipid soluble, which allows it to quickly cross the blood-brain barrier to exert its effects. This accounts for the short effect-site equilibration time for these agents. The context-sensitive half-time of etomidate may be prolonged if repeated or continuous doses of the drug result in saturation of the inactive sites. It is less likely than thiopental to accumulate and have prolonged effects, however. (111, Figure 9-3)

67. The administration of etomidate provides cardiovascular stability in that induction doses of etomidate result in minimal changes in heart rate, mean arterial pressure, central venous pressure, stroke volume, or cardiac index. Minimal decreases in blood pressure may result from the administration of etomidate to hypovolemic patients. The cardiovascular stability associated with etomidate sets it apart from the other induction agents and is the basis for its usefulness as an induction agent in patients with limited cardiac reserve. When etomidate is administered to these patients, it is important to realize that it does not have any analgesic effects. Supplemental agents need to be administered in conjunction with etomidate to blunt the stimulatory effects of direct laryngoscopy. (111)

68. The administration of etomidate alone appears to result in less depressant effects on ventilation than propofol or thiopental. The effects of etomidate on ventilation may be augmented when administered in combination with other anesthetics or opioids. (111)

69. The administration of etomidate results in decreases in cerebral blood flow, intracranial pressure, and cerebral metabolic oxygen requirements. Etomidate has similar effects as barbiturates on the electroencephalogram as well, such that etomidate may be titrated to an isoelectric electroencephalogram to maximally decrease cerebral metabolic oxygen requirements. (111)

70. The administration of etomidate has been shown to increase the activity of seizure foci on an electroencephalogram. Etomidate is similar to methohexital in this regard. Its effects can be used intraoperatively to facilitate intraoperative mapping of seizure foci for surgical ablation. (111)

71. The administration of etomidate is associated with the suppression of adrenocortical function. The suppression of adrenocortical function may last for up to 4 to 8 hours after the induction dose of etomidate has been administered. The concern regarding this suppression of adrenocortical function is the potential for the adrenal cortex to be unresponsive to adrenocorticotropic hormone. Should the adrenal cortex be unresponsive to adrenocorticotropic hormone, desirable protective responses against the stresses that accompany the perioperative period may be prevented. No adverse outcomes have been shown to have occurred secondary to short-term adrenocortical suppression associated with the administration of etomidate, however. (111-112, Figure 9-11)

72. Potential negative effects associated with the administration of etomidate include pain during intravenous injection, superficial thrombophlebitis, involuntary myoclonic movements, and an increased incidence of postoperative nausea and vomiting. (111-112)

DEXMEDETOMIDINE

73. Dexmedetomidine, the active S-enantiomer of medetomidine, is an imidazole. It is also a selective α_2-adrenergic agonist. (112)

74. Dexmedetomidine is a highly selective α_2-adrenergic agonist and exerts its effects through activation of α_2 receptors in the central nervous system. The analgesic effects originate at the level of the spinal cord, and its hypnotic effects likely originate through receptor sites in the locus ceruleus. (113)

75. Some common clinical uses for dexmedetomidine include infusion as an adjunct during general anesthesia in the operating room, sedation for procedures, sedation for airway management (i.e., fiber-optic intubation), and sedation of intubated patients in the intensive care unit. (113)

76. When administered during general anesthesia, dexmedetomidine (0.5- to 1-μg/kg loading dose over a period of 10 to 15 minutes, followed by an infusion of 0.2 to 0.7 μg/kg/hr) decreases the dose requirements for inhaled and injected anesthetics. (113)

77. Dexmedetomidine infusion decreases systemic blood pressure by moderate decreases in heart rate and systemic vascular resistance. Bradycardia associated with dexmedetomidine infusion may sometimes require treatment. Severe bradycardia, heart block, and asystole have been described. A bolus injection may produce transient increases in systemic blood pressure and pronounced decreases in heart rate, an effect that is probably mediated through activation of peripheral α_2-adrenergic receptors. (113)

78. Dexmedetomidine has only minor effects on the respiratory system when compared with other intravenous anesthetics. These effects include small decreases in tidal volume without much change in the respiratory rate. The ventilatory response to carbon dioxide is unchanged. Upper airway obstruction as a result of sedation is possible and may be augmented when dexmedetomidine is combined with other sedative-hypnotics. (113)

79. Dexmedetomidine likely leads to a decrease in cerebral blood flow without significant changes in intracranial pressure and cerebral metabolic oxygen requirements. (113)

Chapter

7 OPIOIDS

Siamak Rahman

STRUCTURE ACTIVITY RELATIONSHIPS

1. Name some of the commonly used opioids in anesthesia practice. Which opioids occur naturally and are obtained from the poppy plant?

MECHANISM OF ACTION

2. What is the mechanism of action of opioids?
3. Describe the location, subtypes, and pharmacologic responses of the opioid receptors. What are the primary receptor subtypes for supraspinal and spinal analgesia?
4. What endogenous neurotransmitters normally bind to and activate opioid receptors?

METABOLISM

5. What are the different ways that opioids are metabolized?
6. How are opioids cleared from the plasma? Which opioids have active metabolites?

PHARMACOKINETICS

7. What are the potency, time of onset, and duration of action of opioids dependent on? How rapid is the effect-site equilibration time of morphine relative to the other opioids?
8. What is the latency time to peak effect of opioids (i.e., bolus front-end kinetics) after a bolus injection?
9. How is the time to steady-state concentration after starting a continuous infusion defined and measured? How is remifentanil different from other opioids when used as a continuous infusion?
10. What is context-sensitive half-time (CSHT)? What are some clinical implications of the CSHT?

PHARMACODYNAMICS

THERAPEUTIC EFFECTS

11. What are some therapeutic effects of opioids?

ADVERSE EFFECTS

12. What are the effects of opioids on the cardiovascular system?
13. What are the effects of opioids on ventilation?
14. What are the effects of opioids on the central nervous system?

15. What are the effects of opioids on the thoracoabdominal muscles? How can they be treated?
16. What are the effects of opioids on the gastrointestinal system?
17. What are the effects of opioids on the genitourinary system?
18. What is the mechanism by which opioids are thought to cause nausea and vomiting?
19. How do opioids modulate immune function?

DRUG INTERACTIONS

20. What is an example of a pharmacokinetic drug interaction of opioids?
21. What is an example of a pharmacodynamic drug interaction of opioids?

SPECIAL POPULATIONS

22. What are some considerations of using opioids in patients with hepatic failure?
23. What are some considerations of using opioids in patients with kidney failure?
24. Does gender have an influence on opioid pharmacology?
25. Does age have an influence on opioid pharmacology?
26. How should opioids be dosed in obese patients?

UNIQUE FEATURES OF INDIVIDUAL OPIOIDS

27. How does the onset time of morphine compare with the other opioids? What are some potential drawbacks of the administration of morphine?
28. How does fentanyl compare with morphine with regard to its effect-site equilibration time? What is the potency of fentanyl relative to morphine?
29. What are some routes for the administration of fentanyl?
30. How are the effects of fentanyl terminated? How does the context-sensitive half-time of fentanyl compare with other opioids?
31. What are some systemic clinical effects associated with the administration of fentanyl?
32. What are some clinical uses of fentanyl in anesthesia practice?
33. How does sufentanil compare with the other opioids with respect to its effect-site equilibration time and its context-sensitive half-time?
34. What is the potency of sufentanil relative to morphine?
35. What are some systemic clinical effects associated with the administration of sufentanil?
36. How does alfentanil compare with the other opioids with respect to its effect-site equilibration time and its context-sensitive half-time?
37. What are some clinical uses of alfentanil?
38. How does remifentanil compare with the other opioids with respect to its effect-site equilibration time and its context-sensitive half-time?
39. What is the potency of remifentanil relative to morphine?
40. What are some clinical uses of remifentanil?

CLINICAL APPLICATION

COMMON CLINICAL INDICATIONS

41. What are some common clinical indications for the use of opioids?

RATIONAL DRUG SELECTION AND ADMINISTRATION

42. What is the basis of opioid selection in different situations?

ANSWERS*

STRUCTURE ACTIVITY RELATIONSHIPS

1. Opioids that are commonly used in anesthesia practice include morphine, meperidine, fentanyl, sufentanil, alfentanil, and remifentanil. The only clinically significant opioids that occur naturally and are derived from the poppy plant are papaverine, codeine, and morphine. Papaverine lacks any opioid activity. Morphine is considered the prototype opioid with which all other opioids are compared. (115, Figure 10-1)

MECHANISM OF ACTION

2. Opioids exert their effects through their agonist actions at the opioid receptors. Opioids bind to the opioid receptors in the ionized state. After an opioid binds to a receptor, there are at least two mechanisms by which opioids alter the activity of the cell. The main action of opioids appears to be through the interaction with G-proteins, resulting in inhibition of the activity of adenylate cyclase and increasing potassium conductance. This ultimately results in hyperpolarization of the cell and leads to a suppression of synaptic transmission. The second mechanism by which opioids may produce their effect is through the interference of calcium ion intracellular transport in the presynaptic cells. This results in interference with the release of neurotransmitters from the presynaptic cell and again suppresses synaptic transmission. Neurotransmitters that are affected by this mechanism of action of opioids include acetylcholine, dopamine, norepinephrine, and substance P. (116, Figure 10-2)

3. Opioid receptors are located in various tissues throughout the central nervous system and exert their therapeutic effects at multiple sites. They inhibit the release of substance P from primary sensory neurons in the dorsal horn of the spinal cord, mitigating the transfer of painful sensations to the brain (spinal analgesia). Opioid actions in the brainstem modulate nociceptive transmission in the dorsal horn of the spinal cord through descending inhibitory pathways. Opioids probably change the affective response to pain through actions in the forebrain (supraspinal analgesia). Three classical opioid receptors have been identified: μ, κ, and δ. More recently, a fourth opioid receptor, ORL1 (also known as NOP), has also been identified, but its function is quite different from that of the classical opioid receptors. Although the existence of opioid receptor subtypes (e.g., μ_1, μ_2, etc.) has been proposed, it is not clear from molecular biology techniques that distinct genes code for them. The responses evoked by opioid agonists at the μ receptor include spinal and supraspinal analgesia, ventilatory depression, gastrointestinal effects (nausea, vomiting, and ileus), and sedation. The responses evoked by agonists at the delta receptor include the modulation of the μ receptor. The responses evoked by agonists at the κ receptor were almost the same as the μ receptor but lacked any ventilatory depression effect. (116-117, Table 10-2)

4. Endorphins and enkephalins are endogenous neurotransmitters that normally bind to and activate opioid receptors. (Table 10-2)

METABOLISM

5. Opioids are transformed and excreted by different metabolic pathways. Codeine is a prodrug and its metabolite, morphine, is the active compound. Codeine is partly metabolized by *O*-demethylation into morphine, a metabolic process mediated by the liver microsomal isoform CYP2D6. Genetic variation in the metabolic pathway of codeine can drastically alter its clinical effects. Patients who lack CYP2D6 because of deletions, frame shift, or splice mutations (i.e., approximately 10% of the white population) or whose CYP2D6 is inhibited (e.g., patients taking quinidine) do not benefit from codeine even though they exhibit a normal response to morphine.

   Morphine is metabolized by hepatic conjugation and subsequent excretion by the kidney. Morphine has a high hepatic extraction ratio (first pass effect), when

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

administered orally, which decreases its effect significantly than when injected intravenously. The hepatic first pass effect of orally administered morphine also results in high morphine-6-glucuronide levels.

Alfentanil, fentanyl, and sufentanil are also metabolized by liver microsomal enzymes. Liver metabolism is unpredictable for alfentanil, and less so for fentanyl and sufentanil. The primary enzyme responsible for alfentanil biotransformation, CYP3A4, has significant individual variability. Remifentanil is a very short-acting drug because of de-esterification (i.e., ester hydrolysis) by nonspecific plasma and tissue esterases to an inactive metabolite. (118, 124, 125, Figure 10-10)

6. Opioids are cleared principally by hepatic metabolism. Morphine is the only opioid that possesses an active metabolite. About 10% of the metabolism of morphine is to the active metabolite morphine-6-glucuronide. Morphine-6-glucuronide has analgesic and ventilatory depressant effects and is eliminated by renal excretion. It is more potent at the μ receptor than morphine and has a similar duration of action. Care must be taken when administering morphine to patients with renal failure because the elimination of the active metabolite of morphine may be prolonged. Morphine's principal metabolite, morphine-3-glucuronide, is inactive. (124)

PHARMACOKINETICS

7. The potency of an opioid is related to its affinity for the opioid receptor. The time of onset, or effect-site equilibration time, and duration of action of an opioid are related to its lipid solubility and degree of ionization at physiologic pH. A greater lipid solubility and greater nonionization allow for quicker crossing of the blood-brain barrier, quicker access to the central nervous system to exert its effects, and quicker redistribution to inactive tissue sites. For example, morphine has relatively low lipid solubility and is only 10% to 20% nonionized at physiologic pH, accounting for its relatively prolonged effect-site equilibration time. (118, Figure 10-3)

8. The latency time to peak effect (bolus front-end kinetics) of common intravenous opioids (morphine, fentanyl, sufentanil, alfentanil, and remifentanil) after administering a bolus is influenced by the opioid's ionization and lipid solubility. Opioids that are un-ionized and unbound, and have high lipid solubility rapidly equilibrate to the effect site. The time on peak effect is also influenced by the amount of drug administered in the initial bolus. The offset of effect after bolus injection is also called bolus back-end kinetics. (118-119)

9. The time required to reach steady state after starting an opioid infusion is defined as the time required to achieve steady-state effect-site concentrations (i.e., infusion front-end kinetics). It is important to understand the clinical relevance of administering a continuous opioid infusion. First, the time required to approach steady-state effect-site concentrations can be very long, often longer than a surgical procedure. To achieve final steady-state concentrations more rapidly, a bolus can be administered before the infusion is started. Additionally, opioid concentrations will increase slowly for many hours after an infusion is started and continued at a constant infusion rate. Because remifentanil rapidly equilibrates to the effect site, it is an exception to this general rule. For this reason, remifentanil is often chosen for total intravenous anesthesia (TIVA). (118)

10. The context-sensitive half-time (CSHT) is defined as the time required for a 50% decrease in drug concentration after stopping a steady-state infusion. The CSHT predicts the termination of drug effect or "infusion back-end" kinetics. It has many clinical utilities. First, for most drugs, the CSHT changes with the length of the infusion time that it has been infused. After a short duration of infusion, the predicted back-end kinetics for the various drugs do not differ much (remifentanil is an exception). But if the duration of infusion is increased, the CSHTs will vary for the different opioids. Second, clinically shorter- or longer-acting drugs should be chosen depending on the duration of opioid effect acceptable after discontinuing it. Finally, the shapes of these curves are not the same if a different degree of concentration decline (20% or an 80% decrease) is required. (118-119)

PHARMACODYNAMICS

THERAPEUTIC EFFECTS

11. Opioids appear to be highly effective for the relief of pain that arises from the viscera, skeletal muscles, and joints, by acting at spinal and brain μ receptors. Other clinical effects of morphine include euphoria, sedation, and altered mentation. Opioids also suppress the cough reflex via the cough centers in the medulla. (120)

ADVERSE EFFECTS

12. There are several mechanisms by which the administration of opioids may result in hypotension. These include histamine release, centrally mediated decreases in sympathetic tone, vagal-induced bradycardia, and direct and indirect venous and arterial vasodilation. For example, morphine may result in hypotension primarily due to histamine release or through centrally mediated decreases in sympathetic tone. The release of histamine is most likely to accompany the administration of morphine when high doses of morphine are administered rapidly. The effects of morphine on blood pressure may manifest clinically only as orthostatic hypotension in the supine, normovolemic patient. The hypotension associated with the administration of morphine may also occur due to vagal stimulation. Hypertension may accompany the administration of opioids secondary to inadequate dosing of the opioid or to the ill-timed administration of the opioid relative to the stimulus inducing the increase in blood pressure. (121, Figure 10-4)

13. All the μ receptor agonist opioids produce a dose-dependent depression of ventilation. This is reflected by an increase in the resting $Paco_2$, an increase in the apneic threshold, a decrease in the responsiveness to the ventilatory stimulant effects of carbon dioxide, and a decrease in the hypoxic ventilatory drive. The administration of opioids also affects the rate of breathing and the tidal volume. The respiratory rate is typically slowed and insufficiently compensated by an increase in the tidal volume. Consequently, the minute ventilation is decreased. The mechanism by which these effects of opioids on ventilation occur is thought to be through the direct depression of the medullary ventilatory centers. (120-121)

14. The administration of opioids results in several central nervous system effects. Opioids are unable to produce a dose-related general depression of the central nervous system typical of other general anesthetics. Instead, opioids have a ceiling effect that is not overcome by increasing the administered dose of opioids. Opioids do contribute to the MAC of anesthesia delivered and decrease the amount of volatile agent required to achieve a given anesthetic depth. Opioids are not considered to be true anesthetics, however, because of their inability to reliably produce unconsciousness even in high doses. Finally, the administration of opioids causes miosis through its cortical inhibition of the Edinger-Westphal nucleus. (122)

15. The administration of opioids can result in increased thoracoabdominal muscle tone, which may result in chest wall stiffness. This "stiff-chest" syndrome can interfere with ventilation. Although the exact mechanism for this muscle rigidity is not known, it appears to occur most frequently when rapid, large boluses of fentanyl congeners are initially administered. Termination of the rigidity to allow for ventilation can be accomplished through the administration of a neuromuscular blocking drug or an opioid antagonist such as naloxone. Prophylaxis against this muscle rigidity can be achieved through the administration of a priming dose of a nondepolarizing neuromuscular blocking drug and the slow, intermittent administration of opioid. (121)

16. Among the several effects opioids have on the gastrointestinal system are effects on gastrointestinal motility, gastric emptying, and biliary smooth muscle tone. Opioids increase tone and decrease propulsive motility in both the small and large

intestines. Opioids also increase the gastric emptying time through both central and peripheral effects of the opioid. Centrally, this effect is mediated by the vagus nerve. Peripherally, binding of an opioid to the opioid receptors in the myenteric plexus and cholinergic nerve terminals inhibits the release of acetylcholine at these nerve terminals. Opioids also increase pyloric sphincter tone, further contributing to a delay in gastric emptying. Opioids can cause spasm of biliary smooth muscle, increasing biliary duct pressure. Opioids also increase the tone of the sphincter of Oddi. In patients receiving intraoperative cholangiograms, approximately 3% of patients who have been administered opioids have opioid-induced spasm of the sphincter of Oddi. Together these can result in an increase in intrabiliary pressure that may manifest as biliary colic or mimic angina pectoris in the awake patient. The clinician can distinguish between opioid-induced biliary colic pain and myocardial ischemia through the administration of naloxone. Naloxone can relieve the pain of biliary colic, but it has no effect on the pain caused by myocardial ischemia. Glucagon also reverses biliary spasm due to opioids. Nitroglycerin has resulted in pain relief in both circumstances, making diagnosis difficult. (121-122)

17. Opioids can decrease bladder detrusor tone and increase the tone of the urinary sphincter. This may lead to urinary retention in some patients, particularly in males, when the opioid is administered intrathecally or epidurally. When this occurs there may be the need to catheterize the patient's bladder to drain it. These effects are in part centrally mediated, although peripheral effects are also likely given the widespread presence of opioid receptors in the genitourinary tract. (122)

18. There are several mechanisms by which opioids are thought to cause nausea and vomiting. The primary mechanism appears to be through the direct stimulation of the chemoreceptor trigger zone in the area postrema on the floor of the fourth ventricle in the brain. In addition to this, opioids also increase gastrointestinal secretions, decrease gastrointestinal tract motility, and prolong gastric emptying time. (121)

19. Both administered and endogenous (e.g., endorphins) opioids depress cellular immunity. For example, opioids have been shown to inhibit the transcription of interleukin-2 in activated T cells. The different opioids may differ in the mechanism and extent of their immunomodulatory effects. Some possible adverse outcomes due to the impairment of cellular immunity may include impaired wound healing, perioperative infections, and cancer recurrence. These effects are not completely understood. (122)

DRUG INTERACTIONS

20. A pharmacokinetic drug interaction is one in which the administration of a drug influences the concentration of another administered drug. An example of this occurs when opioids are administered concurrent with a continuous propofol infusion. Opioid concentrations may be higher when administered with a continuous propofol infusion than they are when the same dose is administered alone. This may be due in part to the hemodynamic changes induced by propofol. (122)

21. A pharmacodynamic drug interaction is one in which the administration of a drug influences the effect of another administered drug. The most common and most important pharmacodynamic drug interaction of opioids is its synergistic effect when administered with sedatives. Opioids also synergistically reduce the minimum alveolar concentration (MAC) when administered with volatile anesthetics. The reduction in the MAC of anesthesia can be substantial, by up to 75% or more. (122)

SPECIAL POPULATIONS

22. With the exception of remifentanil, the liver is the organ primarily responsible for the metabolism of opioids. The anhepatic phase of orthotopic liver transplantation is the only situation in which opioid concentrations may accumulate. Other than that, liver failure is usually not severe enough to have a

major impact on opioid concentrations. Clinically, patients with severe liver disease, such as those with hepatic encephalopathy, may be more sensitive to the sedative effects of opioids. (122-123)

23. Kidney failure may have clinical effects on opioid administration, depending on the opioid. Kidney failure has major clinical relevance when administering morphine and meperidine. Two metabolites of morphine, morphine-3-glucuronide and morphine-6-glucuronide (M3G and M6G), are excreted via the kidney. Indeed, nearly half of morphine conversion to M3G and M6G also happens in the kidney. M3G is inactive, but M6G is an analgesic whose potency approaches that of morphine. Life-threatening respiratory depression can develop in patients with renal failure administered morphine due to very high levels of M6G.

    Normeperidine is the main metabolite of meperidine and is excreted through the kidney. Normeperidine has analgesic and excitatory central nervous system effects. Increasing levels of CNS toxicity of normeperidine include anxiety, tremulousness, myoclonus, and frank seizures. Therefore, normeperidine accumulation is of particular concern in patients with renal failure. For most other opioids, kidney failure has minimal clinical importance. Remifentanil, which is metabolized through ester hydrolysis, is not affected by kidney disease. (123, Figure 10-7).

24. Gender may have an influence on opioid pharmacology. Morphine is more potent in women, but has a slower onset of action. (123)

25. Age has an important influence on opioid pharmacology. For example, fentanyl is more potent in the older patient. Pharmacokinetic changes, decreases in clearance and central distribution volume in older patients, play a lesser role. Pharmacodynamic differences are primarily responsible for the decreased dose requirement in older patients (>65 years of age). Doses of opioids, including remifentanil, should be decreased by at least 50% or more in elderly patients. (123, Figure 10-8)

26. The clearance of opioids appears to be more closely related to lean body mass, such that obese patients do not require as high a dose as would be suggested by their total body weight. For this reason lean body mass should be used to calculate the dose of opioid administered. Pharmacokinetic simulations used to calculate the remifentanil dosage based on total body weight (TBW) or lean body mass (LBM) in obese and lean patients showed dramatically higher concentrations of opioids when TBW was used in obese patients. (124, Figure 10-9)

UNIQUE FEATURES OF INDIVIDUAL OPIOIDS

27. Morphine is the opioid with which other opioids are compared. The onset time of morphine is slower than the other opioids given its high degree of ionization and its low lipid solubility. Some potential drawbacks of the administration of morphine include its active metabolite, the histamine release it causes, and the potential for "stacking" of subsequent doses in patients in pain due to its slow onset time. (124-125)

28. Fentanyl administered intravenously has a more rapid onset and shorter duration of action than morphine. This reflects its greater lipid solubility. The effect-site equilibration time of fentanyl is about 6.5 minutes. Its shorter duration of action is also reflective of its rapid redistribution to inactive tissue sites, leading to a rapid decrease in the plasma concentration of fentanyl. Fentanyl is 75 to 125 times more potent than morphine. (Figure 10-3)

29. Fentanyl can be administered numerous ways. In addition to the intravenous route, transdermal, transmucosal, transnasal, and transpulmonary routes are all effective routes for the administration of fentanyl. The oral transmucosal delivery of fentanyl citrate results in a faster achievement of higher peak levels than when the same dose is swallowed. (125)

30. The effects of fentanyl are terminated through its redistribution to inactive tissue sites followed by its metabolism by the liver. High intravenous doses of fentanyl or a continuous intravenous infusion can lead to saturation of the inactive tissue sites. This may result in prolonged redistribution, prolonged elimination, and prolonged pharmacologic effects of the drug. The cumulative drug effects during continuous intravenous infusions of fentanyl, sufentanil, alfentanil, and remifentanil have been compared. Alfentanil and remifentanil do not seem to produce clinically significant cumulative drug effects, and awakening appears to be prompt with minimal lingering side effects when compared with fentanyl. (118, Figure 10-3)

31. The administration of fentanyl is associated with a decrease in heart rate. The administration of fentanyl alone leads to little change in systemic blood pressure, whereas its administration after a benzodiazepine may lead to decreases in blood pressure. There are also synergistic effects between fentanyl and benzodiazepines on ventilatory depression and sedation. (121-122)

32. Clinical uses of fentanyl in anesthesia practice include perioperative analgesia, the induction and maintenance of anesthesia, the inhibition of the sympathetic nervous system response to direct laryngoscopy or surgical stimulation, and preemptive analgesia. Opioids are most commonly used during the maintenance of anesthesia as a supplement to inhaled anesthetics. Opioids used in this manner are often administered in small intravenous boluses or as a continuous infusion. High doses of a narcotic, especially fentanyl or sufentanil, may be used as the sole anesthetic agent in patients who are unable to tolerate any effects of cardiac depression that inhaled anesthetics may produce. A disadvantage of an opioid-based anesthetic is the potential for patient awareness. (126)

33. Sufentanil has an effect-site equilibration time similar to fentanyl. Its context-sensitive half-time is less than that of alfentanil for infusions lasting less than 8 hours, but it is greater than that of remifentanil. (Figure 10-3)

34. Sufentanil is 500 to 1000 times more potent than morphine. It is the most potent opioid currently in use in anesthesia practice. (125)

35. Systemic clinical effects associated with the administration of sufentanil include depression of ventilation and bradycardia that appears to be greater than that produced by fentanyl. Sufentanil in large doses may result in thoracoabdominal muscle rigidity as well. (121)

36. Alfentanil has an effect-site equilibration time that is shorter than that of fentanyl and sufentanil, about 1.4 minutes. This is a result of its low pKa, which allows for about 90% of the drug to be nonionized and lipid soluble at physiologic pH. The context-sensitive half-time of alfentanil varies by as much as 10 times among individuals. This is believed to be due to individual variations in its metabolism. Even so, the context-sensitive half-time of alfentanil is considered to be short when compared with other opioids. (Figure 10-3, Table 10-1)

37. The rapid, short-acting effect of alfentanil makes it useful for situations in which the response to a single, brief, intense, noxious stimulus requires blunting. Examples include the response to direct laryngoscopy and endotracheal intubation, or the performance of a retrobulbar block. (126)

38. Remifentanil has an effect-site equilibration time of about 1.4 minutes, which is shorter than that of fentanyl and sufentanil, and about equal to that of alfentanil. The context-sensitive half-time of remifentanil is much shorter than that of the other opioids, approximately 4 minutes. It is also independent of the duration of the continuous infusion, which is unique to remifentanil among the opioids. The basis for this is its structure, which has an ester link. The ester link allows for hydrolysis in the plasma to inactive metabolites. This accounts for its rapid titratability, noncumulative effects, and rapid recovery. (Figure 10-3, 125)

39. Remifentanil is 250 times more potent than morphine. (125)

40. Like alfentanil, the unique pharmacokinetic profile of remifentanil makes it desirable in cases where the response to a brief, intense stimulus requires blunting. It can also be used as maintenance anesthesia when rapid recovery might be desired, as during an intraoperative wake-up test for the evaluation of motor nerve integrity during spine surgery. Likewise, a remifentanil infusion is commonly administered along with propofol for total intravenous anesthesia. When remifentanil is used as maintenance anesthesia, a longer-acting opioid may need to be administered before patient arousal for analgesia. (125-126)

CLINICAL APPLICATION

COMMON CLINICAL INDICATIONS

41. Opioids have been used in different areas of anesthesia. Their main and oldest indication is postoperative analgesia. To increase the safety of opioid use for postoperative pain control they can be delivered by a patient-controlled analgesia (PCA) machine. They can be combined with other drugs and techniques to decrease pain as well. Another common indication of opioid use is for "balanced anesthesia." With this technique, the opioids are primarily used for their ability to decrease MAC, thereby avoiding the direct myocardial depression and other untoward hemodynamic effects of the volatile anesthetics. Cardioprotection against ischemia (preconditioning) is another possible beneficial indication of opioids. Total intravenous anesthesia (TIVA) can be achieved when opioids are administered in combination with propofol infusions. This is another recent indication of opioids during anesthesia that may result in postoperative euphoria and less nausea and vomiting. (126)

RATIONAL DRUG SELECTION AND ADMINISTRATION

42. Pharmacokinetic differences between opioids are the main consideration in selecting them for appropriate purpose. All μ agonists are equally efficacious when given in equipotent doses. Among key elements when selecting an opioid for administration is the desired time of onset, the duration of effect, and potential side effects. Side effects for consideration include sedation and respiratory depression. (126-127)

Chapter

8 LOCAL ANESTHETICS

Ken Drasner

HISTORY

1. What was the first local anesthetic introduced into clinical practice? What was its clinical use?

STRUCTURE ACTIVITY RELATIONSHIPS

2. What is the basic structure of local anesthetics?
3. Why are local anesthetics marketed as hydrochloride salts?
4. What are two differences between ester and amide local anesthetics that make classifying local anesthetics important?
5. Name four ester local anesthetics.
6. Name seven amide local anesthetics.
7. What is an easy way to remember whether a local anesthetic is an ester or an amine?

MECHANISM OF ACTION

8. What is the mechanism of action of local anesthetics?
9. Where is the major site of local anesthetic effect?
10. How is the effect of a local anesthetic on the nerve terminated?
11. How is the resting membrane potential and the threshold potential altered in nerves that have been infiltrated by local anesthetic?
12. What is the temporal progression of the interruption of the transmission of neural impulses between the autonomic nervous system, motor system, and sensory system after the infiltration of a mixed nerve with local anesthetic?
13. What is frequency-dependent blockade? How does frequency-dependent blockade relate to the activity of local anesthetics?

CLASSIFICATION OF NERVES AND SENSITIVITY TO LOCAL ANESTHETICS

14. What three characteristics are nerve fibers classified by? What are the three main nerve fiber types?
15. Which types of nerve fibers are myelinated? What is the function of myelin and how does it affect the action of local anesthetics?
16. How many consecutive nodes of Ranvier must be blocked for the effective blockade of the nerve impulse by local anesthetic?
17. Which two nerve fiber types primarily function to conduct sharp and dull pain impulses? Which of these two nerve fibers is more readily blocked by local anesthetic?
18. Which two nerve fiber types primarily function to conduct impulses that result in large motor and small motor activity?
19. What is meant by differential block? Name an anesthetic that has had limited use because of its poor sensory selectivity.
20. How do local anesthetics diffuse through nerve fibers when deposited around a nerve? Which nerve fibers are blocked first as a result?

SPREAD OF ANESTHESIA AND PERIPHERAL NERVE BLOCKADE

21. How are the nerve fibers arranged from the mantle to the core in a peripheral nerve with respect to the innervation of proximal and distal structures? How does this correlate with the temporal progression of local anesthetic-induced blockade of proximal and distal structures?
22. What very fundamental difference exists between the local anesthetics and most systemically administered drugs?

PHARMACOKINETICS

23. Is the pKa of local anesthetics more than or less than 7.4?
24. At physiologic pH, does most local anesthetic exist in the ionized or nonionized form? What form must the local anesthetic be in to cross nerve cell membranes?
25. Does local tissue acidosis create an environment for higher or lower quality local anesthesia? Why?
26. What is the primary determinant of local anesthetic potency?
27. After a local anesthetic has been absorbed from the tissues, what are the primary determinants of local anesthetic peak plasma concentrations?
28. How are ester local anesthetics cleared?
29. How are the amide local anesthetics metabolized?
30. What percent of local anesthetic undergoes renal excretion unchanged?
31. What are two organs that influence the potential for local anesthetic systemic toxicity?
32. What accounts for chloroprocaine's relatively low systemic toxicity?
33. Patients with atypical plasma cholinesterase are at an increased risk for what complication with regard to local anesthetics?
34. What disease states may influence the rate of clearance of lidocaine from the plasma?
35. How extensive is renal excretion of the parent local anesthetic compound?
36. How does the addition of epinephrine or phenylephrine to a local anesthetic solution prepared for injection affect its systemic absorption?
37. How does the addition of epinephrine or phenylephrine to a local anesthetic solution prepared for injection affect its duration of action?
38. How does the addition of epinephrine or phenylephrine to a local anesthetic solution prepared for injection affect its potential for systemic toxicity?
39. How does the addition of epinephrine or phenylephrine to a local anesthetic solution prepared for injection affect the rate of onset of anesthesia?
40. How does the addition of epinephrine or phenylephrine to a local anesthetic solution prepared for injection affect local bleeding?
41. What are some potential negative effects of the addition of epinephrine to a local anesthetic solution prepared for injection?
42. Name some situations in which the addition of epinephrine to a local anesthetic solution prepared for injection may not be recommended.

SIDE EFFECTS

43. What are some potential negative side effects associated with the administration of local anesthetics?
44. What is the most common cause of local anesthetic systemic toxicity?
45. What are the factors that influence the magnitude of the systemic absorption of local anesthetic from the tissue injection site?
46. From highest to lowest, what is the relative order of peak plasma concentrations of local anesthetic associated with the following regional anesthetic procedures: brachial plexus, caudal, intercostal, epidural, sciatic/femoral?
47. Which two organ systems are most likely to be affected by excessive plasma concentrations of local anesthetic?
48. What are the initial and subsequent manifestations of central nervous system toxicity due to increasingly excessive plasma concentrations of local anesthetic?
49. What is a possible pathophysiologic mechanism for seizures that result from excessive plasma concentrations of local anesthetic?
50. What are some potential adverse effects of local anesthetic-induced seizures?
51. How should local anesthetic-induced seizures be treated?

52. What is the indication for and disadvantage of the administration of neuromuscular blocking drugs for the treatment of seizures?
53. Is the cardiovascular system more or less susceptible to local anesthetic toxicity than the central nervous system?
54. What are two mechanisms by which local anesthetics produce hypotension?
55. What is the mechanism by which local anesthetics exert their cardiotoxic effects? How is this manifested on the electrocardiogram?
56. How is the relative cardiotoxicity between local anesthetic agents compared? What is the relative cardiotoxicity between lidocaine, bupivacaine, and ropivacaine?
57. How does bupivacaine differ from lidocaine with respect to their cardiotoxic effects, and what underlying electrophysiologic differences exist between lidocaine and bupivacaine that might contribute to their differing clinical toxicities?
58. What is the maximum recommended concentration of bupivacaine to be administered for obstetric epidural anesthesia? Why?
59. What relatively simple and apparently effective therapy for treatment of systemic local anesthetic toxicity has been recently introduced into clinical practice? What appears to be its predominant mechanism of action?
60. The administration of which local anesthetics have been associated with methemoglobinemia? What is the mechanism by which this occurs? How can it be treated?
61. What is the nature of the neurotoxicity that has been reported in association with the use of chloroprocaine? What is the mechanism by which this occurs?
62. What is TNS?
63. What is the mechanism by which local anesthetics have resulted in cauda equina syndrome?
64. What changes have been recommended with respect to the dose of lidocaine used for spinal anesthesia?
65. What changes in practice have occurred with respect to the relative use of lidocaine for spinal anesthesia?
66. What is the allergenic potential of local anesthetics? What are the potential causes of an allergic reaction associated with administration of local anesthetics?
67. Does cross-sensitivity exist between the classes of local anesthetics?

CLINICAL USES

68. What is the principal use of tetracaine in current clinical practice?
69. What other local anesthetics might be used in place of lidocaine for short-duration or outpatient surgery?
70. What is an enantiomer?
71. What two marketed local anesthetics are chiral compounds?
72. What is eutectic mixture of local anesthetics (EMLA)?

ANSWERS*

HISTORY

1. The first local anesthetic introduced into clinical practice was cocaine. Cocaine's use has been limited by its systemic toxicity, its irritant properties when placed topically or near nerves, and its substantial potential for physical and psychological dependence. (130)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

STRUCTURE ACTIVITY RELATIONSHIPS

2. Local anesthetics consist of a lipophilic end and a hydrophilic end connected by a hydrocarbon chain. The lipophilic end is an aromatic ring, and the hydrophilic end is a tertiary amine and proton acceptor. The bond that links the hydrocarbon chain to the lipophilic end of the structure is either an ester (—CO—) or an amide (—HNC—). The local anesthetic is thus classified as either an ester or an amide local anesthetic. (131, Figure 11-2)
3. Local anesthetics are bases that are poorly water-soluble. For this reason they are marketed as hydrochloride salts. The resulting solution is generally slightly acidic with a pH of about 6. (133)
4. The metabolism and possibly the potential to produce allergic reactions differ between ester and amide local anesthetics, making this classification of local anesthetics important. (131)
5. The ester local anesthetics include procaine, chloroprocaine, cocaine, and tetracaine. (132, Figure 11-3)
6. The amide local anesthetics include lidocaine, mepivacaine, bupivacaine, levobupivacaine, etidocaine, prilocaine, and ropivacaine. (132, Figure 11-3)
7. As a general rule, ester local anesthetics will have only one "i" in their generic name, while the amides will have two. (132, Figure 11-3)

MECHANISM OF ACTION

8. Local anesthetics act by producing a conduction blockade of neural impulses in the affected nerve. This is accomplished through the prevention of the passage of sodium ions through ion-selective sodium channels in the nerve membranes. The inability of sodium ions to pass through their ion selective channels results in slowing of the rate of depolarization. As a result, the threshold potential is not reached and an action potential is not propagated. (131)
9. Local anesthetics are thought to exert their predominant action on the nerve by binding to a specific receptor on the sodium ion channel. The location of the binding site appears to be within the inner vestibule of the sodium channel. (131)
10. The conduction blockade produced by a local anesthetic is normally completely reversible (i.e., reversal of the blockade is spontaneous, predictable, and complete). (130)
11. Neither the resting membrane potential nor the threshold potential is appreciably altered by local anesthetics. (131)
12. The temporal progression of the interruption of the transmission of impulses is autonomic, sensory, and then motor nerve blockade. This yields a temporal progression of autonomic nervous system blockade, then sensory nervous system blockade, followed by skeletal muscle paralysis. (135)
13. According to the modulated receptor model, sodium ion channels alternate between several conformational states, and local anesthetics bind to these different conformational states with different affinities. During excitation, the sodium channel moves from a resting-closed state to an activated-open state, with passage of sodium ions and consequent depolarization. After depolarization, the channel assumes an inactivated-closed conformational state. Local anesthetics bind to the activated and inactivated states more readily than the resting state, attenuating conformational change. Drug dissociation from the inactivated conformational state is slower than from the resting state. Thus, repeated depolarization produces more effective anesthetic binding. The electrophysiologic consequence of this effect is progressive enhancement of conduction blockade with repetitive stimulation, an effect referred to as *use-dependent* or *frequency-dependent* block. For this reason, selective conduction blockade of nerve fibers by local anesthetics may in part be related to the characteristic frequency of activity of the nerve. (132-133)

CLASSIFICATION OF NERVES AND SENSITIVITY TO LOCAL ANESTHETICS

14. Fiber diameter, the presence or absence of myelin, and function are the three characteristics by which nerve fibers are classified. A, B, and C are the three main types of nerve fibers. (133, 135, Table 11-2)

15. The A and B nerve fiber types are myelinated. Myelin is composed of plasma membranes of specialized Schwann cells that wrap around the axon during axonal growth. Myelin functions to insulate the axolemma, or nerve cell membrane, from the surrounding conducting media. It also forces the depolarizing current to flow through periodic interruptions in the myelin sheath called the nodes of Ranvier. The sodium channels that are instrumental in nerve pulse propagation and conduction are concentrated at these nodes of Ranvier. Myelin increases the speed of nerve conduction and makes the nerve membrane more susceptible to local anesthetic-induced conduction blockade. (133, 135, Table 11-2)

16. In general, three consecutive nodes of Ranvier must be exposed to adequate concentrations of local anesthetic for the effective blockade of nerve impulses to occur. (135)

17. The nerve fiber type A-δ, which is myelinated, conducts sharp or fast/first pain impulses. The nerve fiber type C, which is unmyelinated, conducts dull burning pain impulses. The large diameter type A-δ fiber appears to be more sensitive to blockade than the smaller diameter type C fiber. This lends support to the theory that myelination of nerves has a greater influence than nerve fiber diameter on the conduction blockade produced by local anesthetics. In clinical practice, however, the relatively high concentrations of local anesthetic that are generally achieved will overcome this difference. (135, Table 11-2)

18. The nerve fiber types A-α and A-β, which are both myelinated, conduct motor nerve impulses. The nerve fiber type A-α conducts large motor nerve impulses, and the nerve fiber type A-β conducts small motor nerve impulses. (135, Table 11-2)

19. Differential block refers to the relative block of sensory versus motor function. For equivalent analgesia or anesthesia, etidocaine tends to produce more profound motor block than most commonly used local anesthetics, making it an unfavorable choice, particularly for use in labor or postoperative pain management. (135)

20. Local anesthetics diffuse along a concentration gradient from the outer surface, or mantle, of the nerve toward the center, or core, of the nerve. As a result, the nerve fibers located in the mantle of the nerve are blocked before those in the core of the nerve. (135, Figure 11-5)

SPREAD OF ANESTHESIA AND PERIPHERAL NERVE BLOCKADE

21. In a peripheral nerve, the nerve fibers in the mantle generally innervate more proximal anatomic structures. The distal anatomic structures are more frequently innervated by nerve fibers near the core of the nerve. This physiologic orientation of nerve fibers in a peripheral nerve explains the observed initial proximal analgesia with subsequent progressive distal spread as local anesthetics diffuse to reach more central core nerve fibers. (135, Figure 11-5)

22. In contrast to most systemically administered drugs, the local anesthetics are deposited at the target site, and systemic absorption and circulation serve to attenuate or curtail their effect rather than distribute them to their site of action. (135)

PHARMACOKINETICS

23. The pKa of most local anesthetics is greater than 7.4 (benzocaine is a notable exception with a pKa of approximately 3.5). This means that the pH at which the cationic form and nonionized form will be equivalent is greater than 7.4 for almost all of the clinically used anesthetics. (133, Table 11-1)

24. Most local anesthetic molecules exist in the ionized, hydrophilic form at physiologic pH. However, local anesthetics must be in the nonionized, lipid-soluble form to cross the lipophilic nerve cell membranes. (131, 133, Table 11-1)

25. Local tissue acidosis is associated with a lower quality anesthesia. This is presumed to be due to an increase in the ionized fraction of the drug in an acidotic environment, with less of the neutral form available to penetrate the cell membrane. (133, Figure 11-4)

26. The primary determinant of the potency of a local anesthetic is its lipid solubility. (133)

27. The rate of systemic uptake and the rate of clearance of the drug are the two primary determinants of peak plasma concentrations of a local anesthetic after its absorption from tissue sites. (136)

28. Ester local anesthetics are cleared by hydrolysis by pseudocholinesterase enzymes in the plasma. (136)

29. Amide local anesthetics undergo degradation in the liver by hepatic microsomal enzymes. (136)

30. Less than 5% of the injected dose of local anesthetic undergoes renal excretion unchanged. The low water solubility of local anesthetics limits their renal excretion. (136)

31. The lungs and the liver both influence the potential for local anesthetic systemic toxicity. The extent to which the lungs extract local anesthetics from the circulation—so-called first-pass pulmonary extraction—influences systemic toxicity by preventing the rapid accumulation of local anesthetics in the plasma. The liver also influences local anesthetic systemic toxicity, especially for the amide local anesthetics that depend upon the liver for metabolism. (136)

32. The relatively rapid hydrolysis by plasma cholinesterase makes chloroprocaine less likely to produce sustained plasma concentrations. (136)

33. Patients with atypical plasma cholinesterase enzyme may be at increased risk for developing excessive plasma concentrations of ester local anesthetics. Ester local anesthetics rely on plasma hydrolysis for their metabolism, which may be limited or absent in these patients. (136)

34. Lidocaine, an amide local anesthetic, is cleared by hepatic metabolism. The clearance of lidocaine from the plasma parallels hepatic blood flow. Liver disease or decreases in hepatic blood flow as can occur with congestive heart failure or general anesthesia can decrease the rate of metabolism of lidocaine. (136)

35. The low water solubility of the local anesthetics usually limits renal excretion of the parent compound to less than 5% of the administered dose. (136)

36. The addition of epinephrine or phenylephrine to a local anesthetic solution produces a local tissue vasoconstriction. This results in a slowing of the rate of systemic absorption of the local anesthetic. (136)

37. The addition of epinephrine or phenylephrine to a local anesthetic solution produces local tissue vasoconstriction. This results in a prolonged duration of action of the local anesthetic by keeping the anesthetic in contact with the nerve fibers for a longer period of time. (136)

38. The addition of epinephrine or phenylephrine to a local anesthetic solution causes a slower rate of systemic absorption and a prolonged duration of action. This increases the likelihood that the rate of metabolism will match the rate of absorption, resulting in a decrease in the possibility of systemic toxicity. Inclusion of epinephrine may also decrease the potential for toxicity by serving as a marker for misplaced intravascular injection, whereby the elevation of heart rate can serve as a warning of such misplacement, alerting the clinician to halt injection and thus prevent the administration of additional anesthetic. (136)

39. The addition of epinephrine or phenylephrine to a local anesthetic solution has little effect on the rate of onset of anesthesia. (136)

40. The addition of epinephrine or phenylephrine to a local anesthetic solution decreases bleeding in the area infiltrated due to its vasoconstrictive properties. (136)

41. The systemic absorption of epinephrine from the local anesthetic solution may contribute to cardiac dysrhythmias or accentuate hypertension in vulnerable patients. (136)

42. The addition of epinephrine to a local anesthetic solution may not be recommended in patients with unstable angina, cardiac dysrhythmias, uncontrolled hypertension, or uteroplacental insufficiency. The addition of epinephrine to a local anesthetic solution is not recommended for intravenous anesthesia or for peripheral nerve block anesthesia in areas that may lack collateral blood flow, such as the digits (*though the soundness of this latter proscription has been recently questioned*). (136)

SIDE EFFECTS

43. Potential negative side effects associated with the administration of local anesthetics include systemic toxicity, neurotoxicity, and allergic reactions. (136)

44. Local anesthetic systemic toxicity occurs as a result of excessive plasma concentrations of a local anesthetic drug. The most common cause of local anesthetic systemic toxicity is accidental intravascular injection of local anesthetic solution during the performance of a nerve block. (136)

45. The magnitude of the systemic absorption of local anesthetic from the tissue injection site is influenced by the pharmacologic profile of the local anesthetic, the total dose injected, the vascularity of the injection site, and the inclusion of a vasoconstrictor in the local anesthetic solution. (136)

46. The relative order from highest to lowest of peak plasma concentrations of local anesthetic associated with regional anesthesia is intercostal nerve block, caudal block, epidural, brachial plexus, and sciatic/femoral. (136, Figure 11-6)

47. The central nervous system and cardiovascular system are most likely to be affected by excessive plasma concentrations of local anesthetic. (136)

48. The initial manifestations of central nervous system toxicity due to excessive plasma concentrations of local anesthetic include circumoral numbness, facial tingling, restlessness, vertigo, tinnitus, and slurred speech. With progressively increasing concentrations of local anesthetic in the plasma, symptoms may progress to manifestations of central nervous system excitation, such as facial and extremity muscular twitching and tremors. Finally, tonic-clonic seizures, apnea, and death can follow. However, deviations from this classic progression are common. (137)

49. Local anesthetic drugs in excessive plasma concentrations sufficient to cause seizures are believed to initially depress inhibitory pathways in the cerebral cortex. This allows for the unopposed action of excitatory pathways in the central nervous system, which manifests as seizures. As the concentration of local anesthetic in the plasma increases, there is subsequent inhibition of both excitatory and inhibitory pathways in the brain. Ultimately this leads to generalized global central nervous system depression. (137)

50. Potential adverse effects of local anesthetic-induced seizures are arterial hypoxemia, metabolic acidosis, and pulmonary aspiration of gastric contents. The mainstay of treatment of local anesthetic-induced seizures, as with all seizures, is aimed toward supporting the patient while attempting to abort the seizure with anticonvulsant drugs. Supplemental oxygen should be administered. The patient's airway may need to be secured with a cuffed endotracheal tube if there is a need to facilitate adequate ventilation and delivery of oxygen to the lungs, and to protect the airway from the aspiration of gastric contents. (137)

51. Anticonvulsant drugs that can be used to stop local anesthetic-induced seizures include diazepam and propofol. Diazepam is the preferred agent, though propofol is generally more readily accessible for immediate administration. However, propofol should be used cautiously in small doses as seizures may portend cardiovascular toxicity that might be augmented by propofol's cardiovascular depression. (137)

52. The administration of paralyzing doses of a rapidly acting neuromuscular blocking drug may be necessary to facilitate intubation of the trachea during a seizure. The administration of a neuromuscular blocking drug with prolonged paralytic effects during a seizure may be indicated when benzodiazepines and barbiturates have not been effective in stopping the seizure activity. However, while the neuromuscular block aborts the peripheral seizure activity, it does not alter the abnormal cerebral electrical activity, and therefore does not negate the need to adequately control underlying seizure activity with anticonvulsants. (137)

53. The cardiovascular system is generally less susceptible to local anesthetic toxicity than the central nervous system. That is, the dose of local anesthetic required to produce central nervous system toxicity is less than the dose of local anesthetic required to result in cardiotoxicity. (138)

54. Two mechanisms by which local anesthetics produce hypotension include the relaxation of peripheral vascular smooth muscle and direct myocardial depression. (138)

55. Local anesthetics exert their cardiotoxic effects primarily through the blockade of sodium ion channels in the myocardium. This blockade results in an increase in the conduction time throughout the heart, manifested as a prolongation of the P-R interval and widening of the QRS complex. Local anesthetics also produce a dose-dependent negative inotropic effect. Clinically, these may result in a decreased cardiac output. With extremely elevated serum levels of local anesthetic, bradycardia and sinus arrest can result. (138)

56. The relative cardiotoxicity of local anesthetic agents is made through a comparison of the dose (or serum concentration) required to produce cardiovascular collapse relative to central nervous system toxicity. Through the evaluation of these ratios, it has been determined that bupivacaine is roughly twice as cardiotoxic as lidocaine and that levobupivacaine and ropivacaine are intermediate. (138)

57. Bupivacaine is more cardiotoxic than lidocaine per dose administered to achieve a given anesthetic effect. When electrophysiological differences between anesthetics are compared, lidocaine is found to enter the sodium ion channel quickly and to leave quickly. In contrast, recovery from bupivacaine blockade during diastole is relatively prolonged, making it far more potent with respect to depressing the maximum upstroke velocity of the cardiac action potential (Vmax) in ventricular cardiac muscle. As a result, bupivacaine has been labeled a "fast-in, slow-out" local anesthetic. This characteristic likely creates conditions favorable for unidirectional block and reentry. Other mechanisms may contribute to bupivacaine's cardiotoxicity, including disruption of atrioventricular nodal conduction, depression of myocardial contractility, and indirect effects mediated by the central nervous system. (140)

58. The maximum recommended concentration of bupivacaine to be administered for epidural anesthesia in obstetrics is 0.5%. This recommendation emerged as a result of numerous fatal cardiotoxic reactions that occurred with the administration of 0.75% bupivacaine in this patient population. (140)

59. Recently, a series of systematic experimentation and clinical events have identified a practical and apparently effective therapy for systemic anesthetic toxicity. Following experiments in rats and dogs, which demonstrated that administration of a lipid emulsion could attenuate bupivacaine cardiotoxicity, numerous clinical cases were reported in which intravenous lipid appears to have been effective in reversing

local anesthetic systemic toxicity. The mechanism by which lipid is effective is incompletely understood, but its predominant action is most likely related to its ability to extract bupivacaine (or other lipophilic drugs) from aqueous plasma or tissue targets, thus reducing their effective concentration ("lipid sink"). (138)

60. The administration of prilocaine has been associated with methemoglobinemia in a dose-dependent manner, with significant toxicity generally occurring with doses exceeding 600 mg. Methemoglobinemia results from the accumulation of *ortho*-toluidine, a metabolite of prilocaine. Ortho-toluidine is an oxidizing compound that oxidizes hemoglobin to methemoglobin, creating methemoglobinemia. Methemoglobinemia that occurs through the administration of prilocaine is spontaneously reversible. Alternatively, methylene blue may be administered intravenously to treat this condition. Methemoglobinemia can also be a significant clinical problem with benzocaine topically administered on mucosal surfaces. (140)

61. The administration of chloroprocaine has been associated with prolonged motor and sensory deficits when administered at recommended doses for epidural anesthesia that appeared to have been inadvertently administered into the subarachnoid space. Early studies suggested that this effect might have occurred due to a combination of the low pH of the anesthetic solution (pH approximately 3.0)and the antioxidant sodium bisulfite, which resulted in the liberation of sulfur dioxide. However, this mechanism has been challenged by more recent studies, which implicate the high doses of chloroprocaine, per se. (139)

62. Transient neurologic symptoms (TNS) is a syndrome of pain/dysesthesia in the lower back, posterior thighs, or buttocks that generally occurs within 24 hours of recovery from a spinal anesthetic. Full recovery from the symptoms most often occurs within 3 days. Importantly, TNS is not associated with sensory loss, motor weakness, or bowel or bladder dysfunction. Risk factors for TNS following spinal anesthesia include the use of lidocaine, lithotomy position during surgery, and outpatient status. Indeed, when these three risk factors are combined, the incidence rate has been found to be 24%. Similar to lithotomy, positioning for knee arthroscopy appears to dramatically increase risk. (139)

63. Cauda equina syndrome represents the clinical manifestation of injury to the nerve roots caudal to the conus. Symptoms may include perineal sensory loss, bowel and bladder dysfunction, and lower extremity motor weakness. In the past, a cluster of cases was reported in association with the use of lidocaine administered through microbore spinal catheters (also referred to as small-bore and defined as smaller than 27 gauge). It is believed that pooling of local anesthetic in the most dependent portion of the subarachnoid space led to high concentrations of local anesthetic around the nerve roots of the cauda equina and subsequent irreversible neurotoxicity. Small-bore catheters for continuous spinal anesthesia are no longer marketed in the United States. However, risk remains because similar neurotoxic injury can occur with repetitive doses of any local anesthetic even if administered through a large-bore (e.g., epidural) catheter. In fact, this mechanism of neurotoxic injury has also been reported with repeat needle injection after a failed single-injection spinal anesthesia. (139)

64. Recent experience suggests that lidocaine has greater potential for direct neurotoxicity than traditionally appreciated. In addition to the aforementioned cases of cauda equina syndrome with small-bore catheters, lidocaine appears to be capable of inducing injury when administered at the high end of the manufacturer's specified dose range for spinal anesthesia (100 mg). Accordingly, it has been suggested that if this drug is used for spinal anesthesia, the dose should be limited to 75 mg, and the concentration of the anesthetic solution should not exceed 2.5%. However, lidocaine with epinephrine remains an appropriate and popular choice for epidural anesthesia and peripheral blocks. (139)

65. The occurrence of major (cauda equina syndrome) and minor (TNS) sequelae occuring with lidocaine has resulted in near abandonment of this agent for spinal anesthesia.

66. Less than 1% of all adverse reactions to local anesthetics are believed to be true allergic reactions. When an allergic reaction to a local anesthetic is suspected to have occurred, full documentation should be made in the chart regarding the dose and route of local anesthetic administered and the reaction that occurred. There are three potential causes of an allergic reaction to administered local anesthetic. In addition to the anesthetic itself, a reaction might result from exposure to one of its metabolites. For example, it has been traditionally taught that ester local anesthetics have a proclivity to induce allergic reactions due to one of its breakdown products, *para*-aminobenzoic acid, making esters more likely than amides to cause allergic reactions, though some have questioned the validity of this assertion. Allergic reactions may also occur to another component of the anesthetic solution (e.g., the preservative methylparaben, used in some commercial preparations of both amides and esters, appears to have significant antigenic potential). (138)

67. Cross-sensitivity has not been found to exist between the classes of local anesthetics. A patient found to be allergic to ester local anesthetics would not be expected to be allergic to amide local anesthetics.

CLINICAL USES

68. Tetracaine is primarily used as a spinal anesthetic in current clinical practice, where its long duration of action, particularly if used with a vasoconstrictor, can at times be a useful attribute. (139)

69. Of the available local anesthetics, two have received considerable attention as alternatives to lidocaine for short-duration spinal anesthesia: prilocaine and chloroprocaine. However, while prilocaine has an acceptable profile for short-duration anesthesia, it is not available in the United States in a formulation that would be appropriate to administer intrathecally. Consequently, chloroprocaine appears to be the favored contender for lidocaine's replacement. The rationale for using chloroprocaine for deliberate intrathecal administration largely rests on the relative dose (i.e., the dose required for spinal anesthesia is an order of magnitude less than those previously associated with injuries occuring with inadvertent intrathecal injection of anesthetic intended for the epidural space). Chloroprocaine rarely, if ever, results in TNS, and it has a duration of action as a spinal anesthetic that is even shorter than lidocaine, making it extremely well suited for short-duration outpatient spinal anesthesia. Although the issue of bisulfite toxicity has not been adequately resolved, chloroprocaine administered intrathecally should be bisulfite-free, and the dose should not exceed 60 mg.

70. Isomers are different compounds that have the same molecular formula. Subsets of isomers that have atoms connected by the same sequence of bonds but that have different spatial orientations are called stereoisomers. Enantiomers are a particular class of stereoisomers that exist as mirror images. The term chiral is derived from the Greek *cheir* for "hand," because the forms can be considered nonsuperimposable mirror images. Enantiomers have identical physical properties except for the direction of the rotation of the plane of polarized light. This property is used to classify the enantiomer as dextrorotatory (+) if the rotation is to the right or clockwise and as levorotatory (–) if it is to the left or counterclockwise. A racemic mixture is a mixture of equal parts of enantiomers and is optically inactive because the rotation caused by the molecules of one isomer is cancelled by the opposite rotation of its enantiomer. Chiral compounds can also be classified on the basis of absolute configuration, generally designated as R (rectus) or S (sinister). Enantiomers may differ with respect to specific biologic activity. (140)

71. Ropivacaine and levobupivacaine differ from other local anesthetics because they are chiral compounds rather than racemic mixtures. Both are S(−) enantiomers,

and were marketed in response to the cardiotoxic effects of bupivacaine because they appear to cause modestly less myocardial depression and are modestly less arrhythmogenic than bupivacaine. (140-141)

72. EMLA is a topical anesthetic cream that consists of lidocaine 2.5% and 2.5% prilocaine. This mixture has a lower melting point than either component, and it exists as an oil at room temperature that is capable of overcoming the barrier of the skin. EMLA cream is particularly useful in children for relieving pain associated with venipuncture or placement of an intravenous catheter, although it may take up to an hour before adequate topical anesthesia is produced. (141)

Chapter

9 NEUROMUSCULAR BLOCKING DRUGS

Ronald D. Miller, Tula Gourdin

1. Describe the physiologic effect of neuromuscular blocking drugs.

CLINICAL USES

2. What are some clinical situations in which skeletal muscle relaxation is desired?
3. What are some methods by which skeletal muscle relaxation can be achieved without the administration of neuromuscular blocking drugs?
4. What analgesic effects do neuromuscular blocking drugs have?
5. What are some characteristics of neuromuscular blocking drugs that may influence the choice of which drug is administered for clinical use for a given patient?

NEUROMUSCULAR JUNCTION

6. What is the neuromuscular junction?
7. What events lead to the release of neurotransmitter at the neuromuscular junction? What is the neurotransmitter that is released?
8. What class of receptors is located on postjunctional membranes? What clinical effect results from the stimulation of these receptors?
9. How, and in what time course, is the action of acetylcholine terminated in the synaptic cleft? What is the clinical relevance of this?
10. With respect to the neuromuscular junction, what are the three sites at which nicotinic cholinergic receptors are located?
11. What is the role of prejunctional receptors?
12. What is the role of extrajunctional receptors? What is their effect when stimulated?
13. What is the structure of nicotinic cholinergic receptors? How is the junction of the cholinergic receptor related to its structure?
14. What is the binding site for an agonist at the nicotinic cholinergic receptor?

STRUCTURE ACTIVITY RELATIONSHIPS

15. How does the chemical structure of neuromuscular blocking drugs relate to their pharmacologic action?

DEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

16. What is the intubating dose of succinylcholine? What are its approximate time of onset and duration of action when administered at this dose?
17. What is the mechanism of action of succinylcholine?
18. What is phase I neuromuscular blockade?
19. What is phase II neuromuscular blockade? What is the mechanism by which it occurs? When is phase II neuromuscular blockade most likely to occur clinically?
20. What occurs clinically as a result of the opening of the nicotinic cholinergic receptor ion channel that occurs with the administration of succinylcholine?

21. How efficiently does plasma cholinesterase hydrolyze succinylcholine? Where is plasma cholinesterase produced?
22. How is the effect of succinylcholine at the cholinergic receptor terminated?
23. How is the duration of action of succinylcholine influenced by plasma cholinesterase?
24. What are some drugs, chemicals, or clinical diseases that may affect the activity of plasma cholinesterase?
25. What is atypical plasma cholinesterase? What is its clinical significance?
26. What is dibucaine? What is its clinical use?
27. What is the normal dibucaine number? For heterozygous and homozygous atypical cholinesterase patients, what is their associated dibucaine number, duration of action of an intubating dose of succinylcholine, and incidence in the population?
28. Why is succinylcholine usually not administered to children under nonemergent conditions?
29. What are some adverse cardiac rhythms that may result from the administration of succinylcholine? When and why are they likely to occur?
30. How can the potential risk of adverse cardiac rhythms associated with the administration of succinylcholine be minimized?
31. What is the mechanism by which succinylcholine may induce a hyperkalemic response with its administration? Which patients are especially at risk for this effect of succinylcholine?
32. Are renal failure patients at greater risk for a hyperkalemic response to the administration of succinylcholine?
33. What is the mechanism by which succinylcholine may induce postoperative myalgias with its administration? Which muscles are typically affected? Which patients are especially at risk for this effect of succinylcholine?
34. How might the fasciculations associated with the administration of succinylcholine be blunted?
35. What effect does the administration of succinylcholine have on intraocular pressure? What is the clinical significance of this?
36. What effect does the administration of succinylcholine have on intragastric pressure? What is the clinical significance of this?
37. What effect does the administration of succinylcholine have on masseter muscle tension? What is the clinical significance of this?

NONDEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

38. What is the mechanism of action of nondepolarizing neuromuscular blocking drugs?
39. Describe the lipid solubility of nondepolarizing neuromuscular blocking drugs. How does this influence its volume of distribution and clinical effect?
40. What are some of the methods by which nondepolarizing neuromuscular blocking drugs are cleared? How does this influence its duration of action?
41. What are some drugs and physiologic states that may enhance the neuromuscular blockade produced by nondepolarizing neuromuscular blocking drugs?
42. What is the mechanism by which volatile anesthetics are believed to enhance the neuromuscular blockade produced by nondepolarizing neuromuscular blocking drugs?
43. What are some of the methods by which nondepolarizing neuromuscular blocking drugs are able to exert cardiovascular effects?
44. What is a concern regarding patients receiving long-term nondepolarizing neuromuscular blocking drugs in the intensive care unit?
45. Which patients are at risk for developing a myopathy after the administration of nondepolarizing neuromuscular blocking drugs in the intensive care unit? How might they present clinically?

LONG-ACTING NONDEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

46. How is the clearance of pancuronium affected by renal or liver disease?
47. What are the cardiovascular effects associated with the administration of pancuronium? What is the mechanism by which these effects occur?

INTERMEDIATE-ACTING NONDEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

48. Name some intermediate-acting nondepolarizing neuromuscular blocking drugs. What is their approximate time of onset and duration of action?
49. How is vecuronium excreted from the body? How does renal failure affect the clearance of vecuronium?
50. How does the time of onset of rocuronium compare with the time of onset of succinylcholine?
51. How is rocuronium excreted from the body? How does renal failure affect the clearance of rocuronium?
52. How are cisatracurium and atracurium structurally related?
53. How are atracurium and cisatracurium cleared from the plasma? How does renal failure affect the clearance of these drugs?
54. What is the principal metabolite of atracurium and its potential adverse physiologic effect? Which patients are especially at risk for this adverse effect?
55. What are some of the cardiovascular effects of atracurium?
56. What are some differences between cisatracurium and atracurium that make cisatracurium more desirable for clinical use?

SHORT-ACTING NONDEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

57. Name a short-acting nondepolarizing neuromuscular blocking drug. What is its approximate time of onset and duration of action?
58. How is mivacurium cleared from the plasma? How is the duration of action of mivacurium altered in patients who have deficiencies in plasma cholinesterase enzyme, liver disease, or renal disease?
59. Does the administration of neostigmine reverse the neuromuscular blockade produced by mivacurium?
60. What are some of the cardiovascular effects of mivacurium?

MONITORING THE EFFECTS OF NONDEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

61. What is the most common method for monitoring the effects of neuromuscular blocking drugs during general anesthesia?
62. What are two ways in which a peripheral nerve stimulator may be useful during the administration of neuromuscular blocking drugs during general anesthesia?
63. Which nerve and muscle are most commonly used to evaluate the neuromuscular blockade produced by neuromuscular blocking drugs?
64. Which nerves may be used for the evaluation of the neuromuscular blockade produced by neuromuscular blocking drugs through the use of a peripheral nerve stimulator when the arm is not available to the anesthesiologist?
65. How do the neuromuscular blocking drugs vary with regard to their time of onset at the adductor pollicis muscle, orbicularis oculi muscle, laryngeal muscles, and diaphragm?
66. What are some of the mechanical responses evoked by a peripheral nerve stimulator that are used to monitor the effects of neuromuscular blocking drugs? What are the methods to evaluate the mechanically evoked response?
67. What percent of depression of a mechanically evoked single twitch response from its control height correlates with adequate neuromuscular blockade for intubation of the trachea or for the performance of intraabdominal surgery? What approximate percent of nicotinic cholinergic receptors must be occupied by a nondepolarizing neuromuscular blocking drug to achieve this effect?
68. What is the train-of-four stimulus delivered by a peripheral nerve stimulator? What is its clinical use?
69. What is the train-of-four ratio? What is its clinical use?
70. What train-of-four ratio correlates with the complete return to control height of a single twitch response?

71. What is the train-of-four ratio during phase I neuromuscular blockade resulting from the administration of a depolarizing neuromuscular blocking drug such as succinylcholine?
72. How accurate is the estimation of the train-of-four ratio by clinicians evaluating the response visually and manually? What percent of the first twitch control height must be present before the fourth twitch is detectable?
73. What is the double burst suppression stimulus delivered by a peripheral nerve stimulator? What is its clinical use?
74. What is tetany? How might it be mechanically produced by a peripheral nerve stimulator?
75. How is the normal response to tetany altered by the administration of depolarizing and nondepolarizing neuromuscular blocking drugs?
76. What is posttetanic stimulation? What is its clinical use?

ANTAGONISM OF NONDEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

77. What is the mechanism by which the neuromuscular blockade produced by nondepolarizing neuromuscular blocking drugs is antagonized?
78. How are the cardiac muscarinic effects of anticholinesterases attenuated?
79. Name two factors that influence the choice of anticholinesterase drug to be administered to antagonize the neuromuscular blockade produced by nondepolarizing neuromuscular blocking drugs.
80. When might neostigmine or edrophonium be an appropriate choice of anticholinesterase drug to administer to antagonize neuromuscular blockade? What anticholinergic drug is often paired with each?
81. What are some tests that can be done to evaluate the adequacy of the recovery from the effects of neuromuscular blockade?
82. How might the residual effects of neuromuscular blockers be manifest clinically in the awake patient?
83. What are some pharmacologic or physiologic factors that may interfere with the antagonism of the neuromuscular blockade produced by neuromuscular blocking drugs?

ADVERSE OUTCOMES FROM INADEQUATE ANTAGONISM OF NEUROMUSCULAR BLOCKADE

84. What risk factors contribute to adverse respiratory events in the first hour postoperative in the postanesthetic care unit (PACU)?
85. In addition to induction of anesthesia, what is the most dangerous time for anesthetic complications in the postoperative period?
86. What is sugammadex? What is the mechanism of action of sugammadex?
87. What are the major clinical differences between sugammadex and neostigmine?
88. What are some advantages of sugammadex for the antagonism of neuromuscular blockade?

ANSWERS*

1. Neuromuscular blocking drugs interrupt transmission of nerve impulses at the neuromuscular junction and thereby produce paresis or paralysis of skeletal muscles. (144)

CLINICAL USES

2. Skeletal muscle relaxation (i.e., paralysis) is desired most frequently to facilitate intubation of the trachea and provide excellent surgical conditions. Other clinical situations in which skeletal muscle relaxation is desired include to facilitate

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

mechanical ventilation of the lungs either intraoperatively, in the intensive care unit, or during cardiopulmonary resuscitation. (144)

3. Skeletal muscle relaxation can be achieved without the administration of neuromuscular blocking drugs by the administration of high concentrations of volatile anesthetics, regional anesthesia, and by proper patient positioning on the operating table. (81, 252, 300)

4. Neuromuscular blocking drugs do not have any anesthetic or analgesic effects. The potential therefore exists for the patient to be rendered paralyzed without adequate anesthesia and subsequent unrecognized awareness during anesthesia. (144, 737)

5. Neuromuscular blocking drugs vary in their mechanism of action, speed of onset, duration of action, route of elimination, and associated side effects. These characteristics of a neuromuscular blocking drug may influence whether a specific neuromuscular blocking drug is chosen for administration to a given patient. (144)

NEUROMUSCULAR JUNCTION

6. The neuromuscular junction is the location where the transmission of neural impulses at the nerve terminal becomes translated into skeletal muscle contraction at the motor endplate. The highly specialized neuromuscular junction consists of the prejunctional motor nerve ending, a highly folded postjunctional skeletal muscle membrane, and the synaptic cleft in between. (144-146, Figure 12-1)

7. A nerve impulse conducted down the motor nerve fiber, or axon, ends in the prejunctional motor nerve ending. The resulting stimulation of the motor nerve terminal causes an influx of calcium into the nerve terminal. The influx of calcium results in a release of the neurotransmitter acetylcholine into the synaptic cleft. This is why administration of calcium briefly improves neuromuscular function. The nerve synthesizes and stores acetylcholine in vesicles in the motor nerve terminals, which is available for release with the influx of calcium. Acetylcholine released into the synaptic cleft binds to receptors in the postjunctional skeletal muscle membrane, leading to skeletal muscle contraction. (145-146, Figure 12-1)

8. Nicotinic cholinergic receptors are located on the skeletal muscle membrane, or postjunctional membrane. When acetylcholine binds to the nicotinic cholinergic receptor, there is a change in the permeability of the skeletal muscle membrane to sodium and potassium ions. The resultant movement of these ions down their concentration gradients causes a decrease in the membrane potential of the skeletal muscle cell from the resting membrane potential to the threshold potential. The resting membrane potential is the electrical potential of the skeletal muscle cell at rest, usually about -90 mV. The threshold potential is about -45 mV. When the threshold potential is reached, an action potential becomes propagated over the surfaces of skeletal muscle fibers. This leads to the contraction of these skeletal muscle fibers. (146, Figure 12-2)

9. Acetylcholine is hydrolyzed in the synaptic cleft by the enzyme acetylcholinesterase, or true cholinesterase. This occurs rapidly, within 15 ms. Clinically, this allows for the restoration of the membrane to its resting membrane potential. The metabolism of acetylcholine also prevents sustained depolarization of the skeletal muscle cells, and thus prevents tetany from occurring. (145, Figure 12-1)

10. Nicotinic cholinergic receptors are located in three separate sites relative to the neuromuscular junction and are referred to by their varied locations. Each of these receptors also has a different functional capacity with regard to its role in skeletal muscle contraction. The three types of nicotinic cholinergic receptors are prejunctional, postjunctional, and extrajunctional. Prejunctional receptors are located at the motor nerve terminal. Postjunctional receptors are located just opposite the prejunctional receptors in the endplate and are the most important receptors for the action of neuromuscular blocking drugs. Extrajunctional receptors are immature in form and are located throughout the skeletal muscle membrane.

They are located in areas other than the endplate region of the muscle membrane as well as at the motor endplate region. (145-146, Figure 12-1)

11. Prejunctional receptors are located on the motor nerve terminal and influence the release and replenishment of acetylcholine from the nerve terminal. (145-146, Figure 12-1)

12. Extrajunctional receptors are located throughout the skeletal muscle membrane. They differ from the other two types of nicotinic cholinergic receptors both in their location and by their molecular structure. Under normal circumstances, the synthesis of extrajunctional receptors is suppressed by neural activity and has minimal contribution to skeletal muscle action. Extrajunctional receptors may proliferate under conditions of denervation, trauma, strokes, or burn injury. Conversely, when neuromuscular activity returns to normal, extrajunctional receptors quickly lose their activity. Extrajunctional receptors are stimulated more by lower concentrations of acetylcholine and depolarizing neuromuscular blocking drugs than are prejunctional or postjunctional receptors. In addition, extrajunctional receptors remain open longer and permit more ions to flow across the skeletal muscle cell membrane once activated. Clinically, this may manifest as an exaggerated hyperkalemic response when succinylcholine is administered to patients with denervation injuries. (146)

13. Nicotinic cholinergic receptors are made up of glycoproteins divided into five subunits. There are two α subunits and one each of β, γ, and δ subunits. The subunits are arranged in such a way that they form a channel in the membrane, with the binding site for the agonist being the α subunits. When the receptor becomes stimulated by the binding of an agonist or acetylcholine, the channel changes conformation such that it allows the flow of ions through the cell membrane along their concentration gradient. Extrajunctional receptors differ slightly from postjunctional nicotinic cholinergic receptors in that the γ and δ subunits of these receptors are altered from those of the postjunctional receptors. The two α subunits, however, are identical. (146, Figure 12-2)

14. The binding site for agonists at the nicotinic cholinergic receptor is the α subunit. Acetylcholine must bind to both of the two α subunits of the receptor to stimulate the receptor to change conformation and allow the flow of ions through the resulting ion channel. Nondepolarizing neuromuscular blocking drugs also bind to the α subunits of the receptor but only require that one α subunit be bound to exert their pharmacologic effect. With the binding of a nondepolarizing neuromuscular blocking drug to an α subunit on the receptor, acetylcholine is unable to bind to the receptor, the flow of ions across the channel does not occur, and the physiologic effect of skeletal muscle contraction becomes blocked. The binding of a depolarizing neuromuscular blocking drug, like acetylcholine, requires that both α subunits be bound before stimulating the receptor to change conformation and the resulting skeletal muscle contraction. Succinylcholine, a depolarizing neuromuscular blocking drug, exerts its effect in this manner. The elimination of succinylcholine is through its clearance from the plasma and requires a few minutes to occur. This accounts for its prolonged binding period on the nicotinic cholinergic receptor and subsequent skeletal muscle paralysis for the minutes after its administration. (146-148)

STRUCTURE ACTIVITY RELATIONSHIPS

15. Both depolarizing and nondepolarizing neuromuscular blocking drugs have a chemical structure similar to that of acetylcholine, which explains its pharmacologic activity at the nicotinic cholinergic receptor. Succinylcholine is two acetylcholine molecules linked together by methyl groups. The nondepolarizing neuromuscular blocking drugs are much larger and bulkier than acetylcholine but have an internal structure that is chemically related to acetylcholine and allows for interaction with the nicotinic cholinergic receptor. (146-147, Figure 12-3)

DEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

16. The usual intubating dose of succinylcholine when administered intravenously is 1 to 1.5 mg/kg. Complete muscle paralysis after the administration of succinylcholine is typically within 30 to 60 seconds. The duration of action, or duration of skeletal muscle paralysis, after the administration of an intubating dose of succinylcholine is usually 5 to 10 minutes. (148)

17. Succinylcholine acts at the nicotinic cholinergic receptor through a similar mechanism as acetylcholine. Succinylcholine attaches to the two α subunits on the nicotinic cholinergic receptor and causes the ion channel in the muscle cell to open. This results in depolarization of the skeletal muscle cell. Unlike acetylcholine, succinylcholine is not hydrolyzed at the motor endplate but continues to attach to the cholinergic receptors until it is cleared from the plasma. The administration of succinylcholine therefore results in sustained depolarization of the motor endplate. The skeletal muscle paralysis associated with the administration of succinylcholine is due to the inability of the depolarized postjunctional membrane to respond to a subsequent release of acetylcholine. (148)

18. Phase I neuromuscular blockade refers to the blockade of the transmission of neuromuscular impulses caused by succinylcholine with its initial administration. This neuromuscular blockade is due to succinylcholine remaining on the receptor and the sustained depolarization of skeletal muscle cells that results. The sustained depolarization prevents the muscle cell from being able to respond to a subsequent release of acetylcholine. (149, Table 12-2)

19. Phase II neuromuscular blockade refers to the blockade of the transmission of neuromuscular impulses produced by succinylcholine after repolarization of the cell membrane has taken place, but while the cell membrane does not yet respond normally to the release of acetylcholine. Phase II neuromuscular blockade resembles the blockade produced by nondepolarizing neuromuscular blocking drugs. The mechanism of phase II neuromuscular blockade is not completely understood, but it is believed to result from the development of a nonexcitable area around the motor endplate that interferes with the spread of subsequent impulses that have been initiated by the release of acetylcholine. Phase II neuromuscular blockade is most likely to occur when the neuromuscular junction is continuously exposed to a depolarizing neuromuscular blocking drug. This may occur with a succinylcholine infusion, with the administration of a second dose of succinylcholine after the first, or when the intravenous dose of succinylcholine administered exceeds 3 to 5 mg/kg. (149, Table 12-2)

20. The sustained depolarization, and subsequent sustained opening of the cholinergic receptor ion channel, that results from the administration of succinylcholine clinically manifests as skeletal muscle fasciculations. Sustained opening of the nicotinic cholinergic receptor ion channel is also associated with leakage of potassium from the interior of cells into the plasma. The leakage of potassium ions associated with the administration of an intubating dose of succinylcholine is sufficient to increase the serum potassium level by about 0.2 to 0.5 mEq/L. (148, Table 12-2)

21. The enzyme responsible for the hydrolysis of succinylcholine is plasma cholinesterase, or pseudocholinesterase. This is in contrast to acetylcholinesterase, or true cholinesterase, the enzyme responsible for the hydrolysis of acetylcholine. Plasma cholinesterase hydrolyzes succinylcholine at a rapid rate and extremely efficiently, such that only a small fraction of succinylcholine reaches the receptor after its intravenous administration. Plasma cholinesterase is produced in the liver. (148-149, Figure 12-4)

22. The effect of succinylcholine at the cholinergic receptor is terminated by the diffusion of succinylcholine away from the neuromuscular junction and into the extracellular fluid. In the extracellular fluid succinylcholine is rapidly hydrolyzed by plasma cholinesterase. (148)

23. Plasma cholinesterase influences the duration of action of succinylcholine by limiting the amount of succinylcholine that reaches the receptor for its initial action and by hydrolyzing succinylcholine on its diffusion away from the receptor. (148)

24. Potent anticholinesterases often used in insecticides or for the treatment of myasthenia gravis, and certain chemotherapeutic drugs such as nitrogen mustard and cyclophosphamide, can significantly decrease plasma cholinesterase activity and prolong succinylcholine. Prolonged effects of succinylcholine lasting as long as 1 to 3 hours may occur. Liver disease may also result in a decrease in the amount of circulating plasma cholinesterase and a subsequent prolonged clinical effect of succinylcholine. The degree of liver disease must be severe before the synthesis of plasma cholinesterase is sufficiently decreased to result in prolonged muscle paralysis after the administration of succinylcholine, however. (148)

25. Atypical plasma cholinesterase is an abnormal genetic variant of the plasma cholinesterase enzyme that lacks the ability to hydrolyze ester bonds in drugs such as succinylcholine and mivacurium. Patients who are otherwise healthy may have atypical plasma cholinesterase enzyme. Clinically, the presence of this enzyme manifests as prolonged skeletal muscle paralysis after the administration of a conventional dose of succinylcholine. These patients may have skeletal muscle paralysis that persists for over an hour after the administration of succinylcholine. (149)

26. Dibucaine is an amide local anesthetic that greatly inhibits normal plasma cholinesterase activity, but it has limited inhibition of the activity of atypical plasma cholinesterase. This characteristic of dibucaine has led to an evaluation of the percent of inhibition of plasma cholinesterase activity by dibucaine, the result of which is referred to as the dibucaine number. By determining the dibucaine number for a given patient the diagnosis of the presence of atypical plasma cholinesterase may be established. It is important to realize that the dibucaine number reflects the quality, and not the quantity, of the circulating plasma cholinesterase enzyme in the plasma. For instance, patients with liver disease severe enough to decrease the number of circulating plasma cholinesterase enzymes would still have a normal dibucaine number. (149, Table 12-3)

27. The normal dibucaine number is 80. That is, normal plasma cholinesterase enzyme is inhibited by 80% in the presence of dibucaine. An individual heterozygous for atypical plasma cholinesterase would have a dibucaine number between 40 and 60. In these individuals a conventional dose of succinylcholine would lead to neuromuscular blockade that persisted for approximately 20 minutes. The incidence of individuals heterozygous for atypical plasma cholinesterase is about 1 in 480. An individual homozygous for atypical plasma cholinesterase would have a dibucaine number of about 20. In these individuals a conventional dose of succinylcholine would lead to neuromuscular blockade persisting for 60 to 180 minutes. The incidence of individuals homozygous for atypical plasma cholinesterase is about 1 in 3200. (149, Table 12-3)

28. Succinylcholine is usually not administered to children under nonemergent conditions. This is mostly secondary to a number of case reports of cardiac arrest in children and adolescents who were otherwise apparently healthy and had been administered succinylcholine. Hyperkalemia, rhabdomyolysis, and acidosis were frequently documented in these cases. It is believed that many of these children had undiagnosed myopathies. (149)

29. Succinylcholine may induce a wide variety of cardiac dysrhythmias with its administration. Among the most likely adverse cardiac rhythms to result from the administration of succinylcholine are sinus bradycardia, junctional rhythms, and ventricular arrhythmias. This is likely due to the similarity of the chemical structures of succinylcholine and acetylcholine. In addition to stimulating nicotinic receptors, succinylcholine may stimulate cardiac postganglionic muscarinic receptors in the sinus node of the heart and mimic the normal effect of acetylcholine

at these receptors. This potential adverse effect of the administration of succinylcholine is most likely to occur when a second intravenous dose of succinylcholine is administered about 5 minutes after the first. (149-150)

30. The potential risk of adverse cardiac rhythms associated with the administration of succinylcholine may be minimized by pretreating patients before the administration of succinylcholine. The most effective pretreatment regimens include the intravenous administration of atropine or subparalyzing doses of nondepolarizing neuromuscular blocking drugs 1 to 3 minutes before administration of succinylcholine. (150)

31. A hyperkalemic response to succinylcholine in susceptible patients occurs secondary to a proliferation of extrajunctional receptors in the area of skeletal muscle after a denervation injury. These extrajunctional receptors are especially sensitive to succinylcholine. With the administration of succinylcholine to patients with a history of denervation injury there are more ion channels being opened, and more sites for the leakage of potassium out of cells during depolarization. In fact, patients with a history of denervation injury may be placed at risk of hyperkalemia sufficient to cause cardiac arrest when administered succinylcholine. Patients especially at risk are those with disease leading to skeletal muscle atrophy and those with unhealed skeletal muscle injury as produced by third-degree burns, upper motor neuron injury, and multiple trauma. Patients who have had denervation injuries are at risk of a hyperkalemic response to the administration of succinylcholine from 4 days to up to 3 to 6 months after the injury. Susceptibility to the hyperkalemic response peaks 7 to 10 days after the injury. The current recommendation is the avoidance of the administration of succinylcholine to the patient more than 24 hours after the denervation injury has occurred. (150, Figure 12-2)

32. Renal failure patients who are normokalemic can safely receive succinylcholine without being placed at risk for an exaggerated hyperkalemic response. This excludes patients with renal failure who have neuropathy secondary to uremia. (150)

33. Transient, generalized, unsynchronized skeletal muscle contractions referred to as fasciculations often accompany the administration of succinylcholine. This occurs secondary to the depolarization of the skeletal muscle membrane that occurs with the administration of succinylcholine. These fasciculations can result in skeletal muscle damage and myalgias postoperatively. The presence of myoglobinuria may be a clinical sign of skeletal muscle damage in these patients. Postoperative myalgias associated with the administration of succinylcholine most often occur in the muscles of the neck, back, and abdomen. Myalgias localized to the neck may be described as a sore throat by the patient and may be incorrectly attributed to tracheal intubation as the cause of the pain. Young, muscular adults undergoing minor surgical procedures that allow for early ambulation are most likely to complain about myalgias after the administration of succinylcholine. (150)

34. The cause of postoperative myalgias after the administration of succinylcholine has been speculated to be due to the fasciculations associated with the administration of this drug. A nondepolarizing neuromuscular blocking drug can be administered at a dose of 5% to 10% of its ED_{95} dose 2 to 4 minutes before the administration of succinylcholine to blunt the fasciculations. When pretreatment with a nondepolarizing neuromuscular blocking drug has been given to block fasciculations, the subsequent dose of succinylcholine should be increased by 50% to 70%. Pretreatment with a defasciculating dose of a nondepolarizing neuromuscular blocking drug has been shown to decrease the incidence of postoperative myalgias, but not abolish them completely. (150)

35. The administration of succinylcholine is associated with transient increases in intraocular pressure. The mechanism by which this occurs is not clearly understood, but it may be due to the contraction of extraocular muscles. The increase in intraocular pressure peaks 2 to 4 minutes after the administration of succinylcholine. The clinical concern regarding this effect of succinylcholine is the possibility of the extrusion of global contents when succinylcholine is administered to patients with open-eye injuries. Clinical experience with succinylcholine in these patients, however, has not shown this to be the case. For example, the administration of thiopental results in a decrease in intraocular pressure. When thiopental is administered before succinylcholine, the potential increase in intraocular pressure associated with succinylcholine may be attenuated. The prior administration of subparalyzing doses of nondepolarizing neuromuscular blocking drugs may also prevent succinylcholine-induced increases in intraocular pressure. In addition, the benefit of skeletal muscle paralysis associated with the administration of succinylcholine to patients with open-eye injuries far outweighs the risk of the markedly elevated intraocular pressures that are associated with bucking on an endotracheal tube. Intraoperative "bucking" with an endotracheal tube in place can increase intraocular pressure and corneal damage. (150-151)

36. The administration of succinylcholine produces increases in intragastric pressure that are unpredictable. Increases in intragastric pressure with succinylcholine administration, when they do occur, appear to correlate with the magnitude and the intensity of fasciculations. The increase in intragastric pressure is assumed to be due to fasciculation of the abdominal skeletal muscles. There is a theoretical risk of the aspiration of gastric fluid and contents with the increased intragastric pressure associated with the administration of succinylcholine. This risk appears to be increased in patients with ascites, obesity, a hiatal hernia, or an intrauterine pregnancy secondary to the altered angle of entry of the esophagus into the stomach in these patients. Because the magnitude of increase of intragastric pressure appears to be related to the intensity of fasciculations, the prior administration of subparalyzing doses of nondepolarizing neuromuscular blocking drugs may prevent the increase in intragastric pressure from occurring and decrease the theoretical risk of aspiration. (151)

37. The administration of succinylcholine can result in varying degrees of increased masseter muscle tension. In extreme cases this can result in trismus and in difficulty opening the mouth for direct laryngoscopy and intubation of the trachea. Pediatric patients are especially at risk for this complication of succinylcholine administration. Patients who develop trismus in association with the administration of succinylcholine may be susceptible to the subsequent development of malignant hyperthermia. (150)

NONDEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

38. Nondepolarizing neuromuscular blocking drugs compete with acetylcholine for the binding sites on the α subunit of the nicotinic cholinergic receptor. With the binding of a nondepolarizing neuromuscular blocking drug to one or both α subunits on the receptor there are no two α subunits available for acetylcholine to bind. Subsequent depolarization in the postjunctional membrane through the actions of acetylcholine cannot occur, and skeletal muscle paralysis results. Fasciculations do not accompany the administration of nondepolarizing neuromuscular blocking drugs. (151, Table 12-6)

39. Nondepolarizing neuromuscular blocking drugs have very limited lipid solubility. This is due to the highly ionized state of nondepolarizing neuromuscular blocking drugs at physiologic pH. This limits their accessibility to the various tissues and results in a small volume of distribution. The small volume of distribution implies that neuromuscular blocking drugs are limited primarily to the extracellular fluid. Physiologically, the highly ionized state of nondepolarizing neuromuscular blocking drugs minimizes their transfer across lipid membrane barriers. This

includes lipid membranes such as the blood-brain barrier, renal tubular epithelium, gastrointestinal epithelium, and placenta. Clinically, nondepolarizing neuromuscular blocking drugs therefore produce minimal central nervous system effects, undergo minimal renal tubular absorption, are ineffective when administered orally, and do not affect the fetus when administered to a parturient. (151-152)

40. Because of the hydrophilic nature of nondepolarizing neuromuscular blocking drugs, all these neuromuscular blocking drugs may be eliminated by glomerular filtration via the kidneys. When additional methods of clearance of the drugs are possible, the duration of action of the drug shortens. For example, the long-acting neuromuscular blocking drugs, such as pancuronium, undergo little or no metabolism and are primarily cleared by the kidneys. Yet, intermediate-acting and short-acting nondepolarizing neuromuscular blocking drugs are relatively independent of renal function for their clearance from the plasma. For example, vecuronium and rocuronium are cleared primarily through biodegradation in the liver, cisatracurium undergoes chemodegradation by Hofmann elimination and ester hydrolysis, and mivacurium is cleared principally by ester hydrolysis by the enzyme plasma cholinesterase. (151-152, Table 12-6)

41. There are several drugs that are often administered in the perioperative period that may enhance the neuromuscular blockade produced by nondepolarizing neuromuscular blocking drugs. These drugs include volatile anesthetics, local anesthetics, aminoglycoside antibiotics, cardiac antidysrhythmic agents, dantrolene, magnesium, lithium, tamoxifen, and calcium channel blockers. Hypothermia, hypokalemia, and decreases in pH may also prolong the action of nondepolarizing neuromuscular blocking drugs. (152)

42. Volatile anesthetics produce an enhancement of the magnitude and duration of neuromuscular blockade that is dose dependent and drug specific. Volatile anesthetics are thought to enhance the effects of nondepolarizing neuromuscular blocking drugs by directly inducing central nervous system depression and causing a corresponding decrease in skeletal muscle tone. In addition, nondepolarizing neuromuscular blocking drugs may alter the lipid membrane around the nicotinic cholinergic receptors, changing the properties of the ion channel. In this respect, volatile anesthetics may alter the sensitivity of postjunctional membranes to depolarization. (152)

43. Nondepolarizing neuromuscular blocking drugs may exert cardiovascular effects through several methods. First, they may induce the release of histamine. Second, nondepolarizing neuromuscular blocking drugs may have some direct action at cardiac postganglionic muscarinic receptors. Finally, nondepolarizing neuromuscular blocking drugs may have some direct effects on nicotinic receptors at the autonomic ganglia. The clinical significance of the cardiovascular effects produced by neuromuscular blocking drugs is minimal, however. (152, Table 12-5)

44. Most patients receiving neuromuscular blocking drugs for a prolonged period of time in the intensive care unit recover full muscle strength within a few hours of discontinuation of the drug. There have been reports of a subset of patients who, after receiving neuromuscular blocking drugs for several days or weeks, have had persistent skeletal muscle weakness after the discontinuation of the neuromuscular blocking drug. In some cases the skeletal muscle weakness has persisted for months. Weaning the patient from the mechanical ventilation of the lungs is therefore delayed. (152)

45. Risk factors for developing a myopathy secondary to the administration of nondepolarizing neuromuscular blocking drugs in the intensive care unit include patients with asthma, female patients with renal failure receiving vecuronium, the concurrent administration of high doses of corticosteroids, and the administration

of large doses of neuromuscular blocking drugs for prolonged periods. Clinically, these patients may present with flaccid quadriplegia and increased creatine kinase concentrations. The pathophysiology of the myopathy is not known. (152)

LONG-ACTING NONDEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

46. The principal route of clearance of pancuronium, like the other long-acting nondepolarizing neuromuscular blocking drugs, is by glomerular filtration. The clearance of all these long-acting nondepolarizing neuromuscular blocking drugs is greatly affected by renal disease, such that the plasma clearance of pancuronium in patients with renal failure is decreased by 30% to 50%. Patients with renal disease are therefore likely to exhibit prolonged neuromuscular blockade with the administration of conventional doses of pancuronium. Pancuronium is also metabolized by in the liver to a limited degree. A metabolite of pancuronium, 3-desacetylpancuronium, possesses limited muscle relaxant properties. Patients with biliary obstruction or cirrhosis of the liver may also manifest decreased plasma clearance and prolonged elimination half-times of pancuronium, although not to as great an extent as that seen with renal disease. (152)

47. The administration of pancuronium results in a modest increase in heart rate and arterial blood pressure by 10% to 15%. This effect of pancuronium is primarily due to muscarinic receptor blockade at the sinus node of the heart exerted directly by pancuronium. This selective vagal blockade of the heart is similar to the mechanism by which atropine increases heart rate. The increase in heart rate associated with the administration of pancuronium is dose-related and additive, such that subsequent doses of pancuronium will result in similar, additional increases in heart rate as previous doses. This increase in heart rate cannot be blunted or avoided through the slower injection of the drug. A minimal contributor to the increases in heart rate and blood pressure associated with the administration of pancuronium is activation of the sympathetic nervous system. Patients with altered atrioventricular conduction of cardiac impulses, such as patients with atrial fibrillation, appear to be the most likely to have marked increases in heart rate associated with the administration of pancuronium. (152–153)

INTERMEDIATE-ACTING NONDEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

48. The intermediate-acting nondepolarizing neuromuscular blocking drugs include atracurium, cisatracurium, vecuronium, and rocuronium. Their approximate time of onset is 3 to 5 minutes. Their approximate duration of action is 20 to 35 minutes, or 33% to 50% shorter than that of long-acting neuromuscular blocking drugs. The intermediate-acting neuromuscular blocking drug rocuronium stands apart from all the other muscle relaxants with respect to its time of onset, which is 1 to 2 minutes. (153, Figure 12-5, Table 12-6)

49. Vecuronium is metabolized by deacetylation in the liver to 3-, 17-, and 3,17-hydroxy metabolites. Only the 3-hydroxy metabolite has any significant neuromuscular blocking properties. Up to 60% of the injected dose of vecuronium, whether metabolized or unchanged, is excreted in the bile. Vecuronium is also partially cleared by the kidneys. Patients with renal failure may have impaired excretion of the unchanged form of vecuronium as well as the active 3-hydroxy metabolite of vecuronium. This may result in cumulative effects of vecuronium with the administration of large or repeated doses of vecuronium in renal failure patients. There are reports of prolonged neuromuscular blockade in renal failure patients in the intensive care unit being administered continuous infusions of vecuronium. (153)

50. Rocuronium has an onset time of 1 to 2 minutes at its ED_{95} dose, which makes it unique among the intermediate-acting nondepolarizing neuromuscular blocking drugs. In the event that a more rapid onset time is desired, rocuronium may be administered at a dose of three to four times its ED_{95} dose. This increased dose results in an onset time similar to that of succinylcholine. Because of the relatively

increased dose of rocuronium required to produce an onset time similar to succinylcholine, when administered at this dose the duration of action of rocuronium becomes similar to that of pancuronium. (153, Figure 12-5, Table 12-6)

51. Rocuronium is mostly cleared from the plasma through the bile largely unchanged. About 30% of administered rocuronium is excreted renally. Large or repeated doses of rocuronium in patients with renal failure may theoretically produce prolonged effects of the drug, although this has not been seen clinically. (153, Table 12-6)

52. Cisatracurium is an isolated form of a stereoisomer of atracurium. (154, Figure 12-3)

53. The clearance of atracurium and cisatracurium from the plasma is completely independent of the kidneys. Two thirds of administered atracurium or cisatracurium undergoes ester hydrolysis, whereas the remaining third undergoes nonenzymatic spontaneous degradation by Hofmann elimination. Hofmann elimination is dependent on the pH and temperature of the plasma. The metabolism of these drugs is also independent of plasma cholinesterase since nonspecific plasma esterases are responsible for the ester hydrolysis. Both of the routes of metabolism for these drugs are independent of the kidneys or liver, making the duration of action of atracurium or cisatracurium unaltered in patients with hepatic or renal failure. (154, Table 12-6)

54. The principal metabolite of atracurium is laudanosine, which has no neuromuscular blocking effects. Laudanosine freely crosses the blood-brain barrier and, in high concentrations, can act as a central nervous system stimulant. Patients who have been administered continuous infusions of atracurium for several days, as in an intensive care unit setting, are especially at risk for the accumulation of the metabolite laudanosine and its central nervous system stimulatory effects. Laudanosine is primarily cleared through the liver. Patients with impaired hepatic function have a further risk of the adverse effects of laudanosine. (154)

55. The administration of atracurium can result in a transient decrease in systolic blood pressure by as much as 20%, along with facial erythema. These effects of atracurium are related to histamine release and only occur when rapidly doses of three times ED_{95} of atracurium are administered. (154)

56. Cisatracurium undergoes primarily Hofmann elimination to laudanosine and does not seem to undergo ester hydrolysis. In contrast to atracurium, the plasma concentrations of laudanosine after the administration of cisatracurium are very small, making it less likely to exert any central nervous system–stimulating effects. In addition, cisatracurium has minimal cardiovascular effects and does not invoke the release of histamine with its administration. (154)

SHORT-ACTING NONDEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

57. A short-acting nondepolarizing neuromuscular blocking drug is mivacurium. Its approximate time of onset is 3 to 5 minutes. Its approximate duration of action is 10 to 20 minutes, or 30% to 40% shorter than intermediate-acting neuromuscular blocking drugs. (154, Table 12-6)

58. Mivacurium is dependent on the enzyme plasma cholinesterase for its clearance. Patients who have either atypical plasma cholinesterase or a decreased concentration of plasma cholinesterase will have a prolonged duration of action of mivacurium in a similar manner as succinylcholine. For instance, the administration of an intubating dose of mivacurium in patients who are heterozygous for atypical plasma cholinesterase will result in a prolonged duration of effect by 30% to 50%, whereas patients who are homozygous for atypical plasma cholinesterase will have a prolonged effect for 3 to 4 hours. Although the metabolism of mivacurium is completely independent of the kidneys and liver, patients with liver failure may have a prolonged effect of mivacurium secondary to decreases in the concentration of plasma cholinesterase and a subsequent slower rate of clearance. Patients with renal failure who have been receiving

continuous intravenous infusions of mivacurium may also have a mildly prolonged duration of action of mivacurium to 10 to 15 minutes. (154)

59. Neostigmine is an anticholinesterase that inhibits the activity of both plasma cholinesterase and true cholinesterase. The reversal of the neuromuscular blockade produced by mivacurium may be accomplished with the administration of neostigmine. The benefits of increasing the concentration of acetylcholine available to compete for binding sites on the nicotinic cholinergic receptor in the neuromuscular junction outweigh the inhibition of the activity of plasma cholinesterase in this circumstance, and the actions of mivacurium may be reversed. (154)

60. The administration of mivacurium rapidly and at doses of three times ED_{95} may result in histamine release and associated transient decreases in systemic blood pressure. (154, Table 12-6)

MONITORING THE EFFECTS OF NONDEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

61. The most common method for monitoring the effects of neuromuscular blocking drugs during general anesthesia is through the use of a peripheral nerve stimulator. The peripheral nerve stimulator works by stimulating a motor nerve to conduct an impulse. A mechanically evoked muscle response is then evaluated by the clinician. The mechanical motor response of the muscle reflects the number of muscle fibers that are blocked and provides an indication to the clinician of the degree of neuromuscular blockade. (154-155)

62. A peripheral nerve stimulator may be useful during the administration of neuromuscular blocking drugs during general anesthesia in at least two ways. First, a peripheral nerve stimulator allows the clinician to titrate the neuromuscular blocking drug to optimize skeletal muscle relaxation for surgery without unnecessarily overdosing the patient. Second, a peripheral nerve stimulator may be used as an objective means with which to judge the recovery from neuromuscular blockade at the conclusion of surgery either before or after the antagonism of a nondepolarizing neuromuscular blocking drug with an anticholinesterase drug, such as neostigmine. (154-155)

63. The ulnar nerve and adductor pollicis muscle are the nerve and muscle most commonly used for the evaluation of the neuromuscular blockade produced by neuromuscular blocking drugs through the use of a peripheral nerve stimulator. The adductor pollicis muscle is solely innervated by the ulnar nerve. This means that the only source for motor stimulation of the adductor pollicis muscle is through the mechanical stimulation of the ulnar nerve. Different muscle groups differ in their sensitivities to neuromuscular blocking drugs. The adductor pollicis muscle is more sensitive to the effects of neuromuscular blockers than are the diaphragm or upper airway muscles. (155)

64. When the arm is not available to the anesthesiologist, the facial nerve and orbicularis oculi muscle are often used for the evaluation of the neuromuscular blockade produced by neuromuscular blocking drugs through the use of a peripheral nerve stimulator. Other nerves that may be used include the median, posterior tibial, and common peroneal nerves. (155)

65. In general, the administration of nondepolarizing neuromuscular blocking drugs produces laryngeal muscle relaxation and conditions favorable for intubation of the trachea more rapidly than relaxation of the adductor pollicis muscle as measured by ulnar nerve stimulation. Facial nerve stimulation and measurement of neuromuscular blockade of the orbicularis oculi muscle more closely correlates with laryngeal muscle relaxation and vocal cord paralysis than ulnar nerve stimulation. An exception to the pattern of neuromuscular blockade onset in the various muscles is with the administration of succinylcholine. The administration of this neuromuscular blocking drug results in neuromuscular blockade at the adductor pollicis muscle and the laryngeal muscles at approximately the same time. Thus

the measurement of neuromuscular blockade at the ulnar nerve provides a better indication of vocal cord paralysis when succinylcholine is administered. The diaphragm muscle appears to be resistant to the effects of neuromuscular blocking drugs, such that larger doses of drug are required to produce relaxation of the diaphragm than doses required for relaxation of either the laryngeal muscles, orbicularis oculi, or adductor pollicis muscles. (155-156, Figure 12-6)

66. Some of the mechanical responses evoked by a peripheral nerve stimulator and used to monitor the effects of neuromuscular blocking drugs include a single twitch response, a train-of-four ratio, double burst suppression, tetanus, and posttetanic stimulation. The various methods of evaluation of the mechanically evoked response vary with regard to ease and accuracy. The mechanically evoked response can be evaluated visually, manually by touch, or by recording. (154-155)

67. Depression by 90% or more of a mechanically evoked single twitch response from its control height correlates with adequate neuromuscular blockade for the performance of intraabdominal surgery or tracheal intubation. Greater than 70% of nicotinic cholinergic receptors must be occupied by a nondepolarizing neuromuscular blocking drug to achieve this. (158, Table 12-8)

68. The train-of-four stimulus delivered by a peripheral nerve stimulator is four electrical stimuli at 2 Hz each delivered every 0.5 seconds. The train-of-four stimulus is useful for the evaluation of the degree of neuromuscular blockade based on the premise that each successive electrical stimulus will further deplete stores of acetylcholine in the nerve terminal. In the presence of neuromuscular blockade produced by nondepolarizing neuromuscular blocking drugs, there will be a resultant decrease in the mechanically evoked muscle response with each stimulus. The amount of decrease in the mechanical muscle response correlates with the degree of neuromuscular blockade. Only four twitches are used in the train-of-four stimulus because any further stimulation of the nerve after the fourth does not result in any further depletion of acetylcholine stores at the nerve terminal. (158, Table 12-8)

69. The train-of-four ratio is a calculation of the height of the fourth evoked twitch response divided by the height of the first evoked twitch response of a train-of-four stimulus. For example, if the height of the fourth twitch is one half the height of the first twitch, the train-of-four ratio would be 0.5. The train-of-four ratio reflects how much fade has occurred, which correlates with the degree of neuromuscular blockade. The control, or baseline, train-of-four ratio should be 1.0 before the administration of neuromuscular blocking drugs. This corresponds to a height of the fourth mechanically evoked twitch response being equal to the height of the first evoked twitch response. (158, Table 12-8)

70. A train-of-four ratio of 0.7 or greater correlates with the complete return to the control height of a single twitch response. That is, when the height of the fourth mechanically evoked twitch response is 70% of the height of the first evoked twitch response in a train-of-four stimulus, a single twitch response will have returned to its control height. (158, Table 12-8)

71. After the administration of succinylcholine for a neuromuscular blockade, a phase II neuromuscular blockade may be reflected in the train-of-four response as a train-of-four ratio less than 0.3. The train-of-four response thus shows some fade of the fourth twitch when compared with the first twitch of the train-of-four stimulus when phase II neuromuscular blockade is present. (156, Figure 12-8)

72. Estimation of the train-of-four response by clinicians evaluating the response visually and manually is not very accurate. Although clinicians have difficulty assessing the train-of-four ratio, the assessment of the absolute number of twitches evoked by the train-of-four stimulus is much more reliable. When the first twitch is approximately

35% of the control twitch height, the fourth twitch is able to be detected. This corresponds to a train-of-four ratio of about 0.35. (156-157, Figure 12-8)

73. The double burst suppression stimulus delivered by a peripheral nerve stimulator is two bursts of three 50-Hz electrical stimuli separated by 750 milliseconds between each burst, but it is perceived by the clinician as two separate twitches. The use of the double burst suppression stimulus appears to make the estimation of the fade response easier for clinicians. It is thought that the estimation of the ratio between the two twitches is easier for clinicians because the middle two twitches of the train-of-four response are eliminated. A train-of-four ratio of 0.3 or less is most accurately detected by clinicians when using the double burst suppression stimulus. Accuracy of the estimation of a train-of-four ratio greater than 0.7 is still poor, however. (157)

74. Tetany is a continuous skeletal muscle contraction that occurs secondary to continuous stimulation of the postjunctional receptors. Tetany can be mechanically produced through the use of a peripheral nerve stimulator. The delivery of a continuous electrical stimulus of about 50 Hz for 5 seconds is frequently used in clinical anesthesia practice to induce tetany for the evaluation of neuromuscular blockade. (157-158, Figure 12-10)

75. The normal response to tetany is a sustained muscular contraction. This response is altered by the administration of neuromuscular blocking drugs. Phase I neuromuscular blockade subsequent to the administration of depolarizing neuromuscular blocking drugs, such as succinylcholine, induces a mechanical muscle contraction in response to a tetanic stimulus that is greatly decreased from the control response and does not undergo fade over time. The administration of nondepolarizing neuromuscular blocking drugs induces a mechanical muscular contraction in response to a tetanic stimulus that fades over time. (157-158, Figure 12-10)

76. Posttetanic stimulation refers to the evaluation of a train-of-four response after a tetanic stimulus has been delivered. The mechanical muscle response to a train-of-four stimulus after the delivery of a tetanic stimulus is useful during intense neuromuscular blockade when there is no evoked mechanical response to either a single twitch or a train-of-four stimulus. The clinical use of posttetanic stimulation is derived from the transient enhancement of the mechanical muscle response obtained when a train-of-four stimulus is delivered immediately after a tetanic stimulus. This enhancement is due to an increase in the available stores of acetylcholine in the nerve terminals after a tetanic stimulus and is termed posttetanic facilitation. (157, Figure 12-10)

ANTAGONISM OF NONDEPOLARIZING NEUROMUSCULAR BLOCKING DRUGS

77. The antagonism of the neuromuscular blockade produced by nondepolarizing neuromuscular blocking drugs is achieved through the intravenous administration of anticholinesterases. The anticholinesterases most often used for this purpose are neostigmine and edrophonium. These drugs exert their effect by inhibiting the activity of acetylcholinesterase, the enzyme that hydrolyzes acetylcholine in the neuromuscular junction. As a result of the inhibition of the hydrolysis of acetylcholine, acetylcholine accumulates in the neuromuscular junction. With more acetylcholine available at the neuromuscular junction, the competition between acetylcholine and the nondepolarizing neuromuscular blocking drug is altered such that it is more likely that acetylcholine will bind to the postjunctional receptor. In addition to increasing the amount of acetylcholine available in the neuromuscular junction to compete for sites on the nicotinic cholinergic receptors, acetylcholine also accumulates at the muscarinic cholinergic receptor sites through the same mechanism. (158)

78. Anticholinesterases increase the concentration of acetylcholine available at the muscarinic cholinergic receptors as well as at the nicotinic cholinergic receptors. This may result in profound bradycardia through the stimulation of muscarinic

cholinergic receptors in the heart. To attenuate the cardiac muscarinic effects of anticholinesterases, a peripheral-acting anticholinergic such as atropine or glycopyrrolate is administered intravenously before or simultaneous with the intravenous administration of the anticholinesterase. (156, Table 12-7)

79. Two factors that influence the choice of which anticholinesterase drug to administer to antagonize neuromuscular blockade include the approximate duration of action of the nondepolarizing neuromuscular blocking drug that had been administered and the intensity of the neuromuscular blockade that exists at the conclusion of surgery. (159)

80. Neostigmine and edrophonium are the quaternary ammonium-structured anticholinesterases that are most frequently administered for the antagonism of the effects of nondepolarizing muscle relaxants. Neostigmine should be administered for the antagonism of the effects of nondepolarizing neuromuscular blocking drugs when the neuromuscular blockade is intense and/or when the neuromuscular blocking drug that had been administered is long-acting. This is primarily due to the prolonged duration of effect of neostigmine when compared with the duration of effect of edrophonium. Glycopyrrolate is often paired with neostigmine as the anticholinergic of choice because its delayed cardiac anticholinergic effects more closely parallel the time of onset of the muscarinic effects produced by neostigmine. Conversely, edrophonium has a shorter time of onset and shorter duration of action than neostigmine. Edrophonium should be administered for the antagonism of the effects of nondepolarizing neuromuscular blocking drugs when there has been adequate spontaneous recovery from the effects of these drugs and/or when the nondepolarizing neuromuscular blocking drug that had been administered was short- or intermediate-acting. Atropine is often paired with edrophonium as the anticholinergic of choice because its shorter time of onset is similar to the short onset time of edrophonium. (157, Table 12-7)

81. Confirmation of the recovery from the effects of neuromuscular blockade that have occurred either spontaneously or through the administration of anticholinesterases should be obtained before extubation of the patient's trachea at the conclusion of general anesthesia. Often the mechanical muscle response to a train-of-four stimulus is difficult for the clinician to evaluate manually or visually. When this is the case, the evaluation of the muscular response to a continuous tetanic stimulation may be useful. A sustained muscular contraction to a continuous tetanic stimulus usually indicates a train-of-four ratio greater than 0.7 and is an indication of adequate recovery from neuromuscular blockade. Alternatively, a double burst suppression stimulus may be delivered by the peripheral nerve stimulator to facilitate the clinician's ability to evaluate the degree of fade. Clinical tests that may also be used to evaluate the adequacy of the reversal of neuromuscular blockade include the patient's ability to open the eyes, cough, stick out the tongue, and sustain a head lift for 5 to 10 seconds; grip strength; vital capacity; and maximal inspiratory force. Of these clinical tests, a sustained head lift is considered to be the most sensitive test to evaluate the adequacy of the recovery from neuromuscular blockade. (159)

82. Residual effects of neuromuscular blockers may manifest clinically in awake patients as diplopia, decreased hand grip strength, difficulty swallowing, and difficulty speaking. Patients may also have difficulty sustaining their minute ventilation without assistance. (159)

83. There are several pharmacologic and physiologic factors that may interfere with the antagonism of the neuromuscular blockade produced by neuromuscular blocking drugs. Physiologic factors include abnormalities in the patient's temperature, acid-base status, electrolytes, or metabolism pathways. These may all interfere with the metabolism and clearance of the neuromuscular blocking drug. In particular, renal or liver disease may result in markedly prolonged elimination

times and prolonged clinical effects of certain nondepolarizing neuromuscular blocking drugs. Pharmacologic factors include the concurrent administration of aminoglycoside antibiotics, local anesthetics, volatile anesthetics, magnesium, dantrolene, and cardiac antidysrhythmic agents. Another cause of an apparent inability to antagonize the effects of neuromuscular blocking drugs is not allowing sufficient time to pass for an anticholinesterase to begin exerting its effect. Finally, the lack of a mechanically evoked muscular response to a train-of-four stimulus is an indication that the antagonism of the neuromuscular blockade is not possible. (159)

ADVERSE OUTCOMES FROM INADEQUATE ANTAGONISM OF NEUROMUSCULAR BLOCKADE

84. Residual neuromuscular blockade, obesity, the administration of opioids, long duration of surgery, and emergency and abdominal surgery are all risk factors for patients becoming hypoxic in the immediate postoperative period. (158)

85. The most dangerous time for anesthetic complications in the postoperative period starts with the extubation of the trachea, transport to the postanesthesia care unit (PACU), and the first 30 minutes in the PACU. (158)

86. Sugammadex is a neuromuscular blocking drug antagonist that is under development, but not yet approved by the Food and Drug Administration for use in the United States due to hypersensitivity concerns. It has been approved for use in Europe and other countries. The mechanism of action of sugammadex is through encapsulation and inactivation of steroid muscle relaxants (not atracurium). (159-160)

87. Sugammadex differs from neostigmine in several ways. First, it has no cardiovascular effects and does not require other drugs such as glycopyrrolate. Sugammadex, unlike neostigmine, can reverse a profound neuromuscular blockade. For example, if rocuronium, 1.2 mg/kg is given, its neuromuscular blockade can be completely reversed within minutes (e.g., 5 minutes). In this situation, neostigmine would be ineffective. (159)

88. Sugammadex confers several advantages for the antagonism of neuromuscular blockade. First, a rocuronium-sugammadex combination can be used for rapid sequence induction of anesthesia and subsequent reversal. Second, profound neuromuscular blockade can be achieved and maintained through the end of surgery and still have adequate reversal at the conclusion of surgery. Finally, the incidence of residual neuromuscular blockade can be reduced or eliminated. (159)

Chapter

10 PREOPERATIVE EVALUATION AND MEDICATION

Jennifer E. Hofer, Bobbie Jean Sweitzer

1. What is the purpose of the preanesthetic visit before the day of surgery?
2. How does the anesthesiologist classify a patient's physical status?

HISTORY AND PHYSICAL EXAMINATION

3. How is the patient's functional status determined? Why is it important?
4. Why is the airway examination important?
5. What are the components of the airway examination?

COMORBIDITIES IMPACTING ADMINISTRATION OF ANESTHESIA

6. What are the guidelines for cardiovascular evaluation for patients having noncardiac surgery?
7. How long does the patient need to wait after revascularization to undergo elective noncardiac surgery?
8. Should aspirin be continued perioperatively?
9. What can happen if aspirin is stopped abruptly?
10. What percentage of patients with compensated versus decompensated heart failure will have perioperative cardiac complications?
11. What are the main types of heart failure?
12. What are the common causes of systolic and diastolic dysfunction?
13. What finding on an ECG would suggest diastolic dysfunction?
14. For patients with heart failure, which symptoms should prompt echocardiographic evaluation preoperatively?
15. What further evaluation does a patient with heart failure symptoms at rest (decompensated failure or Class IV) need beyond an echocardiogram?
16. Is there a benefit of routine perioperative evaluation of left ventricular (LV) function before surgery?
17. What are the recommendations for preoperative noninvasive evaluation of LV function?
18. Are all cardiac murmurs associated with valvular pathology?
19. Which cardiac murmurs are always pathologic?
20. What are the clinical clues that suggest a patient may have valvular disease?
21. Which planned anesthetics should prompt the anesthesiologist to want an echocardiogram before proceeding with an anesthetic in a patient with a cardiac murmur?
22. When is an echocardiogram indicated in an asymptomatic patient with a cardiac murmur?
23. Are regurgitant or stenotic valvular lesions better tolerated perioperatively?
24. Does aortic stenosis and aortic sclerosis have similar hemodynamic manifestations?

25. Should patients with valvular abnormalities receive antibiotic prophylaxis to prevent infective endocarditis?
26. Which other conditions need antibiotic prophylaxis against infective endocarditis?
27. Should patients undergoing genitourinary (GU) and gastrointestinal (GI) tract procedures take antibiotic prophylaxis to prevent infective endocarditis?
28. For patients meeting criteria for prophylaxis against infective endocarditis, for which procedures is prophylaxis recommended?
29. What conditions are typically associated with a pacemaker and implantable cardioverter-defibrillator (ICD) placement?
30. How should the ICD be managed in the surgical patient?
31. Will a magnet disable an ICD?
32. Which comorbidities are hypertensive patients at risk of?
33. When should surgery be delayed due to elevated blood pressure (BP)? What is severe hypertension?
34. What is the preoperative BP goal for hypertensive patients?
35. Is there a risk in normalizing BP in hypertensive patients?
36. What are predictors of postoperative pulmonary complications?
37. Is chronic obstructive pulmonary disease (COPD) the greatest risk factor for postoperative pulmonary complications?
38. Does well-controlled asthma increase perioperative complications?
39. How can the risk of bronchospasm after tracheal intubation be decreased in patients with obstructive airway disease?
40. If steroids are given, how much steroid should be administered preoperatively to a patient with persistent airway obstruction?
41. Which types of anesthesia are associated with a greater risk of postoperative pulmonary complications (PPC)?
42. Does preoperative testing predict the risk of PPC?
43. Which maneuvers can reduce PPC rates?
44. What is obstructive sleep apnea (OSA)?
45. Which symptoms and risk factors are associated with OSA?
46. What components of the patient's history or physical examination can identify those at risk of OSA?
47. Which comorbidities are associated with OSA?
48. What impact does OSA have for anesthesia?
49. Should patients having anesthesia bring their continuous positive airway pressure (CPAP) devices to the hospital?
50. What are the American Society of Anesthesiologists' (ASA) published recommendations for perioperative care of patients with OSA?
51. What are the most common causes of dyspnea?
52. How should dyspnea be evaluated?
53. Is renal insufficiency a risk factor for perioperative complications?
54. When should a patient with renal insufficiency receive dialysis before surgery?
55. Must chronic hyperkalemia be corrected in a patient with renal insufficiency?
56. Does radiocontrast medium worsen renal function in normal patients?
57. Can the risk of renal injury be reduced in patients receiving radiocontrast medium?
58. What are the goals of perioperative glucose control in diabetic patients?
59. If a diabetic patient has an Hb A_{1c} of 12 on the day of surgery with a glucose level of 350 g/dL, should the surgery be cancelled?
60. What body mass index (BMI) defines extreme obesity?
61. Which comorbidities are associated with obesity?
62. Does anemia predict perioperative morbidity and mortality?
63. Does a patient with anemia require further evaluation to identify its cause?
64. What perioperative concerns surround a pregnant patient who needs a nonobstetric procedure?
65. Are elderly patients at a higher risk for hospital admission after ambulatory surgery?
66. How does a patient's do not resuscitate (DNR) status transfer from the hospital ward to the operating room?

CONSULTATIONS

67. What is the purpose of a preoperative consultation?
68. Is a consultation letter stating "cleared for surgery" or "low risk" adequate?

TESTING

69. Is preoperative testing indicated for every patient?
70. When should preoperative tests be ordered?
71. Should all patients of a certain age receive a preoperative electrocardiogram (ECG)?
72. Do preoperative ECGs or chest radiographs predict postoperative complications?
73. What are the recommendations for obtaining a preoperative ECG?
74. Do all females of childbearing years require a β-human chorionic gonadotropin (β-hCG) assay prior to surgery?
75. Which types of preoperative tests are useful when evaluating patients with severe comorbidities and undergoing intermediate-high risk procedures?
76. What are the minimal recommendations for testing before anesthesia?

MEDICATIONS

77. Should all medications be continued perioperatively?
78. Should β-adrenergic blockers (BB) be continued preoperatively?
79. Are there medications that can lower cardiac risk for high-risk patients scheduled for elective noncardiac surgery?
80. What are the benefits of statins perioperatively?
81. Can statins be abruptly stopped?
82. Can neuraxial or peripheral anesthesia be performed on a patient taking aspirin or clopidogrel?
83. Should psychiatric medications be continued preoperatively?
84. Should angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) be continued preoperatively?
85. When should low-molecular-weight heparin (LMWH) be discontinued before surgery?
86. How many days before surgery should warfarin be stopped?
87. What should be done if the international normalized ratio (INR) is elevated near the day of surgery?
88. When should patients on warfarin be bridged with LMWH before surgery?
89. In which patients is LMWH contraindicated?
90. How should type 1 and type 2 diabetics be managed preoperatively?
91. Should ultra–long-acting insulin such as glargine be continued on the day of surgery?
92. Does metformin need to be discontinued before the day of surgery?
93. Should oral hypoglycemic drugs be withheld on the day of surgery?
94. Which medications should be continued on the day of surgery?
95. Which medications should be discontinued for surgery?
96. Which herbal medication should not be discontinued abruptly before surgery?
97. Is neuraxial anesthesia contraindicated in patients taking herbal medications?
98. Should monoamine oxidase inhibitors (MAOIs) be discontinued before surgery?
99. Should narcotics, anxiolytics, or nicotine replacement be discontinued before surgery?
100. Should patients taking oral steroids take the steroid on the day of surgery?
101. How much cortisol does a patient typically produce a day?
102. Which patients are at risk for adrenal insufficiency?
103. What risks are associated with high-dose steroids?
104. How should perioperative glucocorticoids be dosed for a patient on chronic steroids?
105. How should anxious patients be premedicated before surgery?
106. What medications can be offered preoperatively to patients with a history of severe postoperative nausea and vomiting (PONV)?
107. Who is at risk for pulmonary aspiration, and how should they be premedicated?

FASTING

108. What are the guidelines for food and fluid intake for adult patients before elective surgery?

FORMULATION OF ANESTHETIC PLAN, ASSESSMENT OF RISK, AND INFORMED CONSENT

109. What does the anesthesiologist consider when choosing an anesthetic technique?
110. What side effects of general anesthesia are commonly disclosed to patients?
111. What side effects of regional anesthesia are commonly disclosed to patients?
112. What is entailed in obtaining informed consent?

ANSWERS*

1. The purpose of the visit is to interview the patient or guardian and establish a medical, medication, and anesthesia history, and to determine the patient's functional capacity. At this visit, the anesthesiologist performs a physical examination focusing on the airway, vital signs, and cardiovascular, pulmonary, and neurologic systems; reviews previous diagnostic tests, consultations, and laboratory results; assigns an ASA-physical status (see question 2); and determines whether further tests are necessary before surgery. An anesthetic plan is formulated and discussed with the responsible adult before informed consent is obtained. Medical therapies are optimized, fasting instructions are provided, and preoperative medication recommendations are given. (165-166, Figure 13-1)

2. The American Society of Anesthesiologists (ASA) Physical Status Classification ranges from ASA 1 to ASA 6. A patient who is classified as ASA 1 is healthy, without disease. ASA 2 is for patients with mild systemic disease that is well controlled. ASA 3 refers to patients with systemic disease sufficiently severe to limit daily activity (renal failure on dialysis or class 2 heart failure). ASA 4 is for patients with a severe disease that is a constant threat to life and seriously limits daily activities (acute myocardial infarction or respiratory failure requiring mechanical ventilation). ASA 5 refers to moribund patients likely to die in less than 24 hours with or without surgery. ASA 6 is reserved for brain-dead patients who are organ donors. The letter E is added to a classification if the surgical procedure is an emergency. (Table 13-1)

HISTORY AND PHYSICAL EXAMINATION

3. A patient's functional capacity is measured in metabolic equivalents (MET). One MET is equivalent to the consumption of 3.5 mL O_2/kg/min. A patient able to eat, get dressed, and work at a computer has a MET of 1. A patient who can walk two blocks has a MET of 3. Climbing one flight of stairs equals a MET of 5; a MET of 10 is running or jogging briskly. A MET of 12 is achieved with running rapidly for long distances. A patient's functional capacity predicts outcome, perioperative complications, and indicates the need for further evaluation. (166, Table 13-2)

4. The airway examination is performed to assist in predicting the ease of hand mask ventilation and endotracheal intubation of the patient. If difficult airway management is predicted, then necessary equipment can be set up and skilled personnel alerted and available on the day of surgery. (Figure 13-2, Table 13-3)

5. During the airway examination the following are assessed: the condition of the teeth, the ability of the patient to advance or protrude the mandibular incisors; the tongue size; visibility of the uvula, tonsils, soft palate, or hard palate only

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

(Mallampati classification I-IV); the presence of facial hair; the thyromental distance; and the length, thickness, and range of motion of the neck. (Figure 13-2, Table 13-3)

COMORBIDITIES IMPACTING ADMINISTRATION OF ANESTHESIA

6. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines have decreased the number of recommendations for testing and revascularization. The approach to this algorithm should stop at the first step that applies to the patient.

   Step 1 (emergency surgery): if the patient has ischemic heart disease and needs emergency surgery, the focus is on perioperative surveillance (serial ECG, enzymes, monitoring) and risk reduction (β-adrenergic blockers, statins, pain control), not on preoperative testing.

   If the surgery is not an emergency, then the algorithm is as follows:

   Step 2 (active cardiac conditions): if the patient has an active cardiac condition (unstable angina, acute myocardial infarction, recent myocardial infarction if other myocardium is at risk, decompensated heart failure, significant arrhythmias, or severe valvular disease), surgery should be postponed until the active cardiac condition is stabilized or corrected.

   Step 3 (low-risk surgery): a patient without an active cardiac condition undergoing a low-risk surgery (superficial or endoscopic, cataract, breast, or ambulatory) may proceed to surgery without further testing.

   Step 4 (good functional capacity): if the patient has a MET of 4 or more (refer to question 3), and is asymptomatic, the patient may proceed to surgery without further testing.

   Step 5 (poor functional capacity): if the patient has poor functional capacity and needs intermediate-risk or vascular surgery, then important clinical predictors (not increased age or elevated blood pressure) are used to determine if more testing is necessary. The five important clinical predictors based on the revised cardiac risk index (RCRI) include ischemic heart disease, compensated or prior heart failure, cerebrovascular disease (stroke, transient ischemic attack), diabetes mellitus, and renal insufficiency. If no clinical predictors are present, the patient may proceed to surgery without further testing. If one or more clinical predictors are present, the patient may proceed to surgery with heart rate control, or noninvasive testing may be considered before surgery if it will change management. (166, Figure 13-3)

7. How long the patient needs to wait after revascularization to undergo elective noncardiac surgery depends on the type of revascularization and the associated period of dual antiplatelet therapy to prevent thrombosis or restenosis. For percutaneous coronary intervention (PCI) without stenting, 2 weeks of dual antiplatelet therapy is required. If a drug-eluting stent (DES) is placed, 12 months of aspirin and thienopyridine therapy (clopidogrel or ticlopidine) are required; a bare metal stent (BMS) requires 1 month of dual therapy. Elective surgical procedures should be delayed past this high-risk period. If a patient with a DES requires a procedure that mandates the discontinuation of thienopyridine therapy, aspirin should be continued perioperatively and the thienopyridine restarted as soon as possible. During the preanesthetic visit, the type of stent (DES or BMS) should be identified and managed perioperatively with a cardiologist familiar with these stents, especially to prevent premature withdrawal of antiplatelet drugs. The patient should be made aware of the risks associated with premature discontinuation of the drugs, including stent thrombosis, myocardial infarction, and death. If stent thrombosis does occur, it is best treated in the immediate postoperative period by percutaneous coronary intervention. (169-170, 180, Table 13-4, Figure 13-4)

8. Patients taking aspirin for primary prevention (no known vascular disease but only to prevent ischemic heart disease or stroke) should stop aspirin 7 days before

the procedure. If aspirin is for secondary prevention (for known vascular disease of any type, such as after myocardial infarction, acute coronary syndrome, stent, stroke, or peripheral arterial disease) aspirin should be continued perioperatively unless the procedure is associated with bleeding into a closed space (e.g., intracranial neurosurgery), in which case aspirin is stopped 7 days before the procedure.

If the patient is taking aspirin and clopidogrel, and the condition is low risk (stroke, uncomplicated myocardial infarction, PCI without stenting, or past the high-risk period with stents (see question 8), it is acceptable for the patient to stop clopidogrel 7 days before the surgery and continue aspirin perioperatively. If the patient is taking aspirin and clopidogrel, and the situation is high risk (<2 weeks after PCI without stents, <4 weeks after BMS, <12 months after DES, high-risk stents) then dual antiplatelet therapy is continued unless there is risk of bleeding into a closed space (intracranial), in which case the risk/benefits of antiplatelets are evaluated. If aspirin is stopped, it is best reinstituted early in the postoperative period. (169, 179-180, Table 13-4, Figure 13-4)

9. There is an increased risk of vascular events (including acute coronary syndromes and acute cerebral events) if aspirin is stopped perioperatively. This increase in adverse events may be from a rebound hypercoagulable state when aspirin is withdrawn. (179)

10. The risk of perioperative cardiac complications is 5% to 7% with compensated heart failure and 20% to 30% or higher with decompensated heart failure. (170)

11. Systolic dysfunction (decreased ejection fraction from decreased contractility) and diastolic dysfunction (increased filling pressures with abnormal relaxation but preserved contractility and ejection fraction), or a combination of systolic and diastolic dysfunction. (170-171)

12. Systolic dysfunction is most commonly caused by ischemic heart disease; diastolic dysfunction is associated with hypertension. (171)

13. Left ventricular hypertrophy on an ECG may suggest diastolic dysfunction. (171)

14. Symptoms of recent weight gain, complaints of shortness of breath, fatigue, orthopnea, paroxysmal dyspnea, nocturnal cough, peripheral edema, recent hospitalizations, or necessary changes in medical management prompt echocardiographic evaluation. (171)

15. A patient with heart failure symptoms at rest needs evaluation by a cardiologist before undergoing anesthesia. (171)

16. Routine perioperative evaluation of LV function in patients is not recommended. (Table 13-5)

17. Class IIA (reasonable to perform) recommendations exist for evaluation of LV function in the following patients: patients with dyspnea of unknown origin, with current or previous heart failure with worsening dyspnea, or with another change in clinical status if the LV function has not been evaluated in the previous 12 months. Class IIB (may be considered) recommendations suggest reassessment of LV function in clinically stable patients with previously documented cardiomyopathy, although the recommendations are not well established. (Table 13-5)

18. Not all cardiac murmurs are pathologic. Functional murmurs arise from turbulent flow across the aortic or pulmonary outflow tracts in high output states, such as hyperthyroidism, pregnancy, or anemia. Functional murmurs are not associated with valvular abnormalities. (171, Table 13-6)

19. Diastolic murmurs are always pathologic and require evaluation. (171)

20. Important factors for valvular disease include advanced age, coronary artery disease (CAD), a history of rheumatic fever, volume overload, pulmonary disease, cardiomegaly, an abnormal ECG, or a murmur. (171, Table 13-6)

21. Before general anesthesia, or spinal anesthesia (contraindicated if severe aortic stenosis is present), an anesthesiologist would evaluate a cardiac murmur by echocardiogram. (171)

22. Per ACC/AHA guidelines, there is evidence that echocardiography is useful in murmurs associated with ejection clicks, murmurs that radiate to the neck or back, or grade 3 or louder systolic murmurs. Obtaining an echocardiogram for a patient with a murmur and an abnormal ECG or chest radiograph is a class IIa recommendation; obtaining an echocardiogram for a patient with a grade 2 or softer midsystolic murmur, which is considered innocent or functional by an experienced observer, is a class III recommendation (i.e., not recommended). (171, Table 13-6)

23. Regurgitant valvular lesions are better tolerated perioperatively than stenotic disease. (171)

24. Systolic ejection murmurs are heard in both aortic stenosis and aortic sclerosis. Aortic sclerosis (a calcified valve without narrowing) is associated with a loud murmur, and is more prevalent than aortic stenosis; however, it is aortic stenosis that is associated with a significant compromise in hemodynamics. Patients with severe or critical aortic stenosis should always undergo cardiac evaluation unless the procedure is an emergency. Aortic stenosis is associated with a high risk for perioperative complications. Both conditions are independent predictors of CAD. (171)

25. No, antibiotic prophylaxis is no longer recommended for patients with abnormalities on native valves (e.g., aortic stenosis, tricuspid regurgitation, mitral stenosis from rheumatic heart disease). However, patients with previous episodes of infective endocarditis or a transplanted heart with valvular abnormalities do require infective endocarditis prophylaxis. (171, Table 13-7, Table 13-8)

26. Antibiotic prophylaxis is needed for patients with a prosthetic cardiac valve, previous infective endocarditis, unrepaired congenital heart disease, repaired congenital defects within 6 months of the repair, or lifelong if a residual defect remains. (171, Table 13-8)

27. No, GU and GI tract procedures, unless infection is present, do not require antibiotic prophylaxis against infective endocarditis. (Table 13-7)

28. Antibiotic prophylaxis against infective endocarditis is recommended for all dental procedures that involve manipulation of gingival tissues or the periapical region of the teeth or perforation of oral mucosa, and for procedures on the respiratory tract, or through infected tissue. (Table 13-7)

29. Patients with heart failure, ischemic or valvular disease, cardiomyopathies, or potentially lethal arrhythmias often have a pacemaker or ICD placed. (171-172)

30. First, the patient should carry a wallet card with pertinent information regarding the device. Interference with the device may be caused by monitors, ventilators, chest prepping, cautery, and central line placement. If interference causes unnecessary cardioversion, or an unexpected discharge, patient movement that occurs during a delicate intracranial, spinal, or ocular procedure may be catastrophic. Because of concern for interference causing unexpected discharge and patient movement, ICDs are typically deactivated during procedures. Patients must be connected to monitors, and equipment for cardioversion must be available when ICDs are programmed off. (171-172)

31. A magnet will suspend antishock therapies only. Magnets disable only the antitachycardia function, not the pacing function of an ICD. If the ICD is disabled

by a magnet, a defibrillator must be available as an alternate form of antishock therapy. Once the magnet is removed, the antitachycardia function may not resume in some ICD models. Additionally, some ICDs will not respond to a magnet. If an ICD is reprogrammed or if a magnet is used at any time, the device must be reinterrogated and reenabled before the patient leaves a monitored setting. (172)

32. Hypertensive patients may develop end-organ damage depending on the severity and duration of hypertension. Ischemic heart disease, heart failure, renal insufficiency, and cerebrovascular disease are common in hypertensive patients. (172)

33. Severe hypertension is systolic BP greater than 200 mm Hg or diastolic BP greater than 115 mm Hg. Surgery should be delayed for patients with severe hypertension until the BP is less than 180/110 mm Hg. (172)

34. The preoperative goal is to restore BP to normal levels before surgery if significant end-organ damage is present or intraoperative hypotensive techniques are planned. (172)

35. If BP is lowered rapidly and aggressively, a risk of cerebral or coronary ischemia exists. Extreme lowering of BP resulting in intraoperative hypotension is more dangerous than hypertension. (172)

36. Predictors of postoperative pulmonary complications include advanced age, heart failure, COPD, smoking, poor general health (impaired sensorium, functional dependency), and obstructive sleep apnea. (172-174, Table 13-9)

37. No, COPD is not the greatest risk factor for postoperative pulmonary complications. Heart failure, advanced age, and poor general health are associated with a greater risk of postoperative pulmonary complications than is COPD. However, the more severe the COPD, the greater the risk. (173, Table 13-9)

38. No, well-controlled asthma does not increase perioperative complications; however, patients with poorly controlled asthma as evidenced by wheezing are at a higher risk of complications. (172-173)

39. Administration of corticosteroids and β-adrenergic agonists preoperatively decreases the incidence of bronchospasm upon tracheal intubation. (173-174)

40. Prednisone 0.5 to 1 mg/kg orally for 1 to 4 days before surgery for patients likely to have endotracheal intubation is recommended for patients with persistent airway obstruction despite the use of inhaled medication. (174)

41. General anesthesia is associated with a greater risk of PPC. Neuraxial anesthesia and peripheral nerve blocks are associated with a lower risk of PPC. In addition, percutaneous interventions (endovascular repairs) have a lower risk of PPC than open interventions. (174, Table 13-9)

42. Routine pulmonary function tests, chest radiography, or arterial blood gases do not predict PPC risk. (174)

43. PPC rates can be decreased by maximizing airflow in obstructive disease, treating infections and heart failure, and using lung expansion maneuvers such as coughing, deep breathing, incentive spirometry, positive end-expiratory pressure (PEEP), and continuous positive airway pressure (CPAP). (174)

44. OSA is intermittent airway obstruction during sleep. (174, Figure 13-5)

45. OSA is associated with snoring, daytime sleepiness, hypertension, obesity, and a family history of OSA. (174, Figure 13-5)

46. The STOP-Bang questionnaire can be used to identify patients at risk for OSA. The questions address snoring, daytime fatigue, treatment for high blood pressure,

observed apneas during sleep, BMI of 35 or more, age of 50 or over, neck circumference greater than 15.7 inches (40 cm), and male gender. Patients are at high risk for OSA if they answer yes to three or more items. (174, Figure 13-5)

47. Patients with OSA have increased rates of diabetes, hypertension, atrial fibrillation, bradyarrhythmias, ventricular ectopy, stroke, heart failure, pulmonary hypertension, dilated cardiomyopathy, and CAD. (174, Figure 13-5)

48. Ventilation by mask, direct laryngoscopy, endotracheal intubation, and fiber-optic visualization of the airway are more difficult in patients with OSA. Patients with OSA may have perioperative airway obstruction, hypoxemia, atelectasis, ischemia, pneumonia, and prolonged hospitalizations. (174-175, Figure 13-5)

49. Yes, if CPAP is used at home, the patient should bring the home CPAP device on the day of the procedure for perioperative use. (174)

50. The ASA recommends that patients with OSA have preoperative diagnosis and treatment. The appropriateness of ambulatory surgery should be reviewed since patients with OSA are at a higher risk for perioperative complications and prolonged hospitalization than are patients without OSA. (175, Figure 13-5)

51. The most common pathologic causes of dyspnea are COPD, asthma, and heart failure. Deconditioning is also a common nonpathologic cause of dyspnea. (175, Figure 13-6)

52. In a patient with dyspnea, history and physical examination determine whether the cause is cardiac, pulmonary, both, or other. Dyspnea of cardiac origin may be caused by myocardial ischemia, angina, heart failure, valvular disease, or pericardial disease, such as tamponade or constrictive pericarditis. Evaluation includes an ECG, chest radiograph, stress test, echocardiogram, and a brain natriuretic peptide level. If the etiology of dyspnea is suspected to be pulmonary, this may be caused by COPD, asthma, pneumonia, lung injury, pulmonary embolism, pulmonary hypertension, restrictive lung disease, pulmonary fibrosis, or pleural disease. Evaluation includes a chest radiograph, arterial blood gases, pulmonary function testing, and chest computed tomography. Other causes for dyspnea include anemia, deconditioning, renal failure, neuromuscular disease, hypothyroidism, and psychogenic. For these causes, a complete blood count, blood urea nitrogen, creatinine, electrolytes, thyroid function tests, and comprehensive exercise testing should be obtained. Once the cause of the dyspnea is identified and a diagnosis made, treatment can be implemented to improve the patient's medical condition and decrease the risk of perioperative complications. (175, Figure 13-6)

53. Yes, renal insufficiency is the strongest predictor of perioperative worsening of renal function. It is also equal to CAD as a risk factor for perioperative cardiac complications. (175)

54. Dialysis should be performed within 24 hours of surgery, but not immediately before to avoid acute volume depletion and electrolyte alterations. (175)

55. If the potassium level is less than 6 mEq/dL and within the range of a patient's established levels, then chronic hyperkalemia may not need to be corrected. (175)

56. Radiocontrast medium transiently decreases the glomerular filtration rate (GFR) in almost all patients, but patients with diabetes or renal insufficiency are at highest risk. (175)

57. The risk of renal injury from radiocontrast medium may be reduced by alkalinizing renal tubular fluid with sodium bicarbonate or by simple hydration in patients with a GFR less than 60 mL/kg/min. (175)

58. Perioperative glucose control in diabetic patients focuses on preventing hypoglycemia during fasting, and preventing extreme hyperglycemia and ketosis. (175-176)

59. Targeting tight glucose control in the immediate perioperative period is not likely to substantially impact outcomes in diabetics having surgery. No data support cancellation of procedures for any increased level of blood glucose or even treatment of high levels for noncardiac surgery cases. Perioperative intervention is warranted if a patient has hypoglycemia (glucose $<$50 g/dL). Chronically elevated blood sugars are associated with perioperative morbidity. Long-term optimization of diabetes should be considered for high-risk procedures (e.g., joint replacement). (175-176)

60. A BMI of greater than 40 defines extreme obesity. (176)

61. Obesity is associated with OSA, heart failure, diabetes, hypertension, pulmonary hypertension, difficult airway management, and decreased arterial oxygenation. (176)

62. Anemia is a marker for an increased risk of perioperative death, and a predictor of worse short- and long-term outcomes. (176)

63. For an elective procedure with expected blood loss or anticoagulation, anemia should be evaluated preoperatively. If a patient is asymptomatic with chronic anemia and has no history of CAD, and is undergoing a low-risk procedure, then transfusion is not warranted unless the hemoglobin is less than 6 g/dL. If the cause of the anemia is unknown, an evaluation is indicated. A patient with sickle cell disease should be evaluated by a hematologist perioperatively to guide therapy. (176)

64. Pregnant patients may require fetal monitoring, and the potential for preterm labor or delivery should be anticipated. Perioperative plans should be confirmed with the patient's obstetrician. (176)

65. Patients older than 85 years, and patients with a history of hospital admission within the previous 6 months, are at high risk for postoperative admission after ambulatory surgery. (176)

66. A patient has the right to self-determination in the perioperative period. DNR policies should be reviewed with the patient or the patient's surrogate before surgery and modified as needed to uphold the patient's wishes. There are three parts to the perioperative DNR (A, B, and C). Choice A is full attempt at resuscitation. This choice requests full suspension of existing directives during the anesthetic and immediate postoperative period, thereby consenting to the use of any resuscitation procedures to treat clinical events during this time. Choice B is a limited attempt at resuscitation, which may apply or reject certain specific resuscitation procedures (e.g., chest compressions, defibrillation, tracheal intubation). Choice C is a limited attempt at resuscitation defined with regard to the patient's goals. This choice allows the anesthesiologist and surgical team to use clinical judgment in determining which resuscitation procedures are appropriate in the context of the situation and the patient's stated goals. (176, Figure 13-7, Table 13-10)

CONSULTATIONS

67. The purpose of a preoperative consultation is to diagnose, evaluate, and improve a new or poorly controlled condition, and to create a clinical risk profile to help guide the patient, anesthesiologist, and surgeon to make management decisions. (176)

68. A thorough consultation should summarize a patient's medical problems, condition, and the results of diagnostic tests and provide therapeutic recommendations to help the anesthesiologist provide a safe anesthetic. (176)

TESTING

69. No, preoperative testing is not indicated for every patient. Preoperative tests without specific indications lack utility and may lead to patient injury because of unnecessary interventions, delay of surgery, anxiety, and even inappropriate therapies. (176, 178)

70. Preoperative tests should be ordered if the results will impact the decision to proceed with the planned procedure or alter the care plans. Based on a patient's history (e.g., increased dyspnea on exertion, new onset chest pain, syncope), tests are ordered to establish a diagnosis, evaluate a worsening condition, or aid in preoperative decisions and the management of patients with severe comorbidities. (176, 178)

71. No, age is not an indication for a preoperative ECG. (176, Table 13-11)

72. No, neither preoperative ECGs or chest radiographs predict postoperative complications beyond information available from the patient's history and examination. (176, 178, Table 13-11)

73. The class I recommendation (procedure is indicated) for ordering a preoperative ECG is for patients with at least one RCRI clinical risk factor (ischemic heart disease, heart failure, cerebrovascular disease, diabetes, renal insufficiency) who are undergoing vascular surgery procedures, and for patients with known coronary heart disease (CHD), peripheral arterial disease, or cerebrovascular disease who are undergoing intermediate-risk surgical procedures. The class IIa recommendations (procedure is reasonable to perform) include patients with no RCRI clinical risk factors who are undergoing vascular surgical procedures. Class IIb recommendations (procedure may be considered) include patients with at least one RCRI clinical risk factor who are undergoing intermediate-risk procedures. Class III recommendations (procedure should not be performed because it is not helpful) include asymptomatic patients undergoing low-risk surgical procedures. (176, 178, Table 13-11)

74. Pregnancy testing should be offered to women. Some facilities make it mandatory before anesthesia; other facilities allow women to decline testing. (178, Table 13-12)

75. The recommendations are to check the following: albumin level if a patient has anasarca, liver disease, malnutrition, or malabsorption; a complete blood count (CBC) with platelets if there is alcohol abuse, anemia, dyspnea, hepatic or renal disease, malignancy, malnutrition, personal history of bleeding, poor exercise tolerance, or recent chemotherapy or radiation therapy; creatinine level if the patient has renal disease; chest radiograph if the patient has an active, acute, or chronic pulmonary symptom such as a cough, dyspnea, abnormal unexplained physical findings on chest examination, decompensated heart failure, malignancy within the thorax, or radiation therapy (to chest, breasts, lungs, thorax); an ECG if there is alcohol abuse, an active cardiac condition, an ICD, OSA, pacemaker, pulmonary hypertension, radiation therapy, severe obesity, syncope, or use of amiodarone or digoxin; electrolytes if there is alcohol abuse, cardiovascular, hepatic, renal or thyroid disease, diabetes, malnutrition, or use of digoxin or diuretics; glucose level if the patient has diabetes, is severely obese, or uses steroids; liver function tests (LFTs) if there is a history of alcohol abuse, hepatic disease, recent hepatitis exposure, or an undiagnosed bleeding disorder; a platelet count if there is a history of alcohol abuse, hepatic disease, bleeding disorder, hematologic malignancy, recent chemotherapy or radiation therapy, or thrombocytopenia; a prothrombin time (PT) if there is a history of alcohol abuse, hepatic disease, malnutrition, bleeding disorder (personal or familial), or use of warfarin; a partial thromboplastin time if there is a bleeding disorder (personal or familial), undiagnosed hypercoagulable state, or use of unfractionated heparin; thyroid-stimulating hormone, triiodothyronine, and thyroxine test if there is a goiter, thyroid disease, unexplained dyspnea, fatigue, palpitations, or tachycardia; and a urinalysis if a urinary tract infection is suspected. (178, Table 13-2)

76. A creatinine level should be checked within 3 months if a patient is to receive an injection of contrast dye. A hemoglobin/hematocrit should be checked if the surgery has the potential for significant blood loss, and a type and screen should be obtained if there is a likelihood of transfusion. On the day of surgery it may be useful to obtain a potassium level in a patient with end-stage renal disease, and a glucose determination in a patient with diabetes, although no absolute level of either potassium or glucose has been determined to preclude surgery and anesthesia. The benefits of the procedure must be balanced against the risk of proceeding in a patient with abnormal results. An ECG is indicated if the patient has an active cardiac condition such as decompensated heart failure, arrhythmia, chest pain, or murmur. (178, Table 13-13)

MEDICATIONS

77. Perioperative medications should be evaluated on a case by case basis. Generally, cardiac medications, antihypertensive drugs, and nonloop diuretics when taken for hypertension are continued preoperatively. If ACEIs or ARBs are continued, doses of induction and other anesthetic drugs may be altered, and vasopressin should be available to prevent or mitigate hypotension. (178-184, Table 13-14)

78. There are class I recommendations that BB should be continued preoperatively in patients who take them to treat angina, symptomatic arrhythmias, or hypertension. (179, Table 13-14, Table 13-15)

79. Minimizing risk for high-risk patients includes postponing elective surgery to optimize BB and statin therapy. (179)

80. Statins reduce the length of hospital stay, risk of stroke, renal dysfunction, myocardial infarction, and death. Serious consideration should be given to starting a statin if the patient has risk factors for or has known atherosclerotic disease. (179)

81. Abruptly stopping statins may be associated with an increased risk, including death. (179)

82. According to the American Society of Regional Anesthesia (ASRA), neuraxial and peripheral anesthesia is safe for patients taking aspirin. However, since the risk of spinal hematoma is unknown for patients taking clopidogrel, ASRA guidelines suggest discontinuation of clopidogrel 7 days before a planned neuraxial blockade. (180)

83. Yes, antidepressants, antianxiety, and psychiatric medications including MAOIs should be continued preoperatively. Anesthesia management may need to be altered for patients taking MAOIs. (183, Table 13-14)

84. Continuing ACEIs or ARBs prior to surgery may contribute to hypotension under anesthesia. These medications may be discontinued 12 to 24 hours before surgery if taken only for hypertension, especially if the surgical procedure will be lengthy; there will be significant blood loss or fluid shifts; or planned administration of general anesthesia. Also, if the patient is on multiple antihypertensive medications and has well-controlled blood pressure, ACEi or ARBs may be considered for discontinuation 12 to 24 hours before the procedure. (178, Table 13-14)

85. LMWH is discontinued 12 to 24 hours (12 hours if prophylactic dosing 0.5 mg/kg/day, 24 hours if therapeutic dosing 1 mg/kg/day) before procedures with a risk of bleeding or planned neuraxial blockade. (180, Table 13-16)

86. If the INR is 2 to 3, warfarin administration should be stopped 5 days before surgery (unless the procedure is minor such as cataract surgery without bulbar block) to allow the INR to decrease to within reference limits. (180, Table 13-14, Table 13-16)

87. If the INR is measured a day or two before surgery and is greater than 1.8, a small dose of vitamin K (1 to 5 mg orally or subcutaneously) can reverse anticoagulation. (180, Table 13-16)

88. Patients on warfarin should be bridged with LMWH perioperatively if they have had an acute arterial or venous thromboembolism 1 to 3 months before an operation, if the procedure cannot be postponed, if they have a mechanical heart valve, or if they have high-risk hypercoagulable states. (180, Table 13-16)

89. LMWH is typically contraindicated in patients with creatinine clearance less than 40 mL/min, body weight greater than 150 kg, porcine allergy, heparin-induced thrombocytopenia, or patients with a history of bleeding complications while on LMWH. (180, Table 13-16)

90. Type 1 diabetics have an absolute insulin deficiency and require insulin to prevent ketoacidosis even if they are not hyperglycemic. Type 2 diabetics are often insulin-resistant and prone to extreme hyperglycemia. Both type 1 and type 2 diabetics should discontinue intermittent short-acting regular insulin with the exception of the insulin pump. The insulin pump should be continued at the lowest basal rate, which is generally the nighttime dose. Insulin should be discontinued if the blood sugar level is less than 100. Type 1 diabetics should take half of their usual intermediate- to long-acting morning insulin (lente or NPH) the day of surgery to avoid ketoacidosis. Type 2 diabetics take none or up to a half dose of intermediate- to long-acting insulin (lente or NPH) or a combination of a 70/30 preparation insulin on the day of surgery. (180-182, Table 13-14)

91. Yes, glargine should be continued on the day of surgery, but the dose should be decreased if it is 1 unit/kg or more. (182, Table 13-14)

92. No, metformin does not need to be discontinued before the day of surgery and will not cause hypoglycemia during fasting periods of 1 to 2 days. There is no risk of lactic acidosis with metformin in patients with functioning liver and kidneys. Metformin is not administered postoperatively until the risk of lactic acidosis has passed. (182-183, Table 13-14)

93. Yes, to avoid potential hypoglycemia in fasting patients from some oral agents, these medications are generally held on the day of surgery. (182-183, Table 13-14)

94. On the day of surgery patients should continue asthma medications, birth control pills, cardiac medications, triamterine and hydrochlorothiazide if used for hypertension (while loop diuretics are typically withheld), eye drops, gastrointestinal reflux medications, seizure medications, steroids (oral or inhaled), thyroid medications, and autoimmune medications such as methotrexate if there is no risk of renal failure (while entanercept, infliximab, and adalimumab are generally discontinued). Patients may continue COX-2 inhibitors (unless the surgeon is concerned about bone healing), estrogen compounds when used for birth control or cancer therapy, and narcotics for pain or addiction. (178-184, Table 13-14, Table 13-15)

95. Herbals and nonvitamin supplements should be discontinued 7 to 14 days before surgery. The administration of nonsteroidal antiinflammatory drugs should be discontinued 48 hours before surgery. Topical creams, ointments, and Viagra should be discontinued 24 hours before surgery. Vitamins, minerals, and iron should not be taken on the day of surgery. Sildenafil if taken for right heart failure or pulmonary hypertension should be continued perioperatively. (178-184, Table 13-14)

96. Valerian is a central nervous system depressant, which may cause a benzodiazepine-like withdrawal when abruptly discontinued. It is safest to taper this medication. (183)

97. Herbal therapy alone is not a contraindication to neuraxial or regional anesthesia per ASRA guidelines. (183)

98. MAOIs have a long duration of action, approximately 3 weeks. Discontinuation of MAOIs may produce severe depression or result in suicide. The safest alternative is to continue MAOIs and adjust the anesthetic plan. (183)

99. Patients should continue any narcotic pain medications to prevent withdrawal symptoms and discomfort. Anxiolytics are continued as well. Drugs used to treat addiction, such as methadone or nicotine-replacement therapies, are also continued. (183-184, Table 13-14)

100. Yes, patients taking oral steroids should continue the steroid on the day of surgery. (183-184)

101. A normal daily adrenal output of cortisol is 30 mg, which is equivalent to 5 to 7.5 mg of prednisone. (183)

102. The hypothalamic-pituitary axis (HPA) may be suppressed in patients taking 5 to 20 mg/day of prednisone or its equivalent for more than 3 weeks. The HPA is usually suppressed with more than 20 mg/day of prednisone for more than 3 weeks. The risk of adrenal insufficiency remains for up to 1 year after the cessation of high-dose steroids. A patient with a suppressed HPA may need supplemental perioperative steroids if his or her HPA cannot increase the output of glucocorticoids during the period of surgery, trauma, or infection. (183)

103. High-dose steroids are associated with infections, psychosis, poor wound healing, and hyperglycemia. (183)

104. For a minor procedure (e.g., inguinal herniorrhaphy), the target hydrocortisone equivalent is 25 mg/day, so additional supplementation is not necessary and the patient should just take their usual daily dose of steroid. For a moderate stress surgical procedure (colon resection, total joint replacement, lower extremity revascularization) the target hydrocortisone equivalent is 50 to 75 mg/day for 1 to 2 days. The patient should take their usual daily dose of steroid, receive 50 mg hydrocortisone intraoperatively, then 20 mg hydrocortisone every 8 hours through postoperative day 1, then resume their home dosing of steroid. If a major surgery is planned (pancreatoduodenectomy, esophagectomy), then the target hydrocortisone equivalent is 100 to 150 mg/day for 2 to 3 days. The patient should take their usual daily dose of steroid, receive 50 mg hydrocortisone intraoperatively, and continue with 50 mg hydrocortisone every 8 hours through postoperative day 2. After postoperative day 2, they should then resume their home dose of steroid. (183, Table 13-17)

105. Premedication for anxious patients before surgery may include a short course of benzodiazepines in the days preceding surgery and the day of the operation, or opioids in patients with preoperative pain or discomfort associated with regional anesthesia or insertion of invasive monitors before the induction of anesthesia. (183-184, Table 13-18)

106. Patients at risk for PONV may be prescribed a scopolamine patch to be placed 2 to 4 hours preoperatively. Scopolamine is contraindicated in patients with closed angle glaucoma. (184, Table 13-18)

107. Patients at increased risk for pulmonary aspiration include parturient patients, patients with intraabdominal masses, nonfasting individuals, patients with an incompetent lower esophageal sphincter with reflux, symptomatic hiatal hernia, diabetes mellitus, gastric motility disorders, anticipated difficult airway, bowel obstruction, and ascites. Alteration of gastric contents to increase pH and limit the severity of potential pulmonary aspiration can be achieved with H_2 antagonists, proton pump inhibitors, and non-particulate antacids, along with prokinetic agents to stimulate gastric emptying. (184)

FASTING

108. Up to 8 hours prior to surgery, any food or fluid may be consumed. For patients without risk factors for pulmonary aspiration (see question 107) the following applies: up to 6 hours before surgery, the patient may have a light meal (toast and clear liquids), infant formula, or nonhuman milk; up to 4 hours before surgery, breast milk may be consumed; up to 2 hours before surgery, the patient may take clear liquids without milk, pulp, or alcohol. During the 2 hours before surgery, no solids or liquids may be taken orally. If the patient has risk factors for pulmonary aspiration, no food or fluid should be consumed within 8 hours of the surgery. (184, Table 13-19)

FORMULATION OF ANESTHETIC PLAN, ASSESSMENT OF RISK, AND INFORMED CONSENT

109. The anesthesiologist considers the patient's coexisting diseases, the site of surgery, position of the patient during surgery, risk of aspiration, age of the patient, patient cooperation and preference, anticipated ease of airway management, coagulation status, and the patient's previous response to anesthesia. (185, Table 13-20)

110. With general anesthesia, side effects that occur frequently but have minimal consequences include oral or dental damage, sore throat, hoarseness, postoperative nausea/vomiting, drowsiness/confusion, and urinary retention. Side effects of general anesthesia that occur infrequently but have severe consequences include intraoperative awareness, visual loss, aspiration, organ failure, malignant hyperthermia, drug reactions, failure to wake up/recover, and death. (Table 13-22)

111. With regional anesthesia, side effects that occur frequently but with minimal impact include prolonged numbness/weakness, postdural puncture headache, and failure of technique. Side effects of regional anesthesia that occur infrequently but with severe consequences include bleeding, infection, nerve damage/paralysis, persistent numbness/weakness, seizures, coma, and death. (Table 13-22)

112. Informed consent involves the indications for the treatment in terms a layperson can understand, and elucidation of alternatives. When an anesthesiologist obtains informed consent prior to the day of surgery, anxiety is lower in patients before their operation. (185)

Chapter

11 CHOICE OF ANESTHETIC TECHNIQUE

Ronald D. Miller, Tula Gourdin

1. What should be accomplished in the preoperative evaluation and visit by the anesthesiologist according to the standard adopted by the American Society of Anesthesiologists?
2. What are some important aspects that should be included in the preoperative medical evaluation of the surgical patient?

ANESTHETIC TECHNIQUE

3. What are the several anesthetic options available to the anesthesia provider?
4. Name some considerations that influence the choice of anesthetic technique.
5. What are some of the unpleasant side effects associated with anesthesia?
6. Describe some of the optimal conditions to be achieved with the ideal anesthetic technique.
7. What should be included in the discussion of informed consent for anesthesia by the anesthesiologist? Is it required that the anesthesiologist discuss with the patient all the remote risks of anesthesia, including death?
8. How is the induction of general anesthesia often achieved?
9. What is preoxygenation? What is its purpose?
10. What are some methods by which preoxygenation can be achieved?
11. What are some methods by which the proper placement of an endotracheal tube can be confirmed?
12. What is a rapid sequence induction?
13. Describe a rapid sequence induction.
14. When is a rapid sequence induction indicated?
15. Describe an inhalation induction of anesthesia.
16. When is an inhalation induction indicated?
17. What are some objectives during the maintenance of general anesthesia?
18. What are some advantages of nitrous oxide for general anesthesia? What are some advantages of volatile anesthetics for general anesthesia? Why are the two often administered in combination?
19. Why might neuromuscular blocking drugs be used intraoperatively?
20. What are some of the advantages of injected opioids for general anesthesia? What is a disadvantage of injected opioids for general anesthesia?
21. What are some regional anesthetic techniques?
22. What surgical procedures are regional anesthetics often administered for?
23. What are some advantages of spinal anesthesia when compared with epidural anesthesia?
24. What are some advantages of epidural anesthesia when compared with spinal anesthesia?

25. What are some of the conditions that may increase the risk associated with spinal or epidural anesthesia?
26. When is intravenous regional anesthesia or Bier block used?
27. What are some advantages of peripheral nerve blocks for surgical anesthesia?
28. What are some disadvantages of peripheral nerve blocks for surgical anesthesia?
29. What is monitored anesthesia care?
30. What are some anesthesiologist responsibilities during monitored anesthesia care?
31. What are some of the advantages of using monitored anesthesia care?

PREPARATION FOR ANESTHESIA

32. What are some advantages and disadvantages to having a separate room from the operating room for the induction of anesthesia?
33. Regardless of the anesthetic technique, what are some routine preparations the anesthesiologist should make before anesthetizing a patient?

PHARMACO-ECONOMICS

34. Name some of the ways that costs can be contained in the operating room.

ANSWERS*

1. According to the standard adopted by the American Society of Anesthesiologists, preoperatively the anesthesia provider is responsible for determining the medical status of the patient: obtaining and reviewing tests and consultations necessary for the conduct of anesthesia, developing a plan of anesthesia care, and reviewing with the patient or a responsible adult the proposed anesthesia care plan. (190)

2. Important aspects that should be included in the preoperative medical evaluation of the surgical patient include data gathering and the imparting of information to the patient. The anesthesiologist needs to gather information regarding the patient's history and physical examination and current drug therapy regimen, as well as the ordering and interpretation of laboratory data. In turn, the anesthesia provider must present the patient and the patient's family with information regarding the events of the day of surgery, preoperative instructions regarding medicines and fasting, the anesthetic, and the potential risks of anesthesia. In addition, informed consent for the procedure must be obtained. The overriding goal of the preoperative medical evaluation of the surgical patient is to decrease perioperative morbidity and mortality. (190-191, Table 14-1)

ANESTHETIC TECHNIQUE

3. Several anesthetic options are available to the anesthesia provider including (1) general anesthetic, (2) regional anesthetic, (3) peripheral nerve block, (4) monitored anesthetic care (MAC), or (5) a combination of techniques. (190)

4. Some considerations that influence the choice of anesthetic technique include the patient's history of medical problems and diseases, site of surgery, body position of the patient during surgery, whether the surgery is elective or emergent, the likelihood of the aspiration of gastric contents, the age of the patient, and patient preference. (191, Table 14-1)

5. Some of the unpleasant side effects associated with anesthesia include nausea and vomiting, urinary retention, myalgia, pruritus, anxiety, and apprehension caused by the concern of being awake or aware of operating room sights, sounds, and smells during general anesthesia. (191)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

6. Ideally, the anesthetic technique would achieve optimal patient safety and satisfaction, provide excellent surgical conditions (e.g., relaxation) for the surgeon, allow rapid recovery, and avoid postoperative side effects. In addition, the anesthetic should be economical, allow early transfer or discharge from the postanesthesia care unit, provide optimal postoperative pain control, and permit optimal operating room efficiency including turnover times. (191)

7. The discussion of informed consent for anesthesia should include a discussion of the planned method of anesthesia and specific potential complications relative to the patient, anesthetic technique, and the surgical case. Informed consent does not require that the anesthesia provider discuss with the patient all the remote risks of anesthesia. The patient or responsible adult should sign an informed consent statement before surgery. The anesthesiologist should document that the patient understands and accepts the anesthetic plan as well as the accompanying risks. (191)

8. The induction of general anesthesia is often achieved with the administration of an intravenous anesthetic, typically thiopental, propofol, or etomidate. These drugs are all beneficial in that they rapidly produce unconsciousness. Then, ventilation can be sustained via a face mask or a laryngeal mask airway (LMA). A neuromuscular blocking drug may be given intravenously to facilitate direct laryngoscopy before tracheal intubation. (191)

9. Preoxygenation is the replacement of nitrogen with oxygen (denitrogenation) in the patient's functional residual capacity before the induction of general anesthesia. The purpose of preoxygenation is to increase the time period the patient can safely be apneic. Preoxygenation prolongs the time to oxygen desaturation with the apnea that accompanies the induction of anesthesia. (192)

10. There are a few methods by which preoxygenation can be achieved. The patient can take eight vital capacity breaths of 100% oxygen over a period of 1 minute, or the patient can breathe 100% oxygen for 3 minutes at normal tidal volumes. Another method, which is somewhat less efficacious but faster, is to have the patient breathe four vital capacity breaths of 100% oxygen over a 30-second period. (192)

11. Some methods by which the proper placement of an endotracheal tube can be confirmed include the observation of upper chest expansion and reservoir bag collapse with inspiration, refilling of the reservoir bag with exhalation, cyclic waveforms on end-tidal carbon dioxide tracings that cycle from 0 to more than 20 mm Hg with inhalation and exhalation respectively, continuous pulse oximeter readings above 95%, and bilateral breath sounds. Confirmation of endotracheal tube placement can also be achieved by fiber-optic bronchoscopy. (192, Table 14-2)

12. A rapid sequence induction of anesthesia is the intravenous injection of an anesthetic to produce unconsciousness followed immediately by a neuromuscular blocking drug that produces a rapid onset of skeletal muscle paralysis (succinylcholine, rocuronium). (191)

13. A rapid sequence induction of anesthesia should be preceded with preparations such as the placement of routine monitors, confirmation of a functioning suction catheter, positioning the patient in an advantageous position to achieve intubation of the trachea by direct laryngoscopy, premedication with an antacid to neutralize the acidity of gastric contents, preoxygenation, and cricoid pressure. An induction dose of intravenously administered anesthetic, typically thiopental or propofol, followed by a dose of 1 to 2 mg/kg succinylcholine are then administered together in rapid sequence. After approximately 30 seconds, which corresponds to the onset of muscle relaxation, direct laryngoscopy should be instituted with the laryngoscope blade of choice. Only after successful intubation of the trachea has been confirmed by at least two methods should cricoid

pressure be released. Alternatives to succinylcholine for neuromuscular blockade for a rapid sequence induction include rocuronium at two to three times ED_{95}. (192)

14. A rapid sequence induction of anesthesia is indicated when patients are at an increased risk of the aspiration of gastric contents with the loss of protective laryngeal reflexes. The patients at an increased risk of the aspiration of gastric contents include those: with neurologic compromise, in cardiopulmonary arrest, with ascites, a hiatal hernia, or history of gastroesophageal reflux, with a history of gastroparesis, with an obstructed bowel, undergoing emergency surgery, or patients that are obese, pregnant, or intoxicated. (192)

15. An inhalation induction of anesthesia allows the patient to spontaneously breathe sevoflurane, possibly in conjunction with nitrous oxide via a face mask. Nitrous oxide mixed with sevoflurane has not been shown to improve the inhalation induction of anesthesia with sevoflurane, however. Sevoflurane is chosen most often because of its lack of pungency. In some cases, the prior administration of a premedicant drug may be indicated. The technique for the inhalation induction of anesthesia with sevoflurane is by priming the circuit, dialing the concentration of sevoflurane to 8%, administering high fresh gas flow of at least 8 L/min, and having the patient breathe deeply. The induction of anesthesia is usually achieved within 1 minute using this technique. Care should be taken to dial back down the sevoflurane concentration administered to avoid excessive anesthetic doses. This can be followed by placement of a laryngeal mask airway or endotracheal intubation facilitated by a neuromuscular blocking drug. Desflurane is not suitable for an inhalation induction due to its pungency and airway irritant effects. (192)

16. An inhalation induction of anesthesia is frequently used in pediatric patients in whom intravenous access is difficult to achieve while awake. Another benefit of an inhalation induction is the maintenance of the capacity to breathe spontaneously, which may avoid the need for paralysis and controlled ventilation. (192)

17. Objectives during the maintenance of general anesthesia are to maintain amnesia, analgesia, and skeletal muscle relaxation and to control sympathetic nervous system responses evoked by noxious simulation. These objectives are often achieved by combining drugs to optimize their effects. (193)

18. Advantages of nitrous oxide for general anesthesia include its relative lack of significant cardiovascular effects and its low blood gas solubility. Advantages of volatile anesthetics for general anesthesia include their high potency, their ability to attenuate sympathetic nervous system responses, and their ease of administration. Nitrous oxide and volatile anesthetics are often administered in combination to decrease the concentration of the volatile anesthetic necessary for a given anesthetic effect. Administration of nitrous oxide decreases the cardiovascular depression that may result from the administration of higher concentrations of volatile anesthetics alone. (193)

19. Neuromuscular blocking drugs are used intraoperatively to ensure lack of patient movement during certain operative procedures, as in neurosurgery. With the administration of neuromuscular blocking drugs during general anesthesia there is the inherent risk of paralysis with an inadequate depth of anesthesia and resultant patient awareness. Therefore, neuromuscular blockade must be accompanied with adequate levels of anesthesia. (193)

20. Advantages of injected opioids during general anesthesia are the increase in depth of anesthesia, and analgesia without added cardiovascular depression. A disadvantage of injected opioids when compared with inhaled anesthetics for general anesthesia is the inability to easily titrate opioids intraoperatively. (193)

21. Regional anesthetic techniques include spinal, epidural, and caudal anesthetics. (193-194)

22. Regional anesthetics are often administered for procedures involving the lower abdomen or lower extremities. (194)

23. Some advantages of spinal anesthesia when compared with epidural anesthesia are (1) it takes less time to perform, (2) it produces a more rapid onset and better quality sensory and motor anesthesia, and (3) it is associated with less pain during surgery. (194)

24. Some advantages of epidural anesthesia when compared with spinal anesthesia are (1) a lower risk for postdural puncture headache, (2) less systemic hypotension than with a spinal anesthetic if epinephrine is not added to the local anesthetic solution, (3) the ability to prolong or extend the anesthesia through an indwelling epidural catheter, and (4) the option of using the epidural catheter to provide postoperative analgesia. (194)

25. Certain preexisting conditions increase the relative risk of spinal or epidural anesthesia and the anesthesia provider must balance the perceived benefits of this technique. These conditions include hypovolemia, increased intracranial pressure, coagulopathy (thrombocytopenia), sepsis, infection at the cutaneous puncture site, and preexisting neurologic disease (e.g., multiple sclerosis). (194, Table 14-3)

26. Intravenous regional anesthesia is used for procedures lasting between 20 and 90 minutes. It provides reliable anesthesia for both the upper and lower extremities and is more cost effective than general anesthesia or brachial plexus block for outpatient hand surgery. (194)

27. Peripheral nerve blocks for surgical anesthesia provide the advantage of an isolated anesthetic effect without manipulation of the airway or prolonged systemic effects. They typically do not cause any cardiopulmonary impairment, nor are protective airway reflexes compromised. (194)

28. One disadvantage of peripheral nerve blocks for anesthesia is the unpredictability of the adequacy of the block for surgery. Other disadvantages of peripheral nerve blocks are related to the potential complications of the peripheral nerve block itself, such as nerve injury and systemic local anesthetic toxicity. (194)

29. Monitored anesthesia care describes when an anesthetic provider is requested or required to provide anesthetic during a procedure. This can include the preoperative evaluation, anesthetic care during the procedure, and management after the procedure. General anesthesia is not given in these cases. (194-195)

30. Some anesthesiologist responsibilities during monitored anesthesia care include the diagnosis and treatment of clinical problems during the procedure, the support of vital functions, the administrations of medicines as necessary for sedation, analgesia, or hemodynamic support, psychological support and physical comfort, and the provision of other services necessary to facilitate the safe completion of the procedure. (194-195)

31. Monitored anesthesia care may facilitate the avoidance of side effects of general or regional anesthesia (sympatholysis, respiratory depression, delayed emergence) and may be particularly cost effective in comparison to general or regional anesthetics in the ambulatory care setting. (195)

PREPARATION FOR ANESTHESIA

32. An advantage to having a separate room from the operating room for the induction of anesthesia is that peripheral nerve blocks or epidural catheter placement can be achieved before the operating room is available. The distinct disadvantage to having an induction room is that the practice of moving anesthetized patients may be unsafe. (195)

33. Regardless of the anesthetic technique, there are some routine preparations the anesthesiologist should make before anesthetizing a patient. These include evaluation of the anesthesia machine and monitors, and confirmation of the

availability of emergency drugs, anesthetic drugs, and equipment that might be necessary for controlled ventilation or the emergent intubation of the trachea. (195, Table 14-4)

PHARMACO-ECONOMICS

34. Cost containment in the operating room may lead to recommendations for low cost drugs; for example, antiemetics, intravenous drugs to induce anesthesia, volatile anesthetics, and neuromuscular blocking drugs. In addition, a useful method to decrease the cost of volatile anesthetics is the use of low fresh gas flow (2 L/min) during the maintenance of anesthesia. (196)

Chapter

12 ANESTHESIA DELIVERY SYSTEMS

Patricia Roth

ANESTHESIA WORKSTATION

1. What are some components of an anesthesia workstation?
2. What is the purpose of the fail-safe valve? What triggers the fail-safe valve on the anesthesia machine?
3. Can a hypoxic mixture be delivered from the anesthesia machine with an intact fail-safe valve? Explain.
4. How are oxygen, nitrous oxide, and air gases that are used in anesthesia typically delivered to the anesthesia machine? At what pressure must these gases be delivered for proper function of the anesthesia machine?
5. How is the delivery of erroneous gases to the anesthesia machine minimized?
6. What is the purpose of the cylinders of oxygen and nitrous oxide that are found on the back of the anesthesia machine?
7. How is an erroneous hookup of a gas cylinder to the anesthesia machine minimized?
8. Please complete the following table illustrating the characteristics of compressed gases stored in E-sized cylinders:

Characteristics	*Oxygen*	*Nitrous Oxide*	*Carbon Dioxide*	*Air*
Cylinder color				
Physical state in cylinder (gas/liquid)				
Cylinder contents (liters)				
Cylinder pressure full (psi)				

9. How is the pressure of oxygen related to the volume of oxygen in an oxygen gas cylinder? What does this mean with regard to calculating the volume of oxygen remaining in a used oxygen cylinder?
10. How is the pressure of nitrous oxide related to the volume of nitrous oxide in a nitrous oxide gas cylinder?
11. Why does atmospheric water vapor accumulate as frost on the outside surface of oxygen tanks and nitrous oxide tanks in use?
12. What is the purpose of flowmeters on an anesthesia machine?
13. How do flowmeters on an anesthesia machine work?
14. Are flowmeters for various gases interchangeable?
15. Why is the oxygen flowmeter the last flowmeter in a series on the anesthesia machine with respect to the direction in which the gas flows?

16. What is the purpose of the oxygen flush valve?
17. What is the flow of oxygen delivered to the patient when the oxygen flush valve is depressed?
18. What is the risk of activating the oxygen flush valve during a mechanically delivered inspiration?

VAPORIZERS

19. Why do volatile anesthetics require placement in a vaporizer for their inhaled delivery to patients via the anesthesia machine?
20. What is the heat of vaporization?
21. What is vapor pressure? What influence does temperature have on vapor pressure?
22. Why are contemporary vaporizers unsuitable for use with desflurane?
23. Describe how contemporary vaporizers for volatile anesthetics are classified.
24. What does the term *agent-specific* refer to?
25. What do the terms *variable-bypass* and *flow-over* refer to?
26. What does the term *temperature-compensated* refer to? Between what temperatures is vaporizer output reliably constant?
27. What does the term *out of circuit* refer to?
28. How does tipping of a vaporizer affect vaporizer output?
29. How is the delivery of two different volatile anesthetics to the same patient via the same anesthesia machine prevented?
30. How is the potential risk of filling the agent-specific vaporizer with the erroneous volatile anesthetic minimized?

ANESTHETIC BREATHING SYSTEMS

31. What is the function of anesthetic breathing systems?
32. How do anesthetic breathing systems impart resistance to the spontaneously ventilating patient?
33. What are some features of an anesthetic breathing system that enable them to be classified as either open, semiopen, closed, or semiclosed?
34. What are the most commonly used anesthetic breathing systems?
35. What characterizes the Mapleson systems?
36. Describe the Mapleson F anesthetic breathing system. What is another name for this anesthetic breathing system?
37. When is the Mapleson F system commonly used?
38. What are some advantages of the Mapleson F anesthetic breathing system?
39. What are some disadvantages of the Mapleson F anesthetic breathing system?
40. Describe the Bain circuit anesthetic breathing system.
41. What are some advantages of the Bain circuit anesthetic breathing system?
42. What are some disadvantages of the Bain circuit anesthetic breathing system?
43. How does the circle anesthetic breathing system get its name?
44. How does the circle system prevent rebreathing of carbon dioxide?
45. What are the classifications of a circle system and on what does this depend?
46. What is the most commonly used circle breathing system used in the United States?
47. What are some advantages of the semiclosed and closed circle systems?
48. What are some disadvantages of the circle anesthetic breathing system?
49. What is the impact of the rebreathing of anesthetic gases in a semiclosed circle system?
50. What are the components of a circle system?
51. What is the purpose of unidirectional valves in the circle system? What would occur if one of the unidirectional valves should become incompetent?
52. Where is the dead space in the circle system?
53. What is advantageous about the corrugated tubing in the circle system?
54. What is disadvantageous about the corrugated tubing in the circle system?
55. Describe the Y-piece connector in the circle system circuit.

56. What are other names for the adjustable pressure-limiting (APL) valve?
57. Describe the function of the APL valve when the "bag/vent" selector switch is set to "bag."
58. What are the advantages of the reservoir bag on the circle system?
59. Describe a closed anesthetic breathing system. What is the inflow volume of fresh gases in a closed anesthetic breathing system?
60. What are some advantages to the closed circle anesthetic breathing system?
61. What is a disadvantage to the closed circle anesthetic breathing system?
62. What are the dangers of the closed circle anesthetic breathing system?
63. Are inspired concentrations of oxygen more or less predictable when nitrous oxide is also being delivered in a closed circle anesthetic breathing system? Why?
64. How can the potential problem of the inadequate delivery of oxygen using a closed circle anesthetic breathing system be minimized?
65. In a closed circle anesthetic breathing system, to what extent is the inhaled concentration of anesthetic dependent on the exhaled concentration of anesthetic? What is the potential problem with this? How can this problem be partially offset?

ANESTHESIA MACHINE VENTILATORS

66. What parts of a circle system are eliminated in anesthesia machine ventilators when the "bag/vent" selector switch is set to "vent"?
67. What are two different ways in which anesthesia machine ventilators are powered?
68. Describe the mechanics of a conventional anesthesia machine ventilator during inspiration.
69. Why is oxygen preferred over air as the ventilator driving gas?
70. Describe the mechanics of a conventional anesthesia machine ventilator during exhalation.
71. Describe the mechanically driven piston type of ventilators found on some newer anesthesia machines.
72. Why are standing or ascending bellows preferred over hanging or descending bellows?
73. How are inhaled gases normally humidified in awake patients breathing through their native airway?
74. What effect does tracheal intubation or the use of a laryngeal mask airway have on airway humidification? What are the negative consequences of this?
75. Describe anesthetic breathing system humidification. What effect does chemical neutralization of carbon dioxide have on this process?
76. What are three types of humidifiers used for anesthesia and in the intensive care unit?
77. Describe heat and moisture exchanger (HME) humidifiers. What is the difference between an HME and an HMEF?
78. What are the advantages of HME humidifiers over other types of humidifiers?
79. What are the disadvantages of HME humidifiers?
80. What is the advantage of heated water vaporizers and humidifiers over HME humidifiers? When are they used most frequently?
81. What are the risks of heated water vaporizers and humidifiers?
82. Describe nebulizer humidifiers used for anesthesia and in the intensive care unit.

POLLUTION OF THE ATMOSPHERE WITH ANESTHETIC GASES

83. In the operating room, what are the Occupational Safety and Health Administration (OSHA) recommendations for the maximum concentrations of nitrous oxide and volatile anesthetics in parts per million?
84. What is required to control pollution of the atmosphere with anesthetic gases?
85. Describe operating room scavenging.
86. Describe the two types of scavenging systems used in the operating room.

87. What are the advantages of active scavenging with a waste gas receiver mounted on the side of the anesthesia machine?
88. What are the potential hazards of scavenging systems?
89. What two features do scavenging systems have to minimize their potential hazards?
90. Where might be the source of a high-pressure leak of nitrous oxide?
91. Where might be the source of a low-pressure leak of nitrous oxide?
92. What anesthetic techniques can lead to operating room pollution?
93. How often should the air in the operating room be exchanged?

ELIMINATION OF CARBON DIOXIDE

94. How is carbon dioxide eliminated in open and semiopen breathing systems?
95. How is carbon dioxide eliminated in a semiclosed or closed anesthetic breathing system?
96. What are two types of chemicals that are used to neutralize carbon dioxide? What products are formed? Are the neutralization reactions endothermic or exothermic?
97. What does soda lime consist of?
98. Why is silica added to soda lime?
99. Why is the water in the soda lime carbon dioxide absorbent canister hazardous?
100. What does Amsorb Plus consist of?
101. Why are calcium sulfate and polyvinylpyrrolidine added to Amsorb Plus?
102. Why is the water formed by the neutralization of carbon dioxide useful? What if the carbon dioxide absorbent canister fails to become warm during use?
103. What two factors influence the efficiency of carbon dioxide neutralization?
104. How does the size of the carbon dioxide absorbent granules affect the efficiency of carbon dioxide neutralization?
105. What is the optimal carbon dioxide absorbent granule size? How is this sizing system defined?
106. What does channeling in the carbon dioxide absorbent granule-containing canister refer to? How does channeling in the canister affect the efficiency of carbon dioxide neutralization?
107. What is the most frequent cause of channeling in the carbon dioxide absorbent granule-containing canister? How can it be minimized?
108. Define carbon dioxide absorbent absorptive capacity. What can cause a decrease in absorptive capacity?
109. Why do the carbon dioxide absorbent granules change color?
110. Contrast the color change of soda lime granules with those of Amsorb Plus.
111. Describe the degradation of inhaled anesthetics by soda lime to carbon monoxide.
112. Describe the degradation of inhaled anesthetics by soda lime to compound A.
113. Does Amsorb Plus degrade inhaled anesthetics?
114. What factor contributes to the degradation of inhaled anesthetics by soda lime?
115. Why do most instances of increased blood concentrations of carboxyhemoglobin occur in anesthetized patients on a Monday?
116. What causes the development of fire and extreme heat in the breathing system? How can this be avoided?
117. Complete the following table:

Feature	*Soda Lime*	*Amsorb Plus*
Mesh size		
Generation of compound A with sevoflurane		
Generation of carbon monoxide with inhaled anesthetics		
Risk of exothermic reactions and fire in the presence of sevoflurane		

CHECKING THE ANESTHESIA MACHINE AND CIRCLE SYSTEM FUNCTION

118. What are the current recommendations for preanesthesia checkout procedures? How do these apply to newer machines with automated checkout procedures?
119. How often should these checkout procedures be performed?
120. What are the most important preoperative checks?
121. Does the presence of a Jackson-Rees circuit along with a full oxygen E-cylinder mounted on the back of the anesthesia machine comply with the current checkout recommendations?
122. What does a leak check of the machine's low-pressure system evaluate? Why is this so important?
123. Why is calibration of the oxygen monitor so important?
124. Does a manual positive-pressure leak test check the integrity of the unidirectional valves?

ANSWERS*

ANESTHESIA WORKSTATION

1. Components of an anesthesia workstation include what was previously recognized as the anesthesia machine, (the pressure-regulating and gas-mixing components), as well as the vaporizers, anesthesia breathing circuit, ventilator, scavenging system, and respiratory and physiologic monitoring systems (electrocardiogram, arterial blood pressure, temperature, pulse oximeter, and inhaled and exhaled concentrations of oxygen, carbon dioxide, anesthetic gases, and vapors). (198, Table 15-1)

2. The purpose of the fail-safe valve is to prevent the delivery of hypoxic gas mixtures from the anesthesia machine in the event of failure of the oxygen supply. The fail-safe valve is triggered when the pressure in the oxygen delivery line decreases to less than 30 psi. When the fail-safe valve is triggered, it either shuts off or proportionally decreases the flow of all gases. Note that it is only the pressure of oxygen that triggers the fail-safe valve. (199)

3. An intact fail-safe valve is actually only a pressure-sensor valve. A hypoxic mixture may still be delivered to the patient if the fail-safe valve is sensing an adequate gas pressure in the circuit of the anesthesia machine when the oxygen flow is zero. This confirms the importance of the oxygen analyzer on the anesthesia machine. Far superior to the fail-safe valve or an oxygen analyzer is the continuous presence of a vigilant anesthesiologist. (199)

4. The oxygen, nitrous oxide, and air gases that are used in anesthesia are most often delivered to the anesthesia machine as compressed gases from a central supply source located in the hospital. These hospital supplied gases enter the operating room from a central source through pipelines to operating room wall outlets. Pressure hoses then connect the wall outlets to the anesthesia machine. These gases must be delivered at a pressure of about 50 psi for the anesthesia machine to function properly. (199-200).

5. The delivery of erroneous gases from the central supply source to the pipeline inlet connections on the anesthesia machine is minimized in two ways. First, the wall outlets and pressure hoses are color-coded. Second, and more importantly, the pressure hoses are connected to the wall outlet and anesthesia machine by noninterchangeable gas-specific diameter fittings. This *diameter index* safety system (DISS) is designed to prevent misconnections of pipeline gases. (199-200)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

6. The purpose of the cylinders of oxygen and nitrous oxide that are found on the back of the anesthesia machine is for the delivery of those gases should the central gas supply fail. (200)

7. An erroneous hookup of a gas cylinder to the anesthesia machine is minimized in two ways. First, the cylinders are color-coded. Second, and more importantly, the color-coded cylinders are attached to the anesthesia machine by a hanger yoke assembly, which consists of two metal pins that correspond to holes in the valve casing of the gas cylinder. This *pin index* safety system (PISS) makes it impossible to attach an oxygen cylinder to any yoke on the anesthesia machine other than that designed for oxygen. Otherwise, a cylinder containing nitrous oxide could be attached to the oxygen yoke, which would result in the delivery of nitrous oxide when the oxygen flowmeter was activated. (200)

8.

Characteristics	***Oxygen***	***Nitrous Oxide***	***Carbon Dioxide***	***Air***
Cylinder color	Green	Blue	Gray	Yellow
Physical state in cylinder (gas/liquid)	Gas	Liquid and gas	Liquid and gas	Gas
Cylinder contents (liters)	625	1590	1590	625
Cylinder pressure full (psi)	2000	750	838	1800

(201, Table 15-2)

9. The pressure in an oxygen cylinder is directly proportional to the volume of oxygen in the cylinder. For example, a full oxygen cylinder is evidenced by a pressure of approximately 2000 psi. If the pressure gauge on an oxygen cylinder were to read 500 psi, one fourth of the initial pressure, it can be estimated that only one fourth of the volume remains in the oxygen cylinder. The volume in the cylinder could be estimated to be 625/4, or about 155 L. (201)

10. In contrast to oxygen, the pressure gauge for nitrous oxide does not indicate the amount of gas remaining in the cylinder because the pressure in the gas cylinder remains at 750 psi as long as any liquid nitrous oxide is present. When nitrous oxide leaves the cylinder as a vapor, additional liquid is vaporized to maintain an unchanging pressure in the cylinder. After all the liquid nitrous oxide is vaporized, the pressure begins to decrease, and it can be assumed that about 75% of the contents of the gas cylinder have been exhausted. Because a full nitrous oxide cylinder (E-size) contains about 1590 L, approximately 400 L of nitrous oxide remains when the pressure gauge begins to decrease from its previously constant value of 750 psi. (201)

11. Vaporization of a liquefied gas (nitrous oxide), as well as expansion of a compressed gas (oxygen), absorbs heat, which is extracted from the metal cylinder and the surrounding atmosphere. For this reason, atmospheric water vapor often accumulates as frost on gas cylinders and in valves, particularly during high gas flow from these tanks. Internal icing does not occur because compressed gases are free of water vapor. (201)

12. Flowmeters on the anesthesia machine precisely control and measure gas flow to the common gas inlet. (201)

13. Measurement of the flow of gases is based on the principle that flow past a resistance is proportional to pressure. Typically, gas flow enters the bottom of a vertically positioned and tapered (the cross-sectional area increases upward from site of gas entry) glass flow tube. Gas flow into the flowmeter tube raises a bobbin or ball-shaped float. The float comes to rest when gravity is balanced by the decrease in pressure caused by the float. The upper end of the bobbin

or the equator of the ball indicates the gas flow in milliliters or liters per minute. (201)

14. Proportionality between pressure and flow is determined by the shape of the tube (resistance) and the physical properties (density and viscosity) of the gas. The flowmeters are initially calibrated for the indicated gas at the factory. Because few gases have the same density and viscosity, flowmeters are not interchangeable with other gases. (201)

15. The oxygen flowmeter should be the last in the sequence of flowmeters, and thus oxygen should be the last gas added to the manifold. This arrangement reduces the possibility that leaks in the apparatus proximal to oxygen inflow can diminish the delivered oxygen concentration, whereas leaks distal to that point result in loss of volume without a qualitative change in the mixture. Nevertheless, an oxygen flowmeter tube leak can produce a hypoxic mixture regardless of the flowmeter tube arrangement. (201, Figure 15-4)

16. The purpose of the oxygen flush valve is to provide a large volume of oxygen to the patient quickly. Oxygen delivered to the patient when the oxygen flush valve is depressed bypasses the flowmeters and manifold. (201-202)

17. The flow of oxygen that is delivered to the patient via the oxygen flush valve is 35 to 75 L/min. (201-202, Figure 15-3)

18. Activation of the oxygen flush valve during a mechanically delivered inspiration from the anesthesia machine ventilator permits the transmission of high airway pressure to the patient's lungs, with the possibility of barotrauma. (202)

VAPORIZERS

19. Volatile anesthetics are liquids at room temperature and atmospheric pressure. Vaporization, which is the conversion of a liquid to a vapor, takes place in a closed container, referred to as a vaporizer. The inhaled delivery of volatile anesthetics requires that they be vaporized. The vapor concentration resulting from vaporization of a volatile liquid anesthetic must be delivered to the patient with the same accuracy and predictability as other gases (oxygen, nitrous oxide). (202)

20. The heat of vaporization of a liquid is the number of calories required at a specific temperature to convert 1 g of a liquid into a vapor. (202)

21. Vaporization in the closed confines of a vaporizer ceases when equilibrium is reached between the liquid and vapor phases such that the number of molecules leaving the liquid phase is the same as the number reentering. The molecules in the vapor phase collide with each other and the walls of the container, thereby creating pressure. This pressure is termed vapor pressure and is unique for each volatile anesthetic. Vapor pressure is temperature dependent such that a decrease in the temperature of the liquid is associated with a lower vapor pressure and fewer molecules in the vapor phase. Cooling of the liquid anesthetic reflects a loss of heat (heat of vaporization) necessary to provide energy for vaporization. This cooling is undesirable because it lowers the vapor pressure and limits the attainable vapor concentration. (202)

22. Desflurane has a vapor pressure near 1 atm (664 mm Hg) at 20° C. For this reason, a desflurane vaporizer is electrically heated to 23° C and 25° C and pressurized with a backpressure regulator to 1500 mm Hg to create an environment in which the anesthetic has a relatively lower, but predictable volatility. (202)

23. Contemporary vaporizers are classified as agent-specific, variable-bypass, flow-over, temperature-compensated, and out of circuit. (202, Figure 15-5)

24. Vaporizers are calibrated to accommodate a single volatile anesthetic. (203)

25. Variable-bypass describes dividing (splitting) the total fresh gas flow through the vaporizer into two portions. The first portion of the fresh gas flow (20% or less) passes into the vaporizing chamber of the vaporizer, where it becomes saturated (flow-over) with the vapor of the liquid anesthetic. The second portion of the fresh gas flow passes through the bypass chamber of the vaporizer. Both portions of the fresh gas flow mix at the patient outlet side of the anesthesia machine. The proportion of fresh gas flow diverted through the vaporizing chamber, and thus the concentration of volatile anesthetic delivered to the patient, is determined by the concentration control dial. (202, Figure 15-5)

26. As the vaporizer temperature changes, a temperature-sensitive bimetallic strip or an expansion element inside the vaporizer influences proportioning of total gas flow between the vaporizing and bypass chambers. For example, as the temperature of the liquid anesthetic in the vaporizer chamber decreases, the temperature-sensing elements allow increased gas inflow into this chamber to offset the effect of decreased anesthetic liquid vapor pressure. Vaporizers are often constructed of metals with high thermal conductivity (copper, bronze) to further minimize heat loss. As a result, vaporizer output is nearly linear between 20° C and 35° C. (203, Figure 15-5)

27. Out of circuit describes the fact that vaporizers are isolated from the anesthetic breathing system. (203)

28. Tipping of vaporizers can cause liquid anesthetic to spill from the vaporizing chamber into the bypass chamber with a resultant increased vapor concentration exiting from the vaporizer. (203)

29. A safety interlock mechanism ensures that only one vaporizer at a time can be turned on. (203)

30. Use of an anesthetic-specific keyed filler device prevents placement of a liquid anesthetic into the vaporizing chamber that is different from the anesthetic for which the vaporizer was calibrated. This is uniquely important for desflurane because its vapor pressure is near 1 atm and accidental placement of desflurane in a contemporary vaporizer could result in an anesthetic overdose. (203)

ANESTHETIC BREATHING SYSTEMS

31. The function of anesthetic breathing systems is to deliver oxygen and anesthetic gases to the patient and to eliminate carbon dioxide. (204)

32. Anesthetic breathing systems can add considerable resistance to inhalation because peak flows as high as 60 L/min are reached during spontaneous inspiration. This resistance is influenced by unidirectional valves and connectors. The components of the breathing system, particularly the tracheal tube connector, should have the largest possible lumen to minimize this resistance to breathing. Right-angle connectors should be replaced with curved connectors to minimize resistance. Substituting controlled ventilation of the patient's lungs for spontaneous breathing can offset the increased resistance to inhalation imparted by anesthetic breathing systems. (204)

33. Anesthetic breathing systems are classified as open, semiopen, semiclosed, and closed according to the presence or absence of (1) a gas reservoir bag in the circuit, (2) rebreathing of exhaled gases, (3) means to chemically neutralize exhaled carbon dioxide, and (4) unidirectional valves. (204, Table 15-3)

34. The most commonly used anesthetic breathing systems are the (1) Mapleson F (Jackson-Rees) system, (2) Bain circuit, and (3) circle system. (204)

35. The Mapleson systems are characterized by the absence of valves to direct gases to or from the patient and the absence of chemical carbon dioxide neutralization. (204, Figures 15-6 and 15-8)

36. The Mapleson F system is a T-piece arrangement with a reservoir bag and an adjustable pressure-limiting overflow valve on the distal end of the gas reservoir bag. Another name for this anesthetic breathing system is the Jackson-Rees circuit. (204, Figure 15-6)

37. The Mapleson F system is commonly used for controlled ventilation during transport of endotracheally intubated patients. (206)

38. Advantages of the Mapleson F anesthetic breathing system include its minimal dead space and resistance. This makes this system ideal for pediatric anesthesia. (206)

39. Disadvantages of the Mapleson F system include (1) the need for high fresh gas inflow to prevent rebreathing, (2) the possibility of high airway pressure and barotrauma should the overflow valve become occluded, and (3) the lack of humidification. Lack of humidification can be offset by allowing the fresh gas to pass through an in-line heated humidifier. (206)

40. The Bain circuit is a coaxial version of the Mapleson D system in which the fresh gas supply tube runs coaxially inside the corrugated expiratory tubing. The fresh gas tube enters the circuit near the reservoir bag, but the fresh gas is actually delivered at the patient end of the circuit. The exhaled gases are vented through the overflow valve near the reservoir bag. (206, Figure 15-7)

41. Advantages of the Bain circuit include (1) warming of the fresh gas inflow by the surrounding exhaled gases in the corrugated expiratory tube, (2) conservation of moisture as a result of partial rebreathing, and (3) ease of scavenging waste anesthetic gases from the overflow valve. It is lightweight, easily sterilized, reusable, and useful when access to the patient is limited, such as during head and neck surgery. (207)

42. Hazards of the Bain circuit include unrecognized disconnection or kinking of the inner fresh gas tube. The outer expiratory tube should be transparent to allow inspection of the inner tube. (207)

43. The essential components of a circle anesthetic breathing system are arranged in a circular manner. (207, Figure 15-9)

44. The circle system prevents rebreathing of carbon dioxide by chemical neutralization of carbon dioxide with carbon dioxide absorbents. (207)

45. A circle system can be classified as semiopen, semiclosed, or closed, depending on the amount of fresh gas inflow. (207)

46. A semiclosed system is associated with rebreathing of gases and is the most commonly used breathing system in the United States. (207)

47. The semiclosed and closed circle system are both advantageous in that they allow for the rebreathing of exhaled gases. The rebreathing of exhaled gases results in (1) some conservation of airway moisture and body heat and (2) decreased pollution of the surrounding atmosphere with anesthetic gases when the fresh gas inflow rate is set at less than the patient's minute ventilation. (207)

48. Disadvantages of the circle system include (1) increased resistance to breathing because of the presence of unidirectional valves and carbon dioxide absorbent, (2) bulkiness with loss of portability, and (3) enhanced opportunity for malfunction because of the complexity of the apparatus. (207)

49. The rebreathing of exhaled gases in a semiclosed circle system influences the inhaled anesthetic concentrations of these gases. For example, when uptake of the anesthetic gas is high, as during induction of anesthesia, rebreathing of exhaled gases depleted of anesthetic greatly dilutes the concentration of anesthetic in the fresh gas inflow. This dilutional effect of uptake is offset clinically

by increasing the delivered concentration of anesthetic. As uptake of anesthetic diminishes, the impact of dilution on the inspired concentration produced by rebreathing of exhaled gases is lessened. (207)

50. The circle system consists of (1) a fresh gas inlet, (2) inspiratory and expiratory unidirectional check valves, (3) inspiratory and expiratory corrugated tubing, (4) a Y-piece connector, (5) an adjustable pressure-limiting (APL) valve, also referred to as an overflow or "pop-off" valve, (6) a reservoir bag, (7) a canister containing carbon dioxide absorbent, (8) a bag/vent selector switch, and (9) a mechanical anesthesia ventilator. (207-208)

51. Two unidirectional valves are situated in different limbs of the corrugated tubing in a circle system such that one functions for inhalation and the other for exhalation. These valves (1) permit positive-pressure breathing and (2) prevent the rebreathing of exhaled gases until they have passed through the carbon dioxide absorbent canister and have had their oxygen content replenished. Rebreathing and hypercapnia can occur if the unidirectional valves stick in the open position, and total occlusion of the circuit can occur if they are stuck in the closed position. If the expiratory valve is stuck in the closed position, breath stacking and barotrauma can occur. (208)

52. Dead space in the circle system is between the Y-piece and the patient. (208)

53. The inspiratory and expiratory corrugated tubes serve as conduits for delivery of gases to and from the patient. Their large bore provides minimal resistance, and the corrugations provide flexibility, resist kinking, and promote turbulent instead of laminar flow. (208)

54. During positive-pressure ventilation, some of the delivered gas distends the corrugated tubing and some is compressed within the circuit, which leads to a smaller delivered tidal volume. (208)

55. The Y-piece connector at the patient end of the circuit has (1) a curved elbow, (2) an outer diameter of 22 mm to fit inside a facemask, and (3) an inner diameter of 15 mm to fit onto an endotracheal tube connector. (208)

56. The APL valve is also known as the overflow or "pop-off" valve. (208)

57. When the "bag/vent" selector switch is set to "bag," the APL (overflow or "pop-off") valve (1) allows venting of excess gas from the breathing system into the waste gas scavenging system and (2) can be adjusted to allow the anesthesiologist to provide assisted or controlled ventilation of the patient's lungs by manual compression of the gas reservoir bag. The APL valve should be fully open during spontaneous ventilation so that circuit pressure remains negligible throughout inspiration and expiration. (208)

58. When the "bag/vent" selector switch is set to "bag," the gas reservoir bag maintains an available reserve volume of gas to satisfy the patient's spontaneous inspiratory flow rate (up to 60 L/min), which greatly exceeds conventional fresh gas flows (commonly 3 to 5 L/min) from the anesthesia machine. The bag also serves as a safety device because its distensibility limits pressure in the breathing circuit to less than 60 cm H_2O, even when the APL valve is closed. (208)

59. In a closed anesthetic breathing system, there is total rebreathing of exhaled gases after absorption of carbon dioxide, and the APL valve or relief valve of the ventilator is closed. A closed system is present when the fresh gas inflow into the circle system (150 to 500 mL/min) satisfies the patient's metabolic oxygen requirements (150 to 250 mL/min during anesthesia) and replaces anesthetic gases lost by virtue of tissue uptake. If sidestream gas analyzers are used, the analyzed gas exiting the analyzer must be returned to the breathing system to maintain a closed system. (208)

60. Advantages of a closed circle anesthetic breathing system over a semiclosed circle anesthetic breathing system include (1) maximal humidification and warming of inhaled gases, (2) less pollution of the surrounding atmosphere with anesthetic gases, and (3) economy in the use of anesthetics. (208)

61. A disadvantage of a closed circle anesthetic breathing system is an inability to rapidly change the delivered concentration of anesthetic gases and oxygen because of the low fresh gas inflow. (208)

62. The principal dangers of a closed anesthetic breathing system are delivery of (1) unpredictable and possibly insufficient concentrations of oxygen and (2) unknown and possibly excessive concentrations of potent anesthetic gases. (208)

63. Unpredictable and possibly insufficient delivered concentrations of oxygen when using a closed anesthetic breathing system are more likely if nitrous oxide is included in the fresh gas inflow. For example, decreased tissue uptake of nitrous oxide with time in the presence of unchanged uptake of oxygen can result in a decreased concentration of oxygen in the alveoli. (208, Table 15-4)

64. The potential problem of the inadequate delivery of oxygen using a closed circle anesthetic breathing system can be minimized by the use of an oxygen analyzer placed on the inspiratory or expiratory limb of the closed circle system. (208)

65. Exhaled gases, devoid of carbon dioxide, form a major part of the inhaled gases when a closed anesthetic breathing system is used. This means that the composition of the inhaled gases is influenced by the concentration present in the exhaled gases. The concentration of anesthetic in exhaled gases reflects tissue uptake of the anesthetic. Initially, tissue uptake is maximal, and the concentration of anesthetic in the exhaled gases is minimal. Subsequent rebreathing of these exhaled gases dilutes the inhaled concentration of anesthetic delivered to the patient. Therefore, high inflow concentrations of anesthetic are necessary to offset maximal tissue uptake. Conversely, only small amounts of anesthetic need to be added to the inflow gases when tissue uptake has decreased. The unknown impact of tissue uptake on the concentration of anesthetic in exhaled gases makes it difficult to estimate the inhaled concentration delivered to the patient through a closed anesthetic breathing system. This disadvantage can be partially offset by administering higher fresh gas inflow (3 L/min) for about 15 minutes before instituting the use of a closed anesthetic breathing system. This approach permits elimination of nitrogen from the lungs and corresponds to the time of greatest tissue uptake of anesthetic. (208-209, Table 15-4)

ANESTHESIA MACHINE VENTILATORS

66. When the anesthesia machine ventilator "bag/vent" selector switch is set to "vent," the gas reservoir bag and APL valve are eliminated from the circle anesthetic system and the patient's ventilation is delivered from the mechanical anesthesia ventilator. (209, Figure 15-10)

67. Anesthesia ventilators are powered by compressed gas, electricity, or both. (209)

68. Most conventional anesthesia machine ventilators are pneumatically driven by oxygen or air that is pressurized and, during the inspiratory phase, routed to the space inside the ventilator casing between the compressible bellows and the rigid casing. Pressurized air or oxygen entering this space forces the bellows to empty its contents into the patient's lungs through the inspiratory limb of the breathing circuit. This pressurized air or oxygen also causes the ventilator relief valve to close, thereby preventing inspiratory anesthetic gas from escaping into the scavenging system. (209)

69. Oxygen is preferable to air as the ventilator driving gas because if there is a leak in the bellows, the fraction of inspired oxygen will be increased. If there is a leak in the bellows in a ventilator driven by 50 psi oxygen or air, the peak inspiratory pressure will rise. (209)

70. During exhalation, the driving gas is either vented into the room or directed to the scavenging system, and the bellows refills as the patient exhales. (209)

71. Some newer anesthesia machines have mechanically driven piston type of ventilators. The piston operates much like the plunger of a syringe to deliver the desired tidal volume or airway pressure to the patient. (209)

72. Ventilators with bellows that rises during exhalation (standing or ascending bellows) are preferred because the bellows will not rise (fill) if there is a leak in the anesthesia breathing system or the system becomes accidentally disconnected. Ventilators with a bellows that descends during exhalation (hanging or descending bellows) are potentially dangerous because the bellows will continue to rise and fall during a disconnection. Whenever a ventilator is used, a disconnect alarm must be activated and audible. (209)

73. The upper respiratory tract (especially the nose) functions as the principal heat and moisture exchanger (HME) to bring inspired gas to body temperature and 100% relative humidity in its passage to the alveoli. (209)

74. Water is removed from medical gases (cylinders or piped) to prevent corrosion and condensation. Tracheal intubation or the use of a laryngeal mask airway bypasses the upper airway and thus leaves the tracheobronchial mucosa the burden of heating and humidifying inspired gases. Humidification of inspired gases by the lower respiratory tract in intubated patients can lead to dehydration of the mucosa, impaired ciliary function, impaired surfactant function, inspissation of secretions, atelectasis, and a rise in the alveolar-to-arterial gradient. Breathing of dry and room temperature gases in intubated patients is associated with water and heat loss from the patient. Heat loss is more important than water loss, and the most important reason to provide heated humidification for intubated patients is to decrease heat loss and associated decreases in body temperature. This is especially true in infants and children, who are rendered poikilothermic by general anesthesia. (209)

75. Humidification is a form of vaporization in which water vapor (moisture) is added to the gases delivered by the anesthetic breathing system to minimize water and heat loss. The water formed and the heat generated by chemical neutralization of carbon dioxide help humidify and heat the gases in the breathing circuit. (210)

76. Humidifiers used for anesthesia and in the intensive care unit include (1) heat and moisture exchanger (HME) humidifiers, (2) heated water vaporizers and humidifiers, and (3) nebulizers. (210)

77. HME humidifiers are devices that, when placed between the endotracheal tube and Y-piece of the circle system, conserve some of the exhaled water and heat and return it to the inspired gases. They contain a porous hydrophobic or hygroscopic membrane that traps exhaled humidified gases and returns them to the patient on inspiration. Bacterial and viral filters can be incorporated in HME humidifiers to convert them into heat and moisture exchanging filters (HMEFs). (211)

78. The advantages of HME humidifiers over other types of humidifiers are that they are (1) simple and easy to use, (2) lightweight, (3) not dependent on an external power source, (4) disposable, and (5) low cost. (211)

79. The disadvantages of HME humidifiers are that they (1) are not as effective as heated water vaporizers and humidifiers in maintaining patient temperature, (2) add resistance and increase the work of breathing and therefore should be used with caution in spontaneously ventilating patients, (3) can become clogged with patient secretions or blood, and (4) can increase dead space, which can cause significant rebreathing in pediatric patients. Special low-volume HME humidifiers are available for pediatric patients. (211)

80. Heated water vaporizers and humidifiers are used to deliver a relative humidity higher than that delivered by HME humidifiers. Heated water vaporizers are more frequently used in pediatric anesthesia and intensive care unit patients. (211)

81. Risks from heated water vaporizers and humidifiers include (1) thermal injury, (2) nosocomial infection, (3) increased work of breathing, and (4) increased risk of malfunction because of the complexity of these systems. (211)

82. Nebulizers produce a mist of microdroplets of water suspended in a gaseous medium. The quantity of water droplets delivered is not limited by the temperature of the carrier gas. In addition to water, nebulizers can deliver medications to peripheral airways. (211)

POLLUTION OF THE ATMOSPHERE WITH ANESTHETIC GASES

83. In the operating room, OSHA recommends that the concentration of nitrous oxide not exceed 25 ppm and exposure concentrations of volatile anesthetics not exceed 2 ppm. (211)

84. Control of pollution of the atmosphere with anesthetic gases requires (1) scavenging of waste anesthetic gases, (2) periodic preventive maintenance of anesthesia equipment, (3) attention to the anesthetic technique, and (4) adequate ventilation of the operating rooms. (211)

85. Scavenging is the collection and subsequent removal of vented gases from the operating room. The excess gas comes from either the APL valve if the bag/vent selector switch is set to "bag," or from the ventilator relief valve if the bag/vent selector switch is set to "vent." All excess gas from the patient exits the breathing system through these valves. The amount of delivered gas used to anesthetize a patient commonly far exceeds the patient's needs. In addition, when the bag/vent selector switch is set to vent, some anesthetic breathing systems direct the drive gas inside the bellows canister to the scavenging system. If sidestream gas analyzers are used, the analyzed gas exiting the analyzer must be directed to the scavenging system or returned to the breathing system. (211)

86. Scavenging systems may be characterized as active or passive. An active system is connected to the hospital's vacuum system and gases are drawn from the machine by a vacuum. A passive system is connected to the hospital's ventilation duct and waste gases flow out of the machine on their own. (212)

87. Many anesthesia machines provide active scavenging with a waste gas receiver mounted on the side of the anesthesia machine. Advantages of this system include (1) a needle valve that allows the clinician to manually adjust the amount of vacuum flow through the scavenging system, (2) a needle valve that can be adjusted such that the 3-L reservoir bag will be slightly inflated and appear to "breathe" with the patient, and (3) unlike other active scavenging systems, a waste gas receiver that does not require a strong vacuum to operate. (212)

88. Hazards of scavenging systems include (1) obstruction of the scavenging pathways, which can result in excessive positive pressure in the breathing circuit and possible barotrauma, and (2) excessive vacuum applied to the scavenging system, which can cause negative pressures in the breathing system. (212)

89. Scavenging systems contain two relief valves to minimize their potential hazards. If gas accumulates in the scavenging system and cannot leave the anesthesia machine properly, the positive-pressure scavenge relief valve opens when the pressure reaches 10 cm H_2O to allow the gas to escape into the room. If negative pressure is applied to the scavenging system, the negative-pressure scavenge relief valve opens and allows room air to be drawn in (instead of drawing gas from the patient). Additionally, if the amount of fresh gas flow exceeds the capacity of the scavenging system, the excess waste anesthetic gas exits the scavenging system through the positive-pressure relief valve and pollutes the operating room. (212)

90. High-pressure leakage of nitrous oxide can occur as a result of faulty yokes attaching the nitrous oxide tank to the anesthesia machine or faulty connections from the central nitrous oxide gas supply to the anesthesia machine. (212)

91. Low-pressure leakage of anesthetic gases can occur because of leaks inside the anesthesia machine and leaks between the machine and patient. (212)

92. Anesthetic techniques that can lead to operating room pollution include (1) poorly fitting facemasks, (2) flushing the anesthetic delivery circuit, (3) filling anesthetic vaporizers, (4) the use of uncuffed endotracheal tubes, (5) failure to turn off the nitrous oxide flow or vaporizers at the end of the anesthesia, and (6) the use of semiopen breathing circuits such as the Jackson-Rees, which are difficult to scavenge. (212)

93. The air in the operating room should be exchanged at least 15 times per hour by the operating room ventilation system. This rate should be checked periodically by the hospital's clinical engineering department. (212)

ELIMINATION OF CARBON DIOXIDE

94. Open and semiopen breathing systems eliminate carbon dioxide by venting all exhaled gases to the atmosphere. (212)

95. Semiclosed and closed breathing systems eliminate carbon dioxide by chemical neutralization. (212)

96. Soda lime and Amsorb Plus absorbents are used to neutralize carbon dioxide. The products formed by their reactions with carbon dioxide are carbonates, water, and heat, making them exothermic reactions. (212-213)

97. Soda lime granules consist of water, calcium hydroxide, and small amounts of sodium and potassium hydroxide that serve as activators. (212, Table 15-6)

98. Soda lime granules fragment easily and produce alkaline dust, which can lead to bronchospasm if inhaled. Silica is added to the granules to provide hardness and minimize alkaline dust formation. (213)

99. The water formed from the neutralization of carbon dioxide, the water present in the soda lime granules, and the water condensed from the patient's exhaled gases leach the alkaline bases from the soda lime granules and produce a slurry containing NaOH and KOH in the bottom of the canister. These monovalent bases can be corrosive to the skin. (213)

100. Amsorb Plus granules consist of water, calcium hydroxide, and calcium chloride. (213, Table 15-6)

101. Calcium sulfate and polyvinylpyrrolidine are added to Amsorb Plus to increase hardness. (213)

102. The water formed by the neutralization of carbon dioxide with soda lime and Amsorb Plus is useful for humidifying the gases and for dissipating some of the heat generated in these exothermic reactions. The heat generated during the neutralization of carbon dioxide can be detected by the warmness of the canister. Failure of the canister to become warm should alert the anesthesia provider to the possibility that chemical neutralization of carbon dioxide is not taking place. (213)

103. The efficiency of carbon dioxide neutralization is influenced by the size of the carbon dioxide granules and the presence or absence of channeling in the carbon dioxide canister. (213)

104. The optimal absorbent granule size represents a compromise between absorptive efficiency and resistance to airflow through the carbon dioxide absorbent canister. Absorbent efficiency increases as absorbent granule size decreases because the total surface area coming in contact with carbon dioxide increases. The smaller the

absorbent granules, however, the smaller the interstices through which gas must flow and the greater the resistance to flow. (213)

105. Absorbent granule size is designated as mesh size, which refers to the number of openings per linear inch in a sieve through which the granular particles can pass. The granular size of carbon dioxide absorbents in anesthesia practice is between 4 and 8 mesh, a size at which absorbent efficiency is maximal with minimal resistance. A 4-mesh screen means that there are four quarter-inch openings per linear inch. An 8-mesh screen has eight eighth-inch openings per linear inch. (213)

106. Channeling is the preferential passage of exhaled gases through the carbon dioxide absorber canister via pathways of low resistance such that the bulk of the carbon dioxide absorbent granules are bypassed. (213)

107. Channeling results from loose packing of absorbent granules and can be minimized by gently shaking the canister before use to ensure firm packing of the absorbent granules. Carbon dioxide absorbent canisters are designed to facilitate uniform dispersion of exhaled gas flow through the absorbent granules. (213)

108. Absorptive capacity is determined by the maximum amount of carbon dioxide that can be absorbed by 100 g of carbon dioxide absorbent. Channeling of exhaled gases through the absorbent granules can substantially decrease their efficiency. Carbon dioxide absorber canister design also influences the absorptive capacity of the carbon dioxide absorbent. (213)

109. Carbon dioxide absorbents contain a pH-sensitive indicator dye that changes color when the carbon dioxide absorbent granules are exhausted. When the absorptive components of the granules are exhausted, carbonic acid accumulates and produces a change in the pH and thus in the indicator dye color. (213-214)

110. Soda lime contains the indicator dye ethyl violet, which changes granule color from white to purple when exhausted. Over time, exhausted granules may revert to their original white color even though absorptive capacity does not recover with time. On reuse, the dye quickly produces the purple color change again. Amsorb Plus contains an indicator dye that changes granule color from white to purple when exhausted and, once changed, does not revert to its original color. (214)

111. Desiccated soda lime may degrade sevoflurane, isoflurane, enflurane, and desflurane to carbon monoxide. (214)

112. Soda lime, whether moist or dry, degrades sevoflurane and halothane to unsaturated nephrotoxic compounds (compound A). (214)

113. In contrast to soda lime, Amsorb Plus, whether desiccated or moist, does not degrade inhaled anesthetics. (214)

114. Desiccation of soda lime increases the degradation of inhaled anesthetics. Without a patient attached to the conventional circle system, desiccation of soda lime is enhanced by retrograde gas flow, which is facilitated by fresh gas flows greater than 5 L/min, an open APL valve, and removing the breathing bag. (214)

115. Desiccation of soda lime requires a prolonged period (usually 48 hours) of retrograde gas flow. Accordingly, most instances of increased blood concentrations of carboxyhemoglobin occur in patients anesthetized on a Monday after continuous flow of oxygen (flowmeter accidentally left on) through the carbon dioxide absorbent over the weekend. (214)

116. Desiccation of the carbon dioxide absorbent Baralyme (no longer clinically available) can lead to fire within the circle system with sevoflurane use. A poorly characterized chemical reaction between sevoflurane and Baralyme can produce sufficient heat and combustible degradation products to lead to the

spontaneous generation of fires within the carbon dioxide absorber canister and breathing circuit. Cases of extreme heat without fire associated with desiccated soda lime have been reported in Europe. To avoid this problem, anesthesia providers should make every effort to not use desiccated carbon dioxide absorbents. (214, Table 15-8)

117.

Feature	*Soda Lime*	*Amsorb Plus*
Mesh size	4 - 8	4 - 8
Generation of compound A with sevoflurane	Yes	No
Generation of carbon monoxide with inhaled anesthetics	Yes	No
Risk of exothermic reactions and fire in the presence of sevoflurane	No	No

(212-214, Table 15-6)

CHECKING THE ANESTHESIA MACHINE AND CIRCLE SYSTEM FUNCTION

118. In 2008 the American Society of Anesthesiologists developed new recommendations for preanesthesia checkout (PAC) procedures to provide guidelines applicable to all anesthesia delivery systems. This allows individual departments to develop a PAC specific to the anesthesia delivery systems currently used at their facilities that can be performed consistently and expeditiously. Specifically, for newer anesthesia delivery systems that incorporate automated checkout features, items that are not evaluated by the automated checkout need to be identified, and supplemental manual checkout procedures included as needed. (215, Table 15-9)

119. A complete anesthesia machine and circle system function checkout procedure should be performed each day before the first case. An abbreviated checkout should be performed before each subsequent use that day. (215, Table 15-9)

120. The most important preoperative checks are (1) verification that an auxiliary oxygen cylinder and self-inflating manual ventilation device (Ambu bag) are available and functioning, (2) a leak check of the machine's low-pressure system, (3) calibration of the oxygen monitor, and (4) a positive-pressure leak check of the breathing system. (215-216)

121. No. Failure to ventilate is a major cause of morbidity and death related to anesthesia care. Because equipment failure with resulting inability to ventilate the patient can occur at any time, a self-inflating manual ventilation device (e.g., Ambu bag) should be present at every anesthetizing location for every case and should be checked for proper function. In addition, a source of oxygen separate from the anesthesia machine and pipeline supply, specifically an oxygen cylinder with a regulator and a means to open the cylinder valve, should be immediately available and checked. (215)

122. A leak check of the machine's low-pressure system is performed to confirm the integrity of the anesthesia machine from the flowmeters to the common gas outlet. It evaluates the portion of the anesthesia machine that is downstream from all safety devices, except the oxygen monitor. The low-pressure circuit is the most vulnerable part of the anesthesia machine because the components located within this area are the ones most subject to breakage and leaks. The machine's low-pressure system must be checked because leaks in this circuit can lead to hypoxia or patient awareness, or both. (215)

123. The oxygen monitor is the only machine safety device that detects problems downstream from the flowmeters. The other machine safety devices (the fail-safe valve, the oxygen supply failure alarm, and the proportioning system) are all upstream from the flowmeters. (216)

124. No. A positive-pressure leak check of the breathing system must be performed before every procedure. This test does not check the integrity of the unidirectional valves inasmuch as the breathing system will pass the leak check even if the unidirectional valves are incompetent or stuck shut. (216, Table 15-9, items 12-13)

Chapter

13 AIRWAY MANAGEMENT

Patricia Roth

1. What is the definition of difficult mask ventilation?
2. What is the incidence of difficult mask ventilation?
3. What is the definition of difficult tracheal intubation/laryngoscopy?
4. What is the incidence of difficult tracheal intubation/laryngoscopy?
5. What is the incidence of failed tracheal intubation?

ANATOMY AND PHYSIOLOGY OF THE UPPER AIRWAY

6. How does resistance to airflow through the nasal passages compare to that through the mouth?
7. What nerves innervate the nasal mucosa?
8. What nerves innervate the hard and soft palate?
9. What nerve provides sensation to the anterior two thirds of the tongue?
10. What nerve innervates the posterior third of the tongue, the soft palate, and the oropharynx?
11. What are the three components of the pharynx?
12. What nerves innervate the pharynx?
13. Complete the following table: (223, Table 16-1, Motor and Sensory Innervation of Larynx)

Nerve	*Sensory*	*Motor*
Superior laryngeal, internal division		
Superior laryngeal, external division		
Recurrent laryngeal		

14. Where is the narrowest part of the adult airway?
15. What is special about the cricoid cartilage compared with the other tracheal cartilages?

AIRWAY ASSESSMENT

16. What is the purpose of the Mallampati classification system?
17. Describe the observer/patient position during Mallampati classification.
18. Describe the Mallampati classes.
19. What is the purpose of the Cormack and Lehane score?
20. Describe the Cormack and Lehane grades.
21. What is the purpose of the upper lip bite test (ULBT)?
22. Describe the upper lip bite test (ULBT) classes.

23. What three axes must be aligned to obtain a line of vision during direct laryngoscopy? How is this accomplished? What is this final position called?
24. What is the concern with a "short" thyromental distance?
25. What is the concern with a decreased submandibular compliance?
26. What position is associated with improved alignment of the three axes to obtain a line of vision during laryngoscopy in obese patients?
27. What maneuver facilitates identification of the cricoid cartilage in patients who do not have a prominent thyroid cartilage?

AIRWAY MANAGEMENT TECHNIQUES

28. What is "preoxygenation" prior to the induction of anesthesia? What is its value?
29. How is preoxygenation accomplished?
30. Name ten independent variables that are associated with difficult facemask ventilation.
31. Why is it important to limit ventilation pressure to less than 20 cm H_2O during facemask ventilation?
32. What are contraindications to nasal airway placement?
33. What are some indications for endotracheal intubation?
34. What is another name for cricoid pressure and how is it performed?
35. What is the purpose of cricoid pressure?
36. Describe the proper placement of the tip of a curved (Macintosh) laryngoscope blade versus that of a straight (Miller) laryngoscope blade for exposure of the glottic opening during laryngoscopy.
37. Describe the OELM and BURP maneuvers. What is their purpose?
38. How are endotracheal tubes sized?
39. Why are endotracheal tubes radiopaque and transparent?
40. Why are low-pressure, high-volume cuffs on endotracheal tubes preferred?
41. What are some serious complications attributable to endotracheal cuff pressures?
42. Name some stylets that can be used to facilitate endotracheal intubation.
43. What are some methods to confirm the correct placement of an endotracheal tube?
44. When is an awake fiberoptic endotracheal intubation most frequently chosen?
45. Why is fiberoptic endotracheal intubation recommended for patients with unstable cervical spines?
46. Why is fiberoptic endotracheal intubation recommended for patients who have sustained an injury to the upper airway from either blunt or penetrating trauma?
47. What is an absolute contraindication to fiberoptic endotracheal intubation?
48. What are some relative contraindications to fiberoptic endotracheal intubation?
49. What are some advantages and disadvantages of nasal fiberoptic endotracheal intubation?
50. Why should an antisialagogue be given before fiberoptic endotracheal intubation?
51. On what basis is the choice of sedation for an awake fiberoptic tracheal intubation made?
52. Describe preparation of the nose and nasopharynx for nasal fiberoptic tracheal intubation.
53. Describe preparation of the tongue and oropharynx for nasal or oral fiberoptic tracheal intubation.
54. Describe preparation of the larynx and trachea for nasal or oral fiberoptic tracheal intubation.
55. Why is lidocaine the preferred airway topical local anesthetic?
56. Name two blocks that can be performed to topicalize the larynx and trachea.

FLEXIBLE FIBEROPTIC LARYNGOSCOPY

57. How can the risks of mucosal trauma or submucosal bleeding with nasal endotracheal intubation be minimized?
58. What advantages does inflation of the endotracheal tube cuff during advancement with the fiberoptic scope offer?

59. How is endotracheal tube depth verified during fiberoptic intubation?
60. What are possible causes of resistance when removing the fiberoptic bronchoscope?
61. What is the utility of oral intubating airways during oral fiberoptic endotracheal tracheal intubation?
62. Why is visualization more difficult during fiberoptic endotracheal tracheal intubation in an asleep patient?
63. Why is having a second person trained in anesthesia delivery present recommended for fiberoptic endotracheal tracheal intubation in an asleep patient?
64. Describe a Patil-Syracuse mask.
65. Describe an Aintree airway exchange catheter.

RIGID FIBEROPTIC LARYNGOSCOPES/ VIDEOLARYN GOSCOPES

66. Name some rigid fiberoptic laryngoscopes. When might these laryngoscopes be useful?

RETROGRADE TRACHEAL INTUBATION

Blind Nasotracheal Intubation

67. Describe the retrograde and blind nasal endotracheal intubation techniques and when they might be useful.

SUPRAGLOTTIC AIRWAY DEVICES

68. Describe correct anatomic placement of the laryngeal mask airway (LMA).
69. For what purpose was the LMA Fastrach designed?
70. When using an ILMA, why are silicone Euromedical endotracheal tubes preferred over standard endotracheal tubes? What is the disadvantage of these tubes?
71. Describe the LMA CTrach.
72. Describe the ProSeal LMA.
73. Describe the esophageal-tracheal Combitube (ETC).

TRANSTRACHEAL TECHNIQUES

74. What is transtracheal jet ventilation and when might it be useful? When is it contraindicated? What are some potential risks of transtracheal jet ventilation?
75. What is a cricothyrotomy and when is it usually performed?

TRACHEAL EXTUBATION

76. Why is tracheal extubation during a light level of anesthesia dangerous?
77. What is laryngospasm? When is it most likely to occur?
78. How should laryngospasm be treated?
79. When is deep tracheal extubation contraindicated?
80. What are the steps of tracheal extubation?
81. What is the most common complication during direct laryngoscopy?
82. Describe endotracheal tube movement during head flexion and extension.
83. What are the two most serious complications after tracheal extubation?
84. What is the major complication of prolonged tracheal intubation?

AIRWAY MANAGEMENT IN INFANTS AND CHILDREN

85. What are some differences between the infant and the adult airway? At what age does the pediatric upper airway take on more adultlike characteristics?
86. Contrast the location of the larynx in an infant versus an adult. What effect does this have on the tongue?
87. Contrast the size of an infant's tongue in proportion to the size of the mouth with that of an adult. What are the consequences of this?
88. Contrast an infant's epiglottis with that of an adult.
89. What advantages do straight laryngoscopes offer over curved laryngoscopes when intubating an infant or small child?
90. What is the narrowest portion of an infant's airway versus an adult airway?

91. What is the correct size of an uncuffed endotracheal tube in infants and children?
92. Can cuffed endotracheal tubes be safely used in infants and children? What if nitrous oxide is used during the anesthetic?
93. What are the dangers of an endotracheal tube that is too large for infants and children?
94. Contrast proper head and neck positioning of an adult with that of an infant during direct laryngoscopy.
95. What is different about an infant's nares compared to an adult's? Why is this important?
96. Why is a history of snoring important in infants and children?
97. Why is premedication useful in pediatric anesthesia? At what age does this become important?
98. What is the dose of oral midazolam for infants or children? What is the maximum oral dose? What if the child is uncooperative with taking oral midazolam?
99. Describe an inhaled induction in a child. When should the nitrous oxide be discontinued?
100. Describe maneuvers to overcome airway obstruction during mask induction in infants and children.
101. What determines the appropriate size of an LMA for use in infants and children?
102. What is the LMA Flexible? What advantages does it offer?
103. What advantage does the Air-Q intubating laryngeal airway (ILA) have over an LMA?
104. What formula is often used to estimate the appropriate-sized endotracheal tubes for infants and children?
105. Is the formula used to estimate the appropriate-sized endotracheal tube for infants and children applicable for cuffed or uncuffed endotracheal tubes?
106. How is the formula used to estimate the appropriate-sized endotracheal tubes for infants and children adapted for cuffed endotracheal tubes?
107. What three advantages do Microcuff endotracheal tubes have over conventional pediatric cuffed endotracheal tubes?
108. Are stylets useful in intubating infants and children?
109. What is the disadvantage of a straight laryngoscope blade compared to a curved blade?
110. Describe the most useful sizes of laryngoscope blades according to age.
111. What is the most important first step when an unexpected difficult airway occurs in pediatric patients?
112. Why should repeated attempts at direct laryngoscopy be avoided? What should be done instead?
113. Is an awake fiberoptic endotracheal intubation usually an option in managing an expected pediatric difficult airway?
114. What personnel and equipment should be in the operating room before induction of anesthesia in a pediatric patient with an expected difficult airway?
115. What airway devices are available in smaller sizes to facilitate intubation of a child with a difficult airway?
116. Why is tracheal extubation in infants and children riskier than that of adults?
117. When does postextubation croup most commonly occur? Why is this important?
118. What are the clinical manifestations of postextubation croup?
119. How is postextubation croup treated?
120. Why is obstructive sleep apnea especially important in infants and children?
121. How should opiate therapy be managed in an infant or child with obstructive sleep apnea?
122. Describe tracheal extubation and postoperative monitoring for infants and children with obstructive sleep apnea.
123. How should extubation after a difficult intubation be handled in infants and children?

ANSWERS*

1. Difficult mask ventilation is defined as an inability to maintain oxygen saturation (Spo_2) greater than 90% or an inability to prevent or reverse the signs of inadequate ventilation. (220)
2. The incidence of difficult mask ventilation ranges from 0.07% to 5%. (220)
3. Difficult tracheal intubation/laryngoscopy is defined as successful intubation requiring more than three attempts or taking longer than 10 minutes. (220)
4. Difficult tracheal intubation/laryngoscopy occurs in 1.1% to 8.5% of patients. (220)
5. Failed tracheal intubation occurs at an incidence of 0.01% to 0.03%. (220)

ANATOMY AND PHYSIOLOGY OF THE UPPER AIRWAY

6. Resistance to airflow through the nasal passages is twice that through the mouth and accounts for approximately two thirds of total airway resistance. (220)
7. The ophthalmic (V1) and maxillary divisions (V2) of the trigeminal nerve (cranial nerve V) provide innervation to the nasal mucosa as the anterior ethmoidal, nasopalatine, and sphenopalatine nerves. (220, Figure 16-2)
8. The palatine nerves branch from the sphenopalatine ganglion to innervate the hard and soft palate. (220, Figure 16-2)
9. The mandibular division (V3) of the trigeminal nerve (cranial nerve V) forms the lingual nerve, which provides sensation to the anterior two thirds of the tongue. (220, Figure 16-3)
10. The posterior third of the tongue, the soft palate, and the oropharynx are innervated by the glossopharyngeal nerve (cranial nerve IX). (220, Figure 16-4)
11. The three components of the pharynx are the nasopharynx, the oropharynx, and the hypopharynx. (220)
12. The pharynx is innervated by cranial nerves IX (glossopharyngeal) and X (vagus). (220, Figures 16-4 and 16-5)
13.

Nerve	*Sensory*	*Motor*
Superior laryngeal, internal division	Epiglottis Base of tongue Supraglottic mucosa Thyroepiglottic joint Cricothyroid joint	None
Superior laryngeal, external division	Anterior subglottic mucosa	Cricothyroid m.
Recurrent laryngeal	Subglottic mucosa Muscle spindles	Thyroarytenoid m. Lateral cricoarytenoid m. Interarytenoid m. Posterior cricoarytenoid m.

14. The vocal cords are the narrowest portion of the adult airway. (220)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

15. The cricoid cartilage is the most cephalad tracheal cartilage and is the only one that has a full ring structure. It is shaped like a signet ring, wider in the cephalocaudal dimension posteriorly. (220)

AIRWAY ASSESSMENT

16. Mallampati proposed a classification system (Mallampati score) to correlate the oropharyngeal space with the predicted ease of direct laryngoscopy and tracheal intubation. (223)

17. With the observer at eye level, the patient holds the head in a neutral position, opens the mouth maximally, and protrudes the tongue without phonating. (223)

18. Class I: The soft palate, fauces, uvula, and tonsillar pillars are visible.
Class II: The soft palate, fauces, and uvula are visible.
Class III: The soft palate and base of the uvula are visible.
Class IV: The soft palate is not visible. (223, Figure 16-6)

19. The Cormack and Lehane score classifies laryngoscopic view. (223)

20. Grade I: Most of the glottis is visible.
Grade II: Only the posterior portion of the glottis is visible.
Grade III: The epiglottis, but no part of the glottis, can be seen.
Grade IV: No airway structures are visualized. (223, Figure 16-7)

21. The ULBT correlates the patient's ability to prognath the mandible with visualization of glottic structures on direct laryngoscopy. (225)

22. Class I: Lower incisors can bite above the vermilion border of the upper lip.
Class II: Lower incisors cannot reach vermilion border.
Class III: Lower incisors cannot bite upper lip. (225)

23. The laryngeal, pharyngeal, and oral axes must be aligned to obtain a line of vision during direct laryngoscopy. Flexion of the neck, by elevating the head approximately 10 cm, aligns the laryngeal and pharyngeal axes. Extension of the head on the atlanto-occipital joint aligns the oral and pharyngeal axes. These maneuvers place the head in the "sniffing" position and bring the three axes into optimal alignment. (225, Figure 16-8)

24. A thyromental distance (mentum to thyroid cartilage) less than 6 to 7 cm correlates with a poor laryngoscopic view. Three ordinary fingerbreadths approximate this distance. (226)

25. Decreased submandibular compliance correlates with poor laryngoscopic view. The submandibular space is the area into which the soft tissues of the pharynx must be displaced to obtain a line of vision during direct laryngoscopy. Anything that limits the size of this space or compliance of the tissue will decrease the amount of anterior displacement that can be achieved. (226)

26. Obesity is associated with difficulty in airway management. To increase the likelihood of successful endotracheal intubation, a wedge-shaped bolster placed behind the obese patient's back results in a more optimal sniffing position. (226)

27. In patients who do not have a prominent thyroid cartilage, identification of the cricoid cartilage can be achieved by beginning palpation of the neck at the sternal notch and sliding the fingers up the neck until a tracheal cartilage that is wider and higher (cricoid cartilage) than those below is felt. (227)

AIRWAY MANAGEMENT TECHNIQUES

28. "Preoxygenation" describes the administration of oxygen to patients prior to the induction of anesthesia resulting in apnea. The goal is to achieve an end tidal oxygen level of about 90%. Preoxygenation increases the duration of apnea without oxygen desaturation by filling the functional residual capacity with oxygen, thus increasing the patient's reserve of oxygen while apneic. (227)

29. Methods by which to preoxygenate a patient prior to the induction of anesthesia include having the patient breathe 100% oxygen for 3 minutes or take eight deep breaths in 60 seconds. Although it was previously believed that having a patient take four deep breaths was sufficient for preoxygenation, this has been since proved not to be as effective as the other two methods. In obese patients, adequate preoxygenation may take longer. Having the obese patient sit in an upright position and applying continuous positive airway pressure may facilitate preoxygenation. (227)

30. Independent variables associated with difficult facemask ventilation include: (1) age older than 55 years, (2) a body mass index greater than 26 kg/m^2, (3) a beard, (4) lack of teeth, (5) a history of snoring, (6) repeated attempts at laryngoscopy, (7) Mallampati class III to IV, (8) neck radiation, (9) male gender, and (10) limited ability to protrude the mandible. (227)

31. Ventilating pressure during facemask ventilation should be less than 20 cm H_2O to avoid insufflation of the stomach. (227)

32. Nasal airways are relatively contraindicated in patients with coagulation or platelet abnormalities and those with basilar skull fractures. (228)

33. Indications for endotracheal intubation include: (1) Provide a patent airway. (2) Prevent inhalation (aspiration) of gastric contents; (3) need for frequent suctioning; (4) facilitate positive-pressure ventilation of the lungs; (5) operative position other than supine; (6) operative site near or involving the upper airway; and (7) airway maintenance by mask difficult. (228, Table 16-5)

34. Cricoid pressure, also known as the Sellick maneuver, can be applied by an assistant exerting downward external pressure with the thumb and index finger on the cricoid cartilage to displace the cartilaginous cricothyroid ring posteriorly and thus compress the underlying esophagus against the cervical vertebrae. (228, Figure 16-10)

35. Conceptually, cricoid pressure should prevent spillage of gastric contents into the pharynx during the period from induction of anesthesia (unconsciousness) to successful placement of a cuffed endotracheal tube. This is thought to prevent, or minimize, the aspiration of gastric contents during the induction of anesthesia. The efficacy of cricoid pressure for this purpose is not clear. (229)

36. During laryngoscopy with a Macintosh blade, the distal end of the curved blade is advanced into the space between the base of the tongue and the pharyngeal surface of the epiglottis. During laryngoscopy with a Miller blade, the distal end of the straight blade is advanced beneath the laryngeal surface of the epiglottis. (229, Figure 16-12)

37. Depression or lateral movement of the patient's thyroid cartilage externally on the neck (known as optimal external laryngeal manipulation [OELM] or backward upward rightward pressure [BURP]) with the laryngoscopist's right hand may facilitate exposure of the glottic opening. (229)

38. Endotracheal tube sizes are specified according to their internal diameter (ID), which is marked on each tube. (230, Table 16-6)

39. Endotracheal tubes are radiopaque to ascertain the position of the distal tip relative to the carina. They are transparent to permit visualization of secretions or airflow as evidenced by condensation of water vapor in the lumen of the tube ("breath fogging") during exhalation. (230)

40. Use of the minimum volume of air in a low-pressure, high-volume cuff prevents air leaks during positive ventilation pressure (20 to 30 cm H_2O) while also minimizing the likelihood of mucosal ischemia resulting from prolonged pressure on the tracheal wall. (231)

41. Serious complications attributable to endotracheal cuff pressure include ciliary denudation, tracheal stenosis, tracheal rupture, tracheoesophageal fistula, tracheocarotid fistula, and tracheoinnominate artery fistula. (231)

42. Stylets that can be used to facilitate endotracheal intubation include gum elastic bougie, Schroeder stylet, Frova intubating introducer, lighted stylets, and seeing optical stylets. (231-232)

43. Correct placement of an endotracheal tube is confirmed by:
(1) The presence of end-tidal CO_2: the presence of carbon dioxide in the exhaled gases from the endotracheal tube as detected by capnography. An end-tidal $P_{CO_2} > 30$ mm Hg for three to five consecutive breaths should be immediate and sustained. Carbon dioxide may initially be present in low concentrations, but will not persist in exhaled gases from a tube accidentally placed in the esophagus. (2) Auscultation for bilateral breath sounds: symmetrical bilateral movement of the chest with manual ventilation, combined with the presence of bilateral breath sounds on apical or midaxillary auscultation of the lungs is confirmed after endotracheal intubation. (3) Characteristic feel of the reservoir bag: a characteristic feel of the reservoir bag is evaluated. It should be associated with normal lung compliance during manual inflation of the lungs and the presence of expiratory refilling of the bag. (4) Condensation of water in the tube lumen: condensation of water in the tube lumen (breath fogging) during exhalation is evidence of tracheal placement of the tube. (5) Sustained arterial hemoglobin oxygen saturations: progressive decreases in arterial hemoglobin oxygen saturation as evident on the pulse oximeter may alert the anesthesia provider to a previously unrecognized esophageal intubation. (6) Ballottement of tracheal tube cuff in the suprasternal notch. (232-233)

44. Awake fiberoptic endotracheal intubation is most frequently chosen when a difficult tracheal intubation by direct laryngoscopy is anticipated. This technique is suited to these situations because it can be performed before inducing general anesthesia, thus eliminating the risk of failed tracheal intubation and failed ventilation in anesthetized patients. It is usually safest to maintain spontaneous breathing if there is a question about the ability to manage the patient's airway. (233)

45. Fiberoptic endotracheal intubation is recommended for patients with unstable cervical spines because the technique does not require movement of the patient's neck and can be performed before the induction of general anesthesia, thereby allowing for evaluation of the patient's neurologic function after tracheal intubation and surgical positioning. (233)

46. Patients who have sustained an injury to the upper airway from either blunt or penetrating trauma are at risk for the endotracheal tube creating a false passage by exiting the airway through the disrupted tissue during direct laryngoscopy. By performing a fiberoptic intubation, not only can the injury be assessed, but the tracheal tube can also be placed beyond the level of the injury and thus eliminate the risk of causing subcutaneous emphysema, which could compress and further compromise the airway. (233)

47. An absolute contraindication to fiberoptic endotracheal intubation is a lack of time. The technique requires time to set up the equipment and prepare the patient's airway for tracheal intubation. Therefore, if immediate airway management is required, another technique should be used. (233)

48. Relative contraindications to fiberoptic endotracheal intubation include lack of space around the scope, the presence of excessive blood or secretions, and the presence of a pharyngeal abscess. (233)

49. In general, the nasal route is easier than the oral route for fiberoptic endotracheal intubation because the angle of curvature of the endotracheal tube naturally approximates that of the patient's upper airway. Additionally, nasal fiberoptic

endotracheal intubation tends to be less of a stimulus for the gag reflex. A disadvantage of nasal fiberoptic endotracheal intubation is that the risk of inducing bleeding is higher when the nasal route is used. Therefore, the nasal route is relatively contraindicated in patients with platelet abnormalities or coagulation disorders. (233)

50. An antisialagogue (glycopyrrolate, 0.2 mg IV) should be administered to inhibit the formation of secretions that can obscure fiberoptic visualization. (233)

51. Sedation choices are numerous, but the depth of sedation should be titrated to reflect individual patient needs. Sedation should be administered cautiously in patients in whom the airway management is predicted to be difficult. (233)

52. The nasal mucosa must be anesthetized and vasoconstricted, which is typically done with either a 4% cocaine solution or a combination of 3% lidocaine and 0.25% phenylephrine. Local anesthetic solutions can be applied on soaked cotton-tipped swabs or pledgets. (233)

53. Topicalization of the tongue and oropharynx may be achieved by aerosolized local anesthetic or by performing bilateral blocks of the glossopharyngeal nerve at the base of each anterior tonsillar pillar. (233-234)

54. Topicalization or nerve blocks may be used for the larynx and trachea. Local anesthetic may be sprayed, aerosolized, or nebulized into the airway. It should be noted that the larger particle size of a spray tends to cause it to be deposited in the pharynx, with only a small proportion reaching the trachea. Conversely, the small particle size of a nebulized spray is carried more effectively into the trachea, but also into the smaller airways, where the anesthetic is not needed and undergoes more rapid systemic absorption. (234)

55. Lidocaine is the preferred topical local anesthetic because of its broad therapeutic window. Benzocaine can cause methemoglobinemia even in therapeutic doses. Tetracaine has a very narrow therapeutic window, and the maximum allowable dose (1.2 mg/kg) can easily be exceeded. Cetacaine is a mixture of benzocaine and tetracaine and has the disadvantages of each local anesthetic. (234)

56. Two blocks that can be performed to topicalize the larynx and trachea include the superior laryngeal nerve block and the transtracheal block. (234)

FLEXIBLE FIBEROPTIC LARYNGOSCOPY

57. Softening the endotracheal tube in warm water before use makes it less likely to cause mucosal trauma or submucosal tunneling during nasal intubation. (234)

58. Inflation of the endotracheal tube cuff during advancement with the fiberoptic bronchoscope in the pharynx serves to create an enlarged pharyngeal space. Because secretions tend to adhere to the pharyngeal walls, endotracheal tube cuff inflation also helps keep the optics of the fiberoptic bronchoscope from being obscured. The inflated cuff further aims the tip of the endotracheal tube anteriorly. (234)

59. The appropriate depth of endotracheal tube placement can be verified by observing the distance between the carina and the tip of the endotracheal tube as the fiberoptic bronchoscope is withdrawn. (234)

60. If there is any resistance when removing the fiberoptic bronchoscope, the scope is either through the Murphy eye or kinked in the pharynx. In both instances, the endotracheal tube and the scope must be withdrawn together to prevent damaging the fiberoptic bronchoscope. (234)

61. Use of an oral intubating airway facilitates directing the bronchoscope during oral fiberoptic tracheal intubation. (235)

62. An important difference in performing fiberoptic laryngoscopy in an anesthetized patient is that the soft tissues of the pharynx, in contrast to the awake state, tend to relax and limit space for visualization with the fiberoptic bronchoscope. Using jaw thrust or a tonsil retractor, expanding the endotracheal tube cuff in the pharynx, or applying traction on the tongue, may overcome this problem. (235)

63. It is advisable to have a second person trained in anesthesia delivery assisting when a fiberoptic endotracheal intubation is performed under general anesthesia because it is difficult to maintain the patient's airway, be attentive to the monitors, and perform the fiberoptic intubation alone. (235)

64. The Patil-Syracuse mask is designed with a port that will accommodate an endotracheal tube and a fiberoptic bronchoscope through a diaphragm. This device allows for spontaneous or controlled ventilation while fiberoptic nasal or oral endotracheal intubation is being performed. (235)

65. The Aintree catheter is an airway exchange catheter with connectors that allow ventilation with an anesthesia breathing circuit or jet ventilator. It differs from other exchange catheters by having a lumen of adequate size to accommodate a fiberoptic bronchoscope. (235)

RIGID FIBEROPTIC LARYNGOSCOPES/ VIDEOLARYNGO SCOPES

66. Rigid fiberoptic laryngoscopes include the WuScope system, Bullard Laryngoscope, UpsherScope, GlideScope, McGrath Scope, Pentax-AWS, and Airtraq. These laryngoscopes may provide for better visualization of laryngeal structures and therefore facilitate endotracheal intubation in patients in whom direct laryngoscopy would otherwise be difficult. The laryngoscopes provide for better optics because of their rigid shape and/or because of the distal light source and optics on the laryngoscope blade. (235-236, Figure 16-6)

RETROGRADE TRACHEAL INTUBATION

Blind Nasotracheal Intubation

67. Retrograde endotracheal intubation involves threading a wire retrograde to the mouth through an external hole created by a needle in the cricothyroid membrane. The endotracheal tube can then be thread over the wire into the trachea with or without the aid of a fiberoptic bronchoscope. This technique may be useful in patients in which there is bleeding, limited mouth opening, or neck movement. It should not be performed in cases in which there is pathology.
Blind nasotracheal intubation involves advancing an endotracheal tube blindly from the nose into the trachea while listening to breath sounds or attaching the endotracheal tube to an anesthesia circuit and observing end-tidal CO_2. This technique is rarely used, however, since there are a number of other devices now available for management of the difficult airway. (235)

SUPRAGLOTTIC AIRWAY DEVICES

68. When correctly placed, the distal tip of the cuff should be against the upper esophageal sphincter (cricopharyngeus muscle), the lateral edges rest in the piriform sinuses, and the proximal end seats under the base of the tongue. (237-238)

69. The LMA Fastrach (Intubating LMA, ILMA) was designed to obviate the problems encountered when attempting to blindly intubate the trachea through a classic LMA. (238, Figure 16-18)

70. The ILMA is designed to be used with a silicone Euromedical endotracheal tube (size 7.0 ID, 7.5 ID, or 8.0 ID). These tracheal tubes exit the laryngeal mask at a different angle than do standard endotracheal tubes and thus result in better alignment with the airway. The ILMA is advanced into the pharynx by following the natural curvature of the patient's upper airway. Because Euromedical tubes have low-volume, high-pressure cuffs, it is recommended that the largest size that is appropriate for the patient be used to minimize mucosal pressure from the cuff. (238)

71. The LMA CTrach is a modified LMA Fastrach with fiberoptic bundles located within the bowl of the mask and a lightweight viewer that attaches after the device is inserted. (238-239)

72. The ProSeal LMA is a modification of the classic LMA. The cuff of the ProSeal LMA extends onto the back of the mask, which results in an improved airway seal without increasing mucosal pressure. It has a second lumen that parallels the one for the airway, but opens at the distal tip of the mask to act as an esophageal vent. When optimally seated, the ProSeal LMA effectively isolates the trachea from the esophagus, thus protecting the lungs from aspiration when a minimum of 10 mL of air has been placed in the LMA cuff. (239, Figure 16-19)

73. The ETC is a double-lumen device that can function as either an endotracheal device or an esophageal obturator. It has been used successfully in emergency medical management and requires minimal training. (239)

TRANSTRACHEAL TECHNIQUES

74. Transtracheal jet ventilation is the administration of oxygen under high pressure through a needle placed in the cricothyroid membrane into the trachea. Transtracheal jet ventilation is contraindicated in patients with any upper airway disruption or obstruction. Risks of transtracheal jet ventilation include pneumothorax, pneumomediastinum, bleeding, infection, and subcutaneous emphysema. (241)

75. Cricothyrotomy is almost always performed under emergent circumstances when mask ventilation and/or endotracheal intubation are not possible. This technique involves the placement of a breathing tube through the cricothyroid membrane. (241)

TRACHEAL EXTUBATION

76. Tracheal extubation after general anesthesia must be performed when the patient is either deeply anesthetized or fully awake. Tracheal extubation during a light level of anesthesia (disconjugate gaze, breath holding or coughing, and not responsive to command) increases the risk for laryngospasm. (241)

77. Laryngospasm is an involuntary spasm/closure of the vocal cords that may present as stridor or attempts to breathe without air exchange. Laryngospasm is likely to occur during tracheal extubation, particularly under a light level of anesthesia, when vocal cords are stimulated by mucus, blood, or other substance.

78. Laryngospasm can be treated with mask ventilation with 100% oxygen and continuous positive airway pressure along with forward displacement of the mandible with the anesthesia provider's index fingers to apply pressure at the temporomandibular joints. If laryngospasm persists, a small dose of an anesthetic induction agent or muscle relaxant may be used. (242-243)

79. Contraindications to deep tracheal extubation include previous difficult facemask ventilation or endotracheal intubation, risk of aspiration, and a surgical procedure that may have resulted in airway edema or increased airway irritability. (241)

80. Spontaneous ventilation with 100% oxygen is established before tracheal extubation. As with tracheal intubation, a functional residual capacity filled with oxygen allows for the longest safe period should breath holding or laryngospasm occur immediately after tracheal extubation. The effects of neuromuscular blocking drugs should be fully reversed. The oropharynx is suctioned just before tracheal extubation. The endotracheal tube cuff is deflated and the tracheal tube rapidly removed from the patient's trachea and upper airway while a positive-pressure breath is delivered to help expel any secretions. After tracheal extubation, oxygen is delivered by facemask. (241)

81. Dental trauma is the most frequent type of damage related to direct laryngoscopy. (242, Table 16-9)

82. Flexion of the patient's head may advance the tube up to 1.9 cm and convert an endotracheal placement into an endobronchial intubation, especially in children. Conversely, extension of the head can withdraw the tube up to 1.9 cm and result in pharyngeal placement. (242)

83. Laryngospasm and aspiration of gastric contents are the two most serious potential immediate complications after tracheal extubation. (242-243)

84. The major complication of prolonged tracheal intubation (>48 hours) is damage to the tracheal mucosa, which may progress to destruction of cartilaginous rings and subsequent scar formation and tracheal stenosis. Stenosis becomes symptomatic when the adult tracheal lumen is decreased to less than 5 mm. (243)

AIRWAY MANAGEMENT IN INFANTS AND CHILDREN

85. The difference between the infant and adult airway includes positioning of the larynx in the neck, tongue size, epiglottis size, size of the head relative to the body, neck length, nares size, and location of the narrowest point. Usually by the time the child is about 10 years old, the upper airway has taken on more adultlike characteristics. (243, Table 16-10)

86. The infant larynx is located higher in the neck at the level of C3-C4. In adults the larynx is at the level of C4-C5. In infants this causes the tongue to shift more superiorly, closer to the palate. The tongue more easily apposes the palate, which can cause airway obstruction in situations such as the inhalation induction of anesthesia. (243)

87. An infant's tongue is larger in proportion to the size of the mouth than in adults. The relatively large size of the tongue makes direct laryngoscopy more difficult and can contribute to obstruction of the upper airway during sedation, inhalation induction of anesthesia, or emergence from anesthesia. (243)

88. The epiglottis in an infant's airway is often described as relatively larger, stiffer, and more omega shaped than an adult epiglottis. More importantly, an infant's epiglottis is typically angled in a more posterior position, thereby blocking visualization of the vocal cords during direct laryngoscopy. (243)

89. In infants and small children, it is often necessary to lift the epiglottis with the tip of the blade of the laryngoscope to visualize the vocal cords and successfully intubate the trachea. Straight laryngoscope blades, which have a smaller profile than curved laryngoscope blades, more easily fit in the smaller infant mouth. Straight laryngoscope blades with their narrower tips also more effectively lift the epiglottis allowing better visualization of the vocal cords. (243)

90. The narrowest portion of an infant's airway is at the cricoid cartilage, whereas the narrowest portion of an adult's airway is at the vocal cords. (243)

91. The correct size uncuffed endotracheal tube is one that results in an air leak around the endotracheal tube with the application of 20 to 25 cm H_2O positive pressure. (243)

92. Cuffed endotracheal tubes can be used in infants and children if the inflation of the cuff is carefully adjusted and monitored so that the leak pressure remains at 20 to 25 cm H_2O. If nitrous oxide is used during the anesthetic, the nitrous oxide will diffuse into the air-filled cuff and increase both its volume and the pressure transmitted to the underlying tracheal mucosa. (243)

93. If the leak pressure is too high with either a cuffed or uncuffed endotracheal tube, the tracheal mucosa will be compressed causing subglottic edema either at the level of the cricoid cartilage or below. This complication can result in postextubation croup or stridor in mild cases and tracheal stenosis in more severe cases involving prolonged tracheal intubation. (243)

94. An infant's head and occiput are relatively larger than an adult's. The proper position for direct laryngoscopy and tracheal intubation in an adult is often described as the sniffing position with the head elevated and the neck flexed at C6-C7 and extended at C1-C2. An infant, on the other hand, requires a shoulder roll or neck roll to establish an optimal position for facemask ventilation and direct laryngoscopy. (243)

95. Infant's nares are relatively smaller than an adult's. This can offer significant resistance to airflow, and increase the work of breathing, especially when secretions, edema, or bleeding narrow them. (243-244)

96. A history of snoring should prompt additional questioning about whether the child has obstructive sleep apnea and should alert the anesthesia provider that respiratory obstruction may develop during the induction and emergence phases of anesthesia, as well as in the postoperative period. This is of particular concern if opioids are given for pain management. (244)

97. Preanesthetic medication can facilitate separation of the infant or child from the parents before the induction of anesthesia. Preanesthetic medication is often not necessary in infants younger than 6 months because stranger anxiety does not usually develop until 6 to 9 months of age. (244)

98. Midazolam syrup can be given orally (2 mg/mL) in a dose of 0.5 mg/kg up to a maximum dose of about 20 mg. If the child is uncooperative with taking oral midazolam and preanesthetic medication is essential, midazolam can also be given intranasally, intramuscularly, or rectally. (244)

99. In a child without an intravenous catheter in place, the induction of anesthesia with the odorless mixture of nitrous oxide and oxygen through a facemask and then slowly increasing the concentration of sevoflurane is the best approach in a cooperative child. When the infant or child becomes unconscious, the nitrous oxide should be turned off to administrate 100% oxygen to the child. (244)

100. Airway obstruction during mask induction in infants and children can usually be relieved by opening the mouth, extending the neck, and pushing anteriorly on the angle of the jaw. Occasionally, an oral or nasal airway may need to be inserted. (244)

101. The weight of the infant or child determines the appropriate size of LMA. (245)

102. The LMA Flexible has a wire-reinforced airway tube that resists kinking and can be positioned in such a way that interference with surgical procedures involving the head and neck is minimized. (245)

103. The major advantage of the Air-Q ILA is a design that facilitates endotracheal intubation with standard oral endotracheal tubes. The airway tube has a larger diameter than the LMA, allowing for intubation with a larger ETT than the correspondingly sized LMA. In addition, the Air-Q ILA can be used with a specially designed ILA removal stylet that stabilizes the ETT and allows controlled removal of the ILA without dislodging the ETT from the trachea. (245-246)

104. The appropriately sized endotracheal tube for infants and children can be estimated by using the following formula:

$$(\text{Age} + 16)/4 = \text{Endotracheal Tube size.}\ (246)$$

105. The formula is for uncuffed endotracheal tubes. (246)

106. When using a cuffed endotracheal tube in infants and children, the formula used to estimate the appropriate-sized uncuffed endotracheal tube must be adapted. To adapt the formula it is necessary to subtract half a size from the calculated size to estimate the appropriate size cuffed endotracheal tube. (246)

107. The new Microcuff pediatric endotracheal tubes appear to offer several distinct advantages over conventional pediatric cuffed endotracheal tubes. The Microcuff endotracheal tubes have a cuff that is made from a microthin polyurethane membrane that, while stronger than conventional cuffs, seals the airway at lower cuff pressures than conventional endotracheal tubes. This reduces the potential for mucosal edema and postextubation croup. The cuff on the Microcuff endotracheal tube is also shorter and placed closer to the tip of the endotracheal tube, increasing the chances that the endotracheal tube is correctly placed. The Microcuff endotracheal tube also has an intubation depth mark, which indicates the correct depth for insertion and also increases the ability for correct placement. (246)

108. Using a stylet stiffens the endotracheal tube and makes it easier to manipulate during direct laryngoscopy and tracheal intubation. The trachea of infants and small children can often be intubated without using a stylet, but a stylet may be useful for whenever a difficult tracheal intubation is anticipated. Even if intubating without a stylet, the appropriately sized stylet should always be immediately available. (246, Table 16-6)

109. The disadvantage of a straight blade is that it does not retract the tongue as well to the left side of the mouth. A curved blade has a larger flange that retracts the tongue to the left more effectively and may be useful in certain patient populations in which the tongue is larger than normal. (246-247)

110. In infants younger than 1 year, a Miller 1 straight laryngoscope blade is most useful. In children between 1 and 3 years of age, a 1½ straight laryngoscope blade, such as a Wis-Hipple, is often useful. A longer straight laryngoscope blade such as a Miller 2 is appropriate for most children between 3 and 10 years of age. The tracheas of children older than 11 years are often more easily intubated with a curved laryngoscope blade such as a Macintosh 3. Both straight and curved laryngoscope blades of various sizes should always be available. (247)

111. When an unexpected difficult airway appears in pediatric patients, the most important first step is to call for an additional anesthesia colleague to help. (247, Figure 16-23)

112. It is critical to not persist with repeated attempts at direct laryngoscopy, which can result in trauma to the upper airway, edema, and bleeding. In most situations, an LMA should be inserted to provide an airway to oxygenate and ventilate the patient and allow time to obtain additional personnel and airway equipment. An LMA may be the only way to maintain an airway until the patient wakes up or a surgical airway is established. An LMA is also an excellent conduit for fiberoptic intubation. (247)

113. It is unlikely that infants and children will cooperate with procedures such as an awake fiberoptic endotracheal intubation, so it is usually necessary to induce anesthesia and manage the airway with the patient asleep. (247)

114. An additional anesthesia colleague should be available for help during the induction of anesthesia, inserting an intravenous line, and securing the airway. A surgeon capable of establishing a surgical airway and emergency airway equipment should be in the operating room before beginning the induction of anesthesia. (247)

115. Lighted stylets, the GlideScope video laryngoscope, and fiberoptic bronchoscopes are all available in smaller sizes to facilitate intubation of a child with a difficult airway. (247-248)

116. Infants and small children are at a more likely risk than adults for croup, stridor, and laryngospasm after tracheal extubation. (248)

117. Croup occurs most commonly when either a cuffed or uncuffed endotracheal tube is used that is too large or when the cuff is inflated with too much air. The resulting mechanical pressure on the tracheal mucosa causes venous congestion and edema, and in severe cases can even compromise the arterial blood supply causing mucosal ischemia. The resulting edema can narrow the tracheal lumen, especially in infants and small children. Because resistance to flow in an endotracheal tube is inversely proportional to the radius of the lumen to the fourth power, 1 mm of edema in an infant airway is much more significant than 1 mm of edema in an adult airway. Other risk factors for croup include multiple tracheal intubation attempts, unusual positioning of the head during surgery, increased duration of surgery, and procedures involving the upper airway, such as rigid bronchoscopy. (248-249)

118. An infant or child with postextubation croup usually has respiratory distress in the postanesthesia care unit. Nasal flaring, retractions, an increased respiratory rate, audible stridor, and decreased oxygen saturation are common clinical findings. (249)

119. Treatment of postextubation croup or stridor depends on the degree of respiratory distress. Mild symptoms can be managed with humidified oxygen and prolonged observation in the postanesthesia care unit. More severe cases may require aerosolized racemic epinephrine and postoperative observation in an intensive care unit. Patients whose respiratory distress is severe and not relieved with these measures may need to be reintubated with an endotracheal tube smaller than the one previously used. Steroids administered intravenously for preventing upper airway edema are more beneficial when given before the airway is instrumented and should be administered before procedures such as rigid bronchoscopy. (249)

120. Infants and children with obstructive sleep apnea are at significant risk for airway obstruction, respiratory distress, and the potential for apnea in the postoperative period. At baseline these infants and children hypoventilate, which results in hypercapnia and often arterial hypoxemia while asleep. Residual inhaled anesthetics or residual neuromuscular blockade can depress airway reflexes, skeletal muscle tone and strength, and respiratory drive, and result in significant airway compromise in infants and children with obstructive sleep apnea. (249)

121. Opioids must be very carefully titrated both intraoperatively and postoperatively because they can depress the ventilatory drive and contribute to significant hypercapnia and arterial hypoxemia in these infants and children. (249)

122. Tracheal extubation in patients with obstructive sleep apnea should be considered only when these infants and children are fully awake. All infants and children with obstructive sleep apnea should be monitored postoperatively with pulse oximetry and apnea monitoring. High-risk patients should be monitored postoperatively in an intensive care unit setting. (249)

123. Tracheal extubation of an infant or child after a difficult intubation is considered carefully because reintubation can be more difficult than the initial intubation. The tracheas of infants and children with difficult airways should be extubated only when they are fully awake and there is no residual neuromuscular blockade. An infant or child with a difficult airway should be extubated only when appropriate equipment and personnel are available for urgent reintubation. (250)

Chapter

14 SPINAL AND EPIDURAL ANESTHESIA

Ken Drasner

1. What term is used to collectively describe spinal and epidural anesthesia?
2. Where is medicine deposited during performance of spinal anesthesia? With epidural anesthesia? With caudal anesthesia?
3. What are some advantages of spinal anesthesia when compared with epidural anesthesia?
4. What are some advantages of epidural anesthesia?

ANATOMY

5. What is the relative clinical significance of the curvatures of the spinal canal with respect to spinal and epidural anesthesia?
6. What is the number of each type of vertebrae composing the vertebral column?
7. Describe the anatomic parts of a vertebra by answering the following questions: What are the two parts that make up a vertebra? From what parts of the vertebra does the transverse process arise? From what parts of the vertebra does the spinous process arise?
8. How do the different characteristic features of the spinous processes and laminae of the thoracic and lumbar vertebrae impact clinical performance of neuraxial blocks?
9. What is the sacral hiatus?
10. What are some important surface landmarks used to identify specific spinal interspaces to guide placement of a spinal or epidural needle?
11. How are the laminae of adjacent vertebrae connected?
12. How are the tips of the spinous processes of adjacent vertebrae connected?
13. What passes through the intervertebral foramina?
14. What are the rostral and caudal limitations of the spinal canal? What accounts for the disparity between the vertebral level and spinal level?
15. What is the cauda equina, and what characteristic features are relevant to spinal anesthesia?
16. What are the three meningeal layers surrounding the spinal cord?
17. Where is cerebrospinal fluid relative to the meningeal layers? What are two interchangeable terms for this space?
18. What structures form the boundaries of the epidural space?
19. What structures are contained within the epidural space?
20. As the nerves pass through the intervertebral foramen they become encased by the dura, arachnoid, and pia, forming what three components of a peripheral nerve?
21. Where do the preganglionic nerves of the sympathetic nervous system originate, and what is their course of travel after leaving the spinal cord?
22. What is the plica mediana dorsalis? What might be its clinical significance?
23. Describe the blood supply of the spinal cord. Which area of the cord is most vulnerable to ischemic insult?
24. What is the artery of Adamkiewicz?

PREOPERATIVE PREPARATION

25. What are the potential complications that should be discussed with the patient before proceeding with a spinal or epidural anesthetic?
26. What are the common indications for spinal anesthesia?
27. What are the common indications for epidural anesthesia?
28. What are the absolute contraindications to neuraxial anesthesia?
29. Does bacteremia preclude performance of a neuraxial technique?
30. Does chronic back pain preclude performance of a neuraxial technique?
31. What cardiac disorders warrant specific concern with respect to neuraxial anesthesia?
32. Do coagulation abnormalities preclude performance of a neuraxial anesthetic?

SPINAL ANESTHESIA

33. What are the common positions patients are placed in for administration of a spinal anesthetic?
34. What are some advantages and disadvantages of having a patient in a sitting position during performance of a spinal anesthetic?
35. Why might an anesthetist choose to administer a spinal with a patient in the lateral decubitus position?
36. What vertebral level is crossed by a line drawn across the patient's back at the level of the top of the iliac crests? What interspace is located directly above this line? What interspace is located directly below this line?
37. What is the reason for placing a spinal anesthetic at a level below the L2 vertebra?
38. On what basis are spinal needles generally classified?
39. Which characteristics of a spinal needle will result in the lowest incidence of postdural puncture headache?
40. What are the two approaches used for spinal anesthesia, and what are their relative advantages and disadvantages?
41. When a midline approach is chosen, what are the tissue planes that will be traversed as the needle is advanced toward the subarachnoid space?
42. What accounts for the "pop" the anesthetist may feel when advancing a spinal needle into the subarachnoid space?
43. How is subarachnoid placement of the spinal needle confirmed?
44. How can the spinal needle be handled to stabilize the needle after proper placement in the subarachnoid space is confirmed?
45. After the syringe containing the local anesthetic solution for administration into the subarachnoid space is attached to the spinal needle, how can continued subarachnoid placement of the spinal needle be confirmed?
46. What should be done if blood-tinged cerebral spinal fluid (CSF) appears at the hub of the needle?
47. Describe the lumbosacral (Taylor) approach. When is this approach advantageous?
48. What are the three factors that most influence the distribution of the local anesthetic solution in cerebrospinal fluid after its administration into the subarachnoid space?
49. How is the baricity of a local anesthetic solution to be administered into the subarachnoid space defined? Why is this clinically important?
50. What are the two things that most influence the duration of a spinal anesthetic?
51. What is the baricity of the most commonly used spinal anesthetics? What is added to local anesthetics for spinal anesthesia to make the solution hyperbaric? What is the principal advantage of these solutions?
52. What role does the contour of the vertebral canal play in anesthetic distribution, and hence, level of spinal block?
53. What is a "saddle block"?
54. What situations might warrant use of a hypobaric solution?
55. What are the relative advantages and disadvantages of isobaric solutions?
56. What is the purpose of adding a vasoconstrictor to the local anesthetic solution used for spinal anesthesia? What is their mechanism of action?

57. What are the two potentially useful effects derived from adding an opioid to the local anesthetic used for spinal anesthesia? What is their mechanism of action?
58. How do spinal anesthetics regress during the recovery from spinal anesthesia?
59. What recent events have led to concern regarding the use of lidocaine for spinal anesthesia? What are some modifications in practice that have been suggested should lidocaine be used for this purpose?
60. What is TNS, and what are the factors that increase the risk of its occurrence following spinal anesthesia with lidocaine?
61. List the rank order for the relative incidence of TNS with the following local anesthetics used for spinal anesthesia: bupivacaine; chloroprocaine; lidocaine; mepivacaine; prilocaine; and procaine.
62. What are some important restrictions with respect to the anesthetic solution if using chloroprocaine off-label for spinal administration?
63. What are some distinguishing characteristics between bupivacaine and tetracaine with respect to spinal anesthesia?
64. What is the temporal order of blockade of the motor, sensory, and sympathetic nerves after the administration of a spinal anesthetic?
65. What is a useful way to gain an early indication of the level of spinal anesthesia?
66. How do the ultimate dermatomal levels of motor, sensory, and sympathetic block compare during spinal anesthesia?
67. How is the extent of motor block produced by a spinal anesthetic generally assessed?
68. What surface landmarks are used to determine the approximate level of spinal anesthesia?
69. What are some advantages and disadvantages of a continuous spinal technique?
70. Why were microcatheters used for spinal anesthesia withdrawn from the U.S. market?
71. What is the likely mechanism of injury associated with microcatheters?
72. Has removal of microcatheters eliminated the risk of neurologic injury?
73. What elements of the continuous spinal technique are important to prevent neurologic injury?
74. What dose of anesthetic should be used when repeating a spinal because of a failed block?
75. What are the physiologic effects on the respiratory system of an appropriately instituted spinal anesthetic?
76. What are some physiologic effects on the gastrointestinal tract and the genitourinary system that result from a spinal anesthetic?
77. What is the effect of spinal anesthesia on blood pressure and what accounts for this effect?
78. How is spinal anesthetic-induced hypotension treated?
79. What is the effect of spinal anesthesia on heart rate, and what is believed to be the underlying mechanism?
80. How are spinal anesthetic-induced perturbations in heart rate treated?
81. What is the cause and typical onset of a postdural puncture headache?
82. What is the hallmark feature of a postdural puncture headache?
83. What are some of the other characteristic features of a postdural puncture headache?
84. What serious complications may result from a postdural puncture headache?
85. Which patients are most at risk for development of a postdural puncture headache?
86. What features of a spinal needle will impact the incidence of a postdural puncture headache?
87. What are some of the commonly used treatment options for a postdural puncture headache?
88. What are the likely predominant mechanism(s) by which an epidural blood patch may relieve a postdural puncture headache?
89. What is a “total spinal”?
90. How should a total spinal be managed?

91. What are two possible causes of nausea that present soon after the administration of a spinal anesthetic?
92. What might contribute to backache occurring in a patient who has received a spinal for surgical anesthesia?

EPIDURAL ANESTHESIA

93. Is it acceptable to place a lumbar epidural after the induction of general anesthesia?
94. Is it acceptable to place a thoracic epidural after the induction of general anesthesia?
95. What are the advantages and disadvantages of epidural catheters that have an inner stainless steel core?
96. What are the comparative advantages and disadvantages of epidural catheters with a closed versus open tip?
97. Which approach (midline or paramedian) is most often used for placement of a thoracic epidural, and why is it chosen?
98. What is the "loss-of-resistance" technique?
99. What is the "hanging-drop" technique?
100. What are the potential advantages and disadvantages of the single-injection versus catheter technique for epidural anesthesia?
101. What is the technique used for placement of a catheter following identification of the epidural space?
102. What is the "test dose" for an epidural catheter? What is it testing for? How long must the anesthetist wait after administering the test dose to make this determination?
103. Why is the anesthetic administered in incremental doses?
104. Complete the following table of local anesthetics used for epidural anesthesia:

	Concentration (%)	*Onset (min)*	*Duration (min)*
Chloroprocaine			
Lidocaine			
Ropivacaine			
Bupivacaine			

105. Why are tetracaine and procaine rarely used for epidural anesthesia?
106. How is the caudal epidural space identified?
107. What anatomic variations may impact success and complications with caudal anesthesia?
108. What are the major factors affecting the spread of epidural anesthesia?
109. What patient-related factors might influence spread of epidural anesthesia?
110. How do patient position and anesthetic baricity influence the spread of epidural anesthesia?
111. What are the principal factors affecting the duration of epidural anesthesia?
112. What are some of the potential advantages of adding epinephrine to an anesthetic solution used for epidural anesthesia?
113. What is the effect of sodium bicarbonate when added to the local anesthetic solution used for epidural anesthesia?
114. For which local anesthetics is sodium bicarbonate commonly used as an additive?
115. How does lipophilicity affect the choice of opioids used for epidural administration?
116. What are some potential causes of failure of an epidural block?
117. What are the options for managing a failed epidural block?
118. What is the major site of action of local anesthetics administered epidurally?
119. How do the risks of epidural anesthesia compare with that of spinal anesthesia?
120. What are the commonly used management options following a "wet-tap"?

121. What are the risks associated with accidental subarachnoid injection of an epidural dose of anesthetic, and how should this complication be managed?
122. How do the hemodynamic effects of an epidural compare with those of spinal anesthesia?
123. Why does epidural anesthesia differ from spinal anesthesia with respect to systemic local anesthetic toxicity?
124. What are the clinical characteristics of an accidental subdural injection of anesthetic intended for the epidural space?
125. What is the significance of a paresthesia occuring during performance of an epidural anesthetic?
126. What is "combined spinal-epidural" anesthesia, and in what clinical setting is it commonly used?
127. What are the potential advantages of a combined epidural-general technique?

ANSWERS*

1. Spinal and epidural anesthesia are collectively referred to as central neuraxial block. These procedures are subcategories or specific types of regional or conduction anesthesia. (253)

2. In spinal anesthesia, medicine is deposited into the cerebrospinal fluid within the subarachnoid space, with very rare exception at the lumbar level. In epidural anesthesia, the drug is deposited within the epidural space, and is commonly performed at both the lumbar and thoracic level. In caudal anesthesia, medicine is also deposited in the epidural space but the needle used to inject the medicine approaches the epidural space via the sacral hiatus. (253)

3. When compared with epidural anesthesia, spinal anesthesia takes less time to perform, causes less discomfort during placement, requires less local anesthetic, and produces more intense sensory and motor block. In addition, correct placement of the needle in the subarachnoid space is confirmed by a clearly defined endpoint (appearance of cerebral spinal fluid). (253)

4. Advantages of epidural anesthesia include a decreased risk of a postdural puncture headache (assuming a negligible incidence of inadvertent dural puncture), a lower incidence of systemic hypotension, the ability to produce a segmental sensory block, and greater control over the intensity of sensory anesthesia and motor block achieved by adjustment of the local anesthetic concentration. The routine placement of catheters for epidural anesthesia imparts additional benefit by allowing titration of the block for the duration of surgery. Additionally, maintenance of a catheter provides a means for long-term administration of local anesthetics or opioid-containing solutions (or both), which are highly effective for control of postoperative or obstetric pain. (253)

ANATOMY

5. On a lateral view, the vertebral canal exhibits four curvatures, of which the thoracic convexity (kyphosis) and the lumbar concavity (lordosis) are of major importance to the distribution of local anesthetic solution in the subarachnoid space. In contrast, these curves have little effect on the spread of local anesthetic solutions in the epidural space. (253, Figure 17-1)

6. The vertebral column is composed of 7 cervical vertebrae, 12 thoracic vertebrae, and 5 lumbar vertebrae, as well as the 5 fused sacral and 4 fused coccygeal vertebrae. (253, Figure 17-1)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

7. A vertebra is made up of the vertebral body and the bony arch. The transverse process arises from the junction of the pedicle and laminae. The spinous process arises posteriorly from the joining of the laminae. (253, Figure 17-2)

8. The nearly perpendicular orientation of the spinous process in the lumbar area and the downward angular orientation in the thoracic area define the angle required for placement and advancement of a needle intended to access the vertebral canal. The wide interlaminar space in the lumbar spine reflects the fact that the lamina occupies only about half the space between adjacent vertebrae. In contrast, the interlaminar space is just a few millimeters wide at the level of the thoracic vertebrae. (254, Figure 17-5)

9. The opening between the unfused lamina of the fourth and fifth sacral vertebrae is called the sacral hiatus. There is considerable anatomic variability in the features of the dorsal surface of the sacrum. Indeed, the sacral hiatus is absent in nearly 8% of adult subjects, thereby preventing entry through the sacrococcygeal ligament into the sacral canal and performance of caudal anesthesia. (255, Figure 17-4)

10. Surface landmarks are used to identify specific spinal interspaces. The most important surface landmarks include a line drawn between the iliac crests, which generally traverses the body of the L4 vertebra and is the principal landmark used to determine an appropriate level for insertion of a spinal needle; the C7 spinous process appreciated as a bony knob at the lower end of the neck; and a line drawn between the lower limits of the scapulae roughly correlating with the T7-8 interspace that is often used to guide needle placement for passage of a catheter into the thoracic epidural space. (255, Figure 17-6)

11. The laminae of adjacent vertebrae are connected by the ligamentum flavum. (256, Figure 17-3)

12. The tips of the spinous processes of adjacent vertebrae are connected by the supraspinous ligaments. (256, Figure 17-3)

13. The spinal nerves pass through the intervertebral foramina and supply a specific dermatome. (258, Figure 17-3)

14. The spinal cord begins at the rostral border of the medulla and, in the fetus, extends the entire length of the vertebral canal. However, because of disproportionate growth of neural tissue and the vertebral canal, the spinal cord generally terminates around the third lumbar vertebra at birth and at the lower border of the first lumbar vertebra in adults. As a further consequence of this differential growth, the spinal nerves become progressively longer and more closely aligned with the longitudinal axis of the vertebral canal. (256)

15. The cauda equina—so named because of its resemblance to a horse's tail—is the collection of lumbar and sacral nerves that extend beyond the end of the spinal cord as a collection of nerves in the spinal canal before exiting via the intervertebral foramina at their respective vertebral column levels. The nerve roots of the cauda equina move relatively freely within the CSF, a fortunate arrangement that permits them to be displaced rather than pierced by an advancing needle. (256)

16. The outermost meningeal layer, the dura mater, is a tough fibroelastic membrane that provides structural support. It originates at the foramen magnum and continues caudally to terminate between S1 and S4. Closely adherent to the inner surface of the dura lies the arachnoid membrane. Though far more delicate than the dura, the arachnoid serves as the major pharmacologic barrier preventing movement of the drug from the epidural to the subarachnoid space. The innermost layer of the spinal meninges, the pia, is a highly vascular structure closely applied to the cord that forms the inner border of the subarachnoid space. (258, Figures 17-9 and 17-10)

17. Cerebrospinal fluid is contained between the pia and arachnoid, consequently referred to as the subarachnoid space. Another term for this anatomic compartment is the intrathecal space. (258, Figure 17-10)

18. The epidural space lies between the dura and the wall of the vertebral canal. It is bounded cranially by the foramen magnum, caudally by the sacrococcygeal ligament, anteriorly by the posterior longitudinal ligament, laterally by the vertebral pedicles, and posteriorly by both the ligamentum flavum and vertebral lamina. (259)

19. Although often referred to as a "potential space," the epidural space is actually an irregular column of fat, lymphatics, and blood vessels. It is not a closed space but communicates with the paravertebral spaces by way of the intervertebral foramina. (259)

20. The dura, arachnoid, and pia encasement of the peripheral nerve are the origins of the epineurium, perineurium, and endoneurium, respectively. (258, Figure 17-10)

21. Preganglionic nerves of the sympathetic nervous system originate from the spinal cord at the T1 to L2 levels. From there they travel with the spinal nerves before separating to form the sympathetic chain, and more distant sites such as the celiac plexus. (258, Figure 17-11)

22. There is controversy regarding the existence and clinical significance of a connective tissue band (plica mediana dorsalis) extending from the dura mater to the ligamentum flavum and hence dividing the posterior epidural space into two compartments. Anatomic studies have suggested the presence of this structure and have led to speculation that this tissue band may occasionally be responsible for difficulty threading a catheter into the epidural space or the occurrence of a unilateral sensory block. However, some investigators have been unable to confirm the presence of this structure.

23. The blood supply of the spinal cord arises from a single anterior and two paired posterior spinal arteries (Figure 17-13). The posterior spinal arteries emerge from the cranial vault and supply the dorsal (sensory) portion of the spinal cord. Because they are paired and have rich collateral anastomotic links from the subclavian and intercostal arteries, this area of the spinal cord is relatively protected from ischemic damage. This is not the case with the single anterior spinal artery that originates from the vertebral artery and supplies the ventral (motor) portion of the spinal cord. (260, Figure 17-13)

24. The anterior spinal artery receives branches from the intercostal and iliac arteries, but these branches are variable in number and location. The largest anastomotic link, the radicularis magna (artery of Adamkiewicz), arises from the aorta in the lower thoracic or upper lumbar region. The vessel is highly variable but, most commonly, is on the left and enters the vertebral canal through the L1 intervertebral foramen. The artery of Adamkiewicz is critical to the blood supply of the lower two thirds of the spinal cord, and damage to it will produce characteristic bilateral lower extremity motor loss (anterior spinal artery syndrome). (260, Figure 17-13)

PREOPERATIVE PREPARATION

25. Relevant complications that should be discussed with the patient include (1) those that are rare but serious, including nerve damage, bleeding, and infection, and (2) those that are common but of relatively minor consequence, such as a postdural puncture headache. There are no common serious complications (if there were, these techniques would not be used in clinical practice), and the infrequent minor problems are not of sufficient concern to warrant specific discussion. The possibility of a failed block should be discussed, and the patient should be reassured that in

such circumstances, alternative anesthetic techniques will be provided to ensure their comfort. (262)

26. Spinal anesthesia is generally used for surgical procedures involving the lower abdominal area, perineum, and lower extremities. Although the technique can also be used for upper abdominal surgery, most consider it preferable to administer a general anesthetic to ensure patient comfort. In addition, the extensive block required for upper abdominal surgery and the nature of these procedures may have a negative impact on ventilation and oxygenation. (262)

27. Epidural anesthesia, like spinal anesthesia, is often used as the primary anesthetic for surgeries involving the lower abdomen or lower extremities. However, because of its segmental nature, anesthesia provided by lumbar epidural anesthesia may be suboptimal for procedures involving the lower sacral roots. Epidural anesthesia is also frequently used as a supplement to general anesthesia, particularly for thoracic and upper abdominal procedures. In such cases, significant benefit derives from the ability to provide continuous epidural anesthesia postoperatively to facilitate effective treatment of postoperative pain, as numerous studies confirm the superiority of epidural techniques compared to parenteral opioids. Similarly, continuous epidural anesthesia is very effective and widely used for the control of labor pain. (262)

28. Absolute contraindications to neuraxial anesthesia include patient refusal, infection at the site of planned needle puncture, elevated intracranial pressure, and bleeding diathesis. Patients should never be encouraged against their wishes to accept a regional anesthetic technique. (262)

29. Bacteremia does not necessarily mitigate against performance of a regional anesthetic technique. Although concern that an epidural abscess or meningitis might result from the introduction of infected blood during the procedure, clinical experience suggests that the risk is small and can be weighed against the potential benefit. In such cases, there is evidence to suggest that institution of appropriate antibiotic therapy before the block may decrease the risk for infection. (262)

30. Chronic back pain does not represent a contraindication to neuraxial anesthetic techniques, although they may be avoided because patients may perceive a relationship between postoperative exacerbation of pain and the block, even though they are not causally related. (262)

31. Patients with mitral stenosis, idiopathic hypertrophic subaortic stenosis, and aortic stenosis are intolerant of acute decreases in systemic vascular resistance. Thus, though not a contraindication, neuraxial block should be used cautiously in such cases. (262)

32. The decision to use a neuraxial block in patients with abnormal coagulation, either endogenous or produced by the administration of anticoagulants, must be based on a risk-benefit assessment and include discussion with the patient and the surgical team. Guidelines developed by the American Society of Regional Anesthesia (www.asra.com) are updated periodically based on evolving literature and changes in clincal practice, and can thus provide valuable guidance in the management of these patients. (262)

SPINAL ANESTHESIA

33. Spinal anesthesia can be performed with the patient in the lateral decubitus, sitting, or less commonly, the prone position. To the extent possible, the spine should be flexed by having the patient bend at the waist and bring the chin toward the chest, which will optimize the interspinous space and the interlaminar foramen. (263)

34. The sitting position encourages flexion and facilitates recognition of the midline, which may be of increased importance in an obese patient. Because lumbar cerebral

spinal fluid (CSF) is elevated in this position, the dural sac is distended, thus providing a larger target for the spinal needle. This higher pressure also facilitates recognition of the needle tip within the subarachnoid space, as heralded by the free flow of CSF. When combined with a hyperbaric anesthetic, the sitting position favors a caudal distribution; the resultant anesthesia is commonly referred to as a "saddle block." However, in addition to being poorly suited for a heavily sedated patient, vasovagal syncope can occur. (263)

35. The lateral decubitus position is more comfortable and more suitable for the ill or frail. It also enables the anesthetist to safely provide greater levels of sedation. (263)

36. A line drawn across the patient's back at the level of the top of the iliac crests is generally considered to identify the L4 vertebral level. The interspace palpated directly above this line would be L3-4, and the interspace palpated directly below this line would be L4-5. However, this is not invariant, and not uncommonly, use of this conceptual line will result in estimates that are inaccurate by as much as two interspaces. (263)

37. The caudal limitation of the spinal cord in an adult usually lies between the L1 and L2 vertebrae. For this reason, spinal anesthesia is not ordinarily performed above the L2-3 interspace. Nevertheless, some risk remains because the spinal cord extends to the third lumbar vertebra in approximately 2% of adults. (263)

38. A variety of needles are available for spinal anesthesia and they are generally classified by their size (most commonly 22 to 25 gauge) and the shape of their tip. The two basic designs of spinal needles are (1) an open-ended (beveled or cutting) needle and (2) a closed tapered-tip pencil-point needle with a side port. (263, Figure 17-14)

39. The incidence of postdural puncture headache varies directly with the size of the needle, and it is also lower when a pencil-point (Whitacre or Sprotte) rather than a beveled-tip (Quincke) needle is used. Consequently, a 24- or 25-gauge pencil-point needle is usually selected when spinal anesthesia is performed on younger patients in whom postdural puncture headache is more likely to develop. (263, Figure 17-14)

40. Spinal anesthesia can be accomplished using a midline or a paramedian approach. The midline approach is technically easier, and the needle passes through less sensitive structures, thus requiring less local anesthetic infiltration to ensure patient comfort. However, the paramedian approach is better suited to challenging circumstances when there is narrowing of the interspace or difficulty in flexion of the spine. (264)

41. As the spinal needle progresses toward the subarachnoid space, it passes through the skin, subcutaneous tissue, supraspinous ligament, interspinous ligament, ligamentum flavum, and the epidural space to reach and pierce the dura/arachnoid. (264, Figure 17-3)

42. The anesthetist may feel a characteristic "pop" just before accessing the subarachnoid space as the spinal needle is being advanced. This "pop" is produced by the spinal needle passing through the dura mater. (265)

43. Subarachnoid placement of the spinal needle is confirmed by the appearance of cerebrospinal fluid in the hub of the spinal needle. (265)

44. After proper positioning in the subarachnoid space, the spinal needle may be stabilized by holding the hub of the spinal needle between the anesthesiologist's thumb and forefinger and resting the dorsum of the same hand on the patient's back. When the spinal needle is held in this manner, it should remain stabilized even with patient movement. (265)

45. After the syringe containing the local anesthetic solution for administration into the subarachnoid space is attached to the spinal needle, the anesthetist typically aspirates back on the syringe to confirm continued subarachnoid placement of the spinal needle tip. Confirmation is made by the characteristic swirl in the syringe as cerebrospinal fluid enters the syringe and mixes with the local anesthetic solution. The local anesthetic solution can then be deposited into the subarachnoid space over approximately 3 to 5 seconds. After completion of the deposition of the local anesthetic solution into the subarachnoid space, cerebrospinal fluid can again be aspirated to verify delivery of the anesthetic. The spinal needle and syringe should be removed together as a single unit, and the antiseptic wiped from the patient's back. (265)

46. Occasionally, blood-tinged CSF initially appears at the hub of the needle. If clear CSF is subsequently seen, the spinal anesthetic can be completed. Conversely, if blood-tinged CSF continues to flow, the needle should be removed and reinserted at a different interspace. Should blood-tinged CSF still persist, the attempt to induce spinal anesthesia should be terminated. (265)

47. The Taylor approach (first described by Dr. John A. Taylor, a urologist) describes the paramedian technique to access the L5-S1 interspace. Though generally the widest interspace, it is often inaccessible from the midline because of the acute downward orientation of the L5 spinous process. The spinal needle is passed from a point 1 cm caudad and 1 cm medial to the posterior superior iliac spine and advanced cephalad at a 55-degree angle with a medial orientation based on the width of the sacrum. The Taylor approach is technically challenging but very useful because it is minimally dependent on patient flexion for successful passage of the needle into the subarachnoid space. (265, Figure 17-15)

48. The three factors that most influence the distribution of local anesthetic solution in the subarachnoid space are the baricity of the solution, the contour of the spinal canal, and the position of the patient during, and for the first few minutes after, its administration. (266)

49. Local anesthetic solutions are classified as hypobaric, isobaric, and hyperbaric based on their density relative to the density of CSF. Baricity is an important consideration because it predicts the direction that local anesthetic solution will move after injection into the CSF. (266)

50. The two things that most influence the duration of a spinal anesthetic are the particular drug selected and whether a vasoconstrictor, such as epinephrine or phenylephrine, is present in the local anesthetic solution. (266)

51. The most commonly selected local anesthetic solutions for spinal anesthesia are hyperbaric (achieved by the addition of glucose), and their principal advantage is the ability to achieve greater cephalad spread of anesthesia. Commercially available hyperbaric local anesthetic solutions include 0.75% bupivacaine with 8.25% glucose and 5% lidocaine with 7.5% glucose. Tetracaine is formulated as a 1% plain solution and is most often used as a 0.5% solution with 5% glucose, which is achieved by dilution of the anesthetic with an equal volume of 10% glucose. (266)

52. The contour of the vertebral canal is critical to the subarachnoid distribution of hyperbaric local anesthetic solutions. For example, in the supine horizontal position, the patient's thoracic kyphosis will be dependent relative to the peak created by the lumbar lordosis. Anesthetic delivered cephalad to this peak will thus move toward the thoracic kyphosis, which is normally around T6-8. Placing the patient in a head-down (Trendelenburg) position will further accentuate this cephalad spread of local anesthetic solution. (266, Figure 17-1)

53. Hyperbaric local anesthetic solutions can be administered with the patient seated and this position maintained during the initial movement of anesthetic to deliberately encourage restricted sacral anesthesia (referred to as a "saddle block," reflecting sensory anesthesia of the area that would be in contact with a saddle). (266)

54. Hypobaric local anesthetic solutions find limited use in clinical practice and are generally reserved for patients undergoing perineal procedures in the "prone jackknife" position or undergoing hip arthroplasty where anesthetic can "float up" to the nondependent operative site. (267)

55. Isobaric local anesthetic solutions undergo limited spread in the subarachnoid space, which may be considered an advantage or disadvantage depending on the clinical circumstances. Because the distribution of local anesthetic solutions is not affected by gravity, spinal anesthesia can be performed without concern that the resultant block might be influenced by patient position. Isobaric spinal anesthesia is particularly well suited for perineal or lower extremity procedures, as well as surgery involving the lower part of the trunk (hip arthroplasty, inguinal hernia repair). (267)

56. Vasoconstrictors are frequently added to spinal anesthetic solutions to increase the duration of spinal anesthesia. This is most commonly achieved by the addition of epinephrine (0.1 to 0.2 mg, which is 0.1 to 0.2 mL of a 1:1000 solution) or phenylephrine (2 to 5 mg, which is 0.2 to 0.5 mL of a 1% solution). Increased duration of spinal anesthesia is believed to result from a reduction in spinal cord blood flow, which decreases loss of local anesthetic from the perfused areas and thus increases the duration of exposure to local anesthetic. However, with epinephrine, there may be a small contribution as a result of its α_2-adrenergic analgesic activity. (267)

57. Opioids may be added to local anesthetic solutions to enhance surgical anesthesia and provide postoperative analgesia. This effect is mediated at the dorsal horn of the spinal cord, where opioids mimic the effect of endogenous enkephalins. Commonly, fentanyl (25 μg) is used for short surgical procedures, and its administration does not preclude discharge home on the same day. The use of morphine (0.1 to 0.5 mg) can provide effective control of postoperative pain for roughly 24 hours, but it necessitates in-hospital monitoring for respiratory depression. (267)

58. During recovery from spinal anesthesia, regression of the anesthetic is from the highest dermatome in a caudad direction. (266)

59. Recent reports of major and minor complications associated with spinal lidocaine have tarnished its reputation and jeopardize its continued clinical use. Initial reports of permanent neurologic deficits were restricted to its use for continuous spinal anesthesia, where extremely high doses were administered. However, subsequent reports suggest that injury may occur even with the administration of a dose historically recommended for single-injection spinal anesthesia. These injuries have led to suggested modifications in practice that include a reduction in the lidocaine dose from 100 mg to 60 or 75 mg and dilution of the commercial formulation of 5% lidocaine with an equal volume of saline or CSF before subarachnoid injection. (267)

60. Lidocaine has been linked to the development of transient neurologic symptoms or "TNS" (pain and/or dysesthesia in the back, buttocks, and lower extremities) in up to a third of patients receiving this anesthetic for spinal anesthesia. Factors that increase the risk for TNS in association with lidocaine spinal anesthesia include patient positioning (lithotomy, knee arthroscopy) and outpatient status. (268)

61. With respect to TNS, the approximate rank order with respect to its incidence is lidocaine>procaine, mepivacaine>prilocaine, bupivacaine, chloroprocaine. (268)

62. When using chloroprocaine off-lable for spinal administration, the solution should be preservative-free, and epinephrine should not be used. (268)

63. The recommended doses (5 to 20 mg) and reported durations of action (90 to 120 minutes) of bupivacaine and tetracaine are similar. However, bupivacaine produces slightly more intense sensory anesthesia (as evidenced by a lower incidence of tourniquet pain), whereas motor block with tetracaine appears to be slightly more pronounced. The more important distinction between these local anesthetics is that the duration of tetracaine spinal anesthesia is more variable and more profoundly affected by the addition of a vasoconstrictor. Consequently, tetracaine remains the most useful spinal anesthetic in circumstances in which a prolonged block is sought. Unfortunately, the inclusion of a vasoconstrictor with tetracaine results in a significant incidence of transient neurologic symptoms, as opposed to the rarity of these symptoms when tetracaine is used alone. (268)

64. Sympathetic nerves are blocked before both motor nerves and sensory nerves after the administration of a spinal anesthetic. (268)

65. A useful way to gain an early indication of the level of spinal anesthesia is by testing the patient's ability to discriminate temperature in the relevant dermatomes. For example, in an unblocked area, an alcohol sponge will produce a cold sensation, whereas in the blocked areas the same alcohol sponge will feel warm or neutral. (268)

66. The dermatomal order of blockade produced by a spinal anesthetic, from highest to lowest, is sympathetic, sensory, then motor. (268)

67. Skeletal muscle strength can be tested by asking the patient to dorsiflex the foot (S1-2), raise the knees (L2-3), or tense the abdominal rectus muscles (T6-12). (269)

68. The surface landmarks and their respective dermatomal level most often used clinically are: nipple, T4-5; tip of xiphoid, T7; umbilicus, T10; inguinal ligament, T12. (269)

69. Inserting a catheter into the subarachnoid space increases the utility of spinal anesthesia by permitting repeated drug administration as necessary to maintain the level and duration of sensory and motor block. Anesthesia can thus be provided for prolonged operations without delaying recovery. An added benefit is the possibility of using lower doses of anesthetic. (With a catheter in place, smaller doses can be titrated to the patient's response. In contrast, with the single-injection technique, relatively high doses must be administered to all patients to ensure successful anesthesia in a large percentage of cases.) However, use of large-bore epidural needles and catheters for continuous spinal anesthesia poses significant risk of postdural puncture headache. (269, Figure 17-4)

70. Microcatheters (27 gauge and smaller) used for continuous spinal anesthesia were withdrawn from clinical practice in the United States after reports of cauda equina syndrome associated with their use. (269)

71. It is likely that the injury associated with the use of microcatheters resulted from the combination of maldistribution and repetitive injection of local anesthetic solution. It is speculated that pooling of local anesthetic solution in the dependent sacral sac produced a restricted block that was inadequate for surgery. In response to inadequate anesthesia, injections were repeated and ultimately achieved adequate sensory anesthesia, but not before neurotoxic concentrations were reached in the caudal region of the subarachnoid space. It is possible that the microcatheter contributed to this problem because the long narrow-bore tubing creates resistance to injection and thereby results in a low flow rate that can encourage a restricted distribution. (269)

72. Removal of microcatheters from clinical practice has not eliminated risk. The problem of maldistribution is not restricted to microcatheters or lidocaine, and the same injuries have occurred with larger "epidural" catheters used for continuous spinal anesthesia and other local anesthetics. (269)

73. Guidelines for continuous spinal anesthesia include the following elements:

- Insert the catheter just far enough to confirm and maintain placement
- Use the lowest effective local anesthetic concentration
- Place a limit on the dose of local anesthetic to be used
- Administer a test dose and assess the extent of any sensory and motor block
- If maldistribution is suspected, use maneuvers to increase the spread of local anesthetic (change the patient's position, alter the lumbosacral curvature, switch to a solution with a different baricity)
- If well-distributed sensory anesthesia is not achieved before the dose limit is reached, abandon the technique (269, Figure 17-4)

74. Similar to continuous spinal anesthesia, single-injection spinal anesthesia may fail due to local anesthetic maldistribution. This issue becomes important when considering whether to repeat a "failed" spinal and, if so, the dose of anesthetic that should be used for the second injection. In the past, it was considered acceptable to readminister a "full dose." However, if failure derives from maldistribution of the local anesthetic solution, this strategy may introduce a risk of injury. Accordingly, if a spinal anesthetic is to be repeated, it should be assumed that the first injection was delivered in the subarachnoid space as intended, and the combination of the two doses should not exceed that considered reasonable as a single injection for spinal anesthesia. (270)

75. Spinal anesthesia has little, if any, effect on resting alveolar ventilation (arterial blood gases unchanged), but high levels of motor anesthesia that produce paralysis of abdominal and intercostal muscles can lead to a decreased ability to cough and expel secretions. Additionally, patients may complain of difficulty breathing (dyspnea)—despite adequate ventilation—because of inadequate sensation of breathing from the loss of proprioception from abdominal and thoracic muscles. (270)

76. Spinal anesthesia above T5 inhibits sympathetic nervous system innervation to the gastrointestinal tract, and the resulting unopposed parasympathetic nervous system activity results in contracted intestines and relaxed sphincters. Similarly, the ureters are contracted, and the ureterovesical orifice is relaxed.

77. Hypotension (systolic blood pressure $<$90 mm Hg) is estimated to occur in about a third of patients receiving spinal anesthesia. This hypotension results from a sympathetic nervous system block that (1) decreases venous return to the heart and decreases cardiac output and/or (2) decreases systemic vascular resistance. Modest decreases in systemic blood pressure are most likely due to decreases in systemic vascular resistance, whereas large decreases in systemic blood pressure are believed to be the result of decreases in venous return and cardiac output. (270)

78. Spinal anesthesia–induced hypotension is treated physiologically by restoration of venous return to increase cardiac output. In this regard, the internal autotransfusion produced by a modest head-down position (5 to 10 degrees) will facilitate venous return without greatly exaggerating cephalad spread of the spinal anesthetic. Adequate hydration before the institution of spinal anesthesia is important for minimizing the effects of venodilation from sympathetic nervous system block. Sympathomimetics with positive inotropic and venoconstrictor effects, such as ephedrine (5 to 10 mg IV), are often chosen as first-line drugs to maintain perfusion pressure during the first few minutes after the institution of spinal anesthesia. Phenylephrine (50 to 100 μg IV) and other

sympathomimetics that increase systemic vascular resistance may decrease cardiac output and do not specifically correct the decreased venous return contributing to the spinal anesthesia–induced hypotension. Nevertheless, anesthesiologists have long used phenylephrine successfully to treat decreases in systemic blood pressure associated with spinal anesthesia. Furthermore, this drug is of particular value when administration of ephedrine is associated with significant increases in heart rate. (270)

79. The heart rate does not change significantly in most patients during spinal anesthesia. However, in an estimated 10% to 15% of patients, significant bradycardia occurs. As with hypotension, the risk for bradycardia increases with increasing sensory levels of anesthesia. Speculated mechanisms for this bradycardia include the block of cardioaccelerator fibers originating from T1 through T4 and decreased venous return (Bezold-Jarisch reflex). (271)

80. Although bradycardia is usually of moderate severity and promptly responsive to atropine or ephedrine, there are reports of precipitous bradycardia and asystole in the absence of any preceding event. This catastrophic event can probably be prevented through maintenance of preload and reversal of bradycardia by aggressive stepwise escalation of treatment (ephedrine, 5 to 50 mg IV; atropine, 0.4 to 1.0 mg IV; epinephrine, 0.05 to 0.25 mg IV), whereas the development of profound bradycardia or asystole mandates immediate treatment with full resuscitative doses of epinephrine. (271, Figure 17-16)

81. Postdural puncture headache is a direct consequence of the hole in the dura, which results in the loss of CSF at a rate exceeding its production. Loss of CSF causes downward displacement of the brain and a resultant stretch on sensitive supporting structures. Pain also results from distention of the blood vessels, which must compensate for the loss of CSF because of the fixed volume of the skull. The pain associated with postdural puncture headache generally begins 12 to 48 hours after transgression of the dura, but it can occur immediately and has been reported to occur up to several months after the event. (271, Figure 17-17)

82. The hallmark of a postdural puncture headache is its postural component: it appears or intensifies with sitting or standing and is partially or completely relieved by recumbency. This feature is so distinctive that it is difficult to consider the diagnosis in its absence. (271)

83. Postdural puncture headache is typically occipital or frontal (or both) and is usually described as dull or throbbing. Associated symptoms such as nausea, vomiting, anorexia, and malaise are common. Ocular disturbances, manifested as diplopia, blurred vision, photophobia, or "spots," may occur and are believed to result from the stretch of the cranial nerves, most commonly cranial nerve VI, as the brain descends because of the loss of CSF. Although symptomatic hearing loss is unusual, formal auditory testing will routinely reveal abnormalities. (271)

84. Though generally a transient problem, loss of CSF may rarely result in significant morbidity because caudal displacement of the brain can result in tearing of bridging veins with the development of a subdural hematoma. (271)

85. Age is one of the most important factors affecting the incidence of postdural puncture headache. Children are at low risk, but after puberty, risk increases substantially and then slowly declines with advancing age. Females have long been suspected to be at increased risk, and a recent meta-analysis confirms this impression, even in the absence of pregnancy. A previous history of postdural puncture headache places one at increased risk for the development of this complication after a subsequent spinal anesthetic. (272)

86. The incidence of postdural puncture headache varies directly with the diameter of the needle that has pierced the dura. The shape of the hole created by the needle also has an impact on loss of CSF; this has led to the development of "pencil-point"

needle tips, which appear to spread the dural and arachnoid fibers, and to produce less tear and a smaller hole for a given diameter needle. (272)

87. Initial treatment of postdural puncture headache is usually conservative and consists of bed rest, fluids, analgesics, and possibly caffeine. More definitively, a blood patch can be performed in which 15 to 20 mL of the patient's blood, aseptically obtained, is injected into the epidural space. (272)

88. The immediate effect is related to the volume effect of the injected blood, whereas long-term relief is thought to occur from sealing or "patching" of the dural tear. (272)

89. Total spinal anesthesia is the term applied to excessive sensory and motor anesthesia associated with a loss of consciousness. Apnea and loss of consciousness are often attributed to ischemic paralysis of the medullary ventilatory centers because of profound hypotension and associated decreases in cerebral blood flow. However, loss of consciousness may also be the direct consequence of local anesthetic effect above the foramen magnum inasmuch as patients may lose or fail to regain consciousness despite restoration of systemic blood pressure. Total spinal anesthesia is typically manifested soon after injection of the local anesthetic solution into the subarachnoid space. (272)

90. Treatment of high or total spinal anesthesia consists of maintenance of the airway and ventilation, as well as support of the circulation with sympathomimetics and intravenous fluid administration. Patients are placed in a head-down position to facilitate venous return. An attempt to limit the cephalad spread of local anesthetic solution in CSF by placing patients in a head-up position is not recommended, because this position will encourage venous pooling and potentially jeopardize cerebral blood flow, which may contribute to medullary ischemia. Tracheal intubation is usually warranted and is mandated for patients at risk of aspiration (e.g., pregnant women). It may be appropriate to administer an intravenous induction drug before tracheal intubation if consciousness is retained and cardiovascular status is acceptable. (273)

91. Nausea occurring after the initiation of spinal anesthesia must alert the anesthetist to the possibility of systemic hypotension sufficient to produce cerebral ischemia. In such cases, treatment of hypotension with a sympathomimetic should eliminate the nausea. Alternatively, nausea may occur because of a predominance of parasympathetic activity as a result of selective block of sympathetic nervous system innervation to the gastrointestinal tract. Similar to bradycardia, the incidence of nausea and vomiting parallels the sensory level of spinal anesthesia. (273)

92. Backache presenting after spinal anesthesia is frequently due to the position that was maintained during surgery. Patients with decreased sensory perception induced by a spinal anesthetic may remain in positions for long periods of time that may otherwise have been too uncomfortable, thus resulting in ligament strain that might not have otherwise occurred. In support of this is the fact that roughly 25% of patients complain of backache after surgery regardless of the anesthetic technique. (273)

EPIDURAL ANESTHESIA

93. Controversy exists regarding the wisdom of placing lumbar epidural catheters after the induction of general anesthesia. Although there is concern that an inability to elicit a patient response might increase the risk for neural injury, a retrospective review challenges this assertion. Nonetheless, many anesthesiologists believe that lumbar epidural anesthesia and catheter placement are best performed in a communicative patient. (273)

94. Performance of thoracic epidural anesthesia in an anesthetized patient should be avoided. However, the same considerations do not apply to pediatric anesthesia, where a conscious patient would probably impart no benefit but instead add

substantial risk. Consequently, it is standard practice to place caudal, lumbar, and even thoracic epidural catheters in children after induction of general anesthesia. (273)

95. Some catheters have an inner stainless steel wire coil that imparts flexibility and prevents kinking. This characteristic makes them less likely to (1) pierce an epidural vessel, (2) find false passage into a fascial plane, or (3) be advanced out of the epidural space through the intervertebral foramen. However, their flexibility also makes them more difficult to thread into the epidural space. (274, Figure 17-18)

96. The tip of an epidural catheter may be open or have a closed "bullet" tip with proximal ports. Bullet-tipped or multiorifice catheters tend to produce more uniform distribution of local anesthetic solution, but they have the disadvantage of requiring greater insertion depth to ensure complete delivery of local anesthetic solution into the epidural space. (274, Figure 17-18)

97. In contrast to procedures performed in the lumbar area, thoracic epidural anesthesia is generally accomplished through a paramedian approach. In this region the spinous processes are angulated and closely approximated, which makes it difficult to avoid bony obstruction when approaching from the midline. (275, Figure 17-5)

98. With the loss-of-resistance technique, a syringe containing saline, air, or both is attached to the needle, and the needle is slowly advanced while assessing resistance to injection. One method is to use a syringe containing 2 to 3 mL of saline with a small air bubble (0.1 to 0.3 mL). If the needle is properly seated in the ligamentum flavum, it will be difficult to inject the saline or the air bubble, and the plunger of the syringe will "spring back" to its original position. The needle is advanced while continuous pressure is exerted on the plunger of the syringe. An abrupt loss of resistance to injection signals passage through the ligamentum flavum and into the epidural space, at which point the contents of the syringe are delivered. Another technique uses repeated advances of the needle without continuous pressure, and an assessment of the resistance to injection is made after each advancement. (275, Figure 17-19)

99. The "hanging-drop" technique is an alternative method for identifying the epidural space. With this technique, a small drop of saline is placed at the hub of the epidural needle. As the needle passes through the ligamentum flavum into the epidural space, the saline drop is retracted into the needle by the negative pressure in the epidural space. Interestingly, the hanging-drop technique can be used in the lumbar region despite the lack of negative pressure in the lumbar epidural space. In this region, the needle pushing the dura away from the ligamentum flavum creates negative pressure. Accordingly, this technique is likely to be associated with a higher incidence of accidental dura penetration ("wet tap"). (275)

100. The advantage of the single-injection technique is its simplicity, and the distribution of local anesthetic solution tends to be more uniform than when administered through an indwelling catheter. The disadvantage is the lack of ability to reinject, and thus the inability to provide prolonged anesthesia titrated to the duration of surgery. Additionally, with the catheter technique, anesthetic administration can extend into the postoperative period to provide highly effective postoperative analgesia. (276)

101. Following identification of the epidural space, the catheter is advanced 3 to 5 cm beyond the tip of the needle positioned in the epidural space. Further advancement increases the risk that the catheter might enter an epidural vein, exit an intervertebral foramen, or wrap around a nerve root. The epidural needle is withdrawn over the catheter, with care taken to not move the catheter. No attempt should be made to withdraw a catheter back through the needle because

shearing (transection) of the catheter might result, with retention of the transected tip of the catheter in the epidural space. An empty 3-mL syringe is then attached to the distal end of the catheter, and negative pressure is applied to the syringe. Failure to aspirate CSF or blood helps rule out accidental subarachnoid or intravascular placement. It is also important to reconfirm negative aspiration of CSF or blood from the catheter before any subsequent dose of local anesthetic is administered. (276)

102. The test dose commonly used for an epidural catheter is 3 mL of 1.5% lidocaine with 1:200,000 epinephrine. Failure of the test dose to produce sensory and motor anesthesia is assessed after 3 minutes to rule out accidental subarachnoid injection (spinal anesthesia has a more rapid onset of sensory and motor block). If epinephrine has been included in the test dose, the heart rate is monitored to detect an increase that may signal accidental intravascular injection. The local anesthetic solution is then injected in fractionated doses (e.g., multiple injections of 5-mL aliquots) over a 1- to 3-minute period at an appropriate volume and concentration (dose) for the planned surgical procedure. (276)

103. Intermittent dosing is critical because a negative test result does not conclusively rule out intravascular placement. This becomes even more critical with the single-injection epidural technique, where the needle's position may change during or between injections. (276)

104. The following are local anesthetics commonly used for epidural anesthesia, their concentration, time of onset, and duration of action. (277, Figure 17-5)

	Concentration (%)	***Onset (min)***	***Duration (min)***
Chloroprocaine	2-3	5-15	45-60
Lidocaine	1-2	10-15	60-120
Ropivacaine	0.25-1	10-20	120-180
Bupivacaine	0.25-0.5	15-20	120-200

105. Tetracaine and procaine are rarely used for epidural anesthesia because of their slow onset of action. (277)

106. After sterile preparation, the sacral cornu (typically 3 to 5 cm above the coccyx) is identified by the anesthetist's palpating fingers. The depression between the cornu is the sacral hiatus, and a skin wheal is raised. The needle is introduced perpendicular to the skin through the sacrococcygeal ligament (generally felt as a rather distinct pop) and advanced until the sacrum is contacted. The needle is then slightly withdrawn, the angle is reduced, and the needle is advanced about 2 cm into the epidural caudal canal. Confirmation that the needle is properly positioned can be obtained by rapidly injecting 5 mL of air or saline through the needle while palpating the skin directly covering the caudal canal. Subcutaneous crepitus or midline swelling indicates that the needle is positioned posterior to the bony sacrum and requires replacement. (276, Figure 17-20)

107. Subarachnoid injection may occur if the needle is advanced too far cephalad in the sacral canal, or it may result from anatomic variation (the dural sac extends beyond S2 in approximately 10% of individuals). Anatomic variation may also hinder success inasmuch as the sacral hiatus is absent in nearly 10% of patients.

108. The principal factors affecting the spread of epidural anesthesia are dose (volume times concentration) and site of injection. However, administration of an equivalent dose (mass) at lower concentration may foster greater spread,

particularly with lower concentrations of local anesthetic. Cephalad-to-caudad extension of epidural anesthesia depends on the site of administration of the local anesthetic solution into the epidural space. Lumbar epidural injections produce preferential cephalad spread because of negative intrathoracic pressure transmitted to the epidural space, whereas resistance to caudad spread of local anesthetic solution is created by narrowing of the space at the lumbosacral junction. In contrast, thoracic injections tend to produce symmetric anesthesia and result in greater dermatomal spread for a given dose of local anesthetic. This latter effect results, at least in part, from the smaller volume of the thoracic epidural space. The site of placement of the local anesthetic solution in the epidural space also defines the area of peak anesthetic effect, which decreases with increasing distance from the injection site.

109. The spread of epidural anesthesia varies directly with age and inversely with height, although these effects are small, and likely to be overshadowed by interpatient variability. (277)

110. In contrast to spinal anesthesia, the baricity of local anesthetic solutions does not influence the level of epidural anesthesia. Likewise, patient position during performance of an epidural block is less important than with a spinal block, but the dependent portion of the body may still manifest more intense anesthesia than the nondependent side. This effect is most noticeable in a pregnant woman who has remained in a specific lateral position for a prolonged period during labor. (277)

111. The duration of epidural anesthesia, as with spinal anesthesia, is principally affected by the choice of local anesthetic and whether a vasoconstrictor drug is added to the anesthetic solution. (277)

112. The addition of epinephrine (generally 1:200,000; 5 μg/mL) decreases vascular absorption of the local anesthetic from the epidural space, thus maintaining effective anesthetic concentrations at the nerve roots for more prolonged periods. Decreased vascular absorption also serves to limit systemic uptake and reduce the risk of systemic anesthetic toxicity. In addition, the inclusion of epinephrine serves as a marker of intravascular injection that may occur with cannulation of an epidural vein. (277)

113. Local anesthetic effect requires transfer across the nerve membrane. Because local anesthetics are weak bases, they exist largely in the ionic form in commercial preparations. Adding sodium bicarbonate to the solution favors the nonionized form of the local anesthetic and promotes more rapid onset of epidural anesthesia. (278)

114. Most commonly, 1 mL of 8.4% sodium bicarbonate is added to 10 mL of a solution containing lidocaine or chloroprocaine. Alkalinization of a bupivacaine solution is not recommended because this local anesthetic precipitates at alkaline pH. (278)

115. In contrast to spinal administration, lipid solubility of the opioid is a critical factor in determining the selection and appropriate use of epidural opioids. For example, morphine, which is relatively hydrophilic, spreads rostrally within the CSF and can produce effective analgesia for thoracic surgery, even when administered into the lumbar epidural space. In contrast, a lipophilic opioid such as fentanyl is rapidly absorbed into the systemic circulation and exhibits little rostral spread. (278)

116. Failed epidural anesthesia may occur when local anesthetic solution is not delivered into the epidural space or because spread of the local anesthetic solution is inadequate to cover the relevant dermatomes. A false loss of resistance can occur in the interspinous ligament before entry into the ligamentum flavum or as the needle passes through fascial planes. In some cases, failure results from

advancement of the catheter through an intervertebral foramen, which generally gives rise to a limited unilateral block. Fortunately, these blocks can often be salvaged by retracting the catheter a few centimeters. Opinion varies on the presence of a midline barrier to diffusion of local anesthetics. (278)

117. If epidural anesthesia is nearly adequate and there are concerns that additional local anesthetic would create a risk for systemic toxicity, small doses of chloroprocaine, which are rapidly hydrolyzed in plasma, may provide adequate extension to permit surgery. At other times, failure of epidural anesthesia may be managed by replacement of the epidural catheter or abandonment of the technique in favor of a general or spinal anesthetic. However, subarachnoid injection after a failed epidural produces unpredictable and often excessive spinal anesthesia. This effect probably results from compression of the dural sac by the volume of anesthetic solution in the epidural space. (278)

118. The major site of action of local anesthetic solutions placed in the epidural space appears to be the spinal nerve roots, where the dura is relatively thin. To a lesser extent, anesthesia results from diffusion of local anesthetic solutions from the epidural space into the subarachnoid space. (278)

119. Side effects of epidural anesthesia resemble those described for spinal anesthesia, with the added risks of accidental subarachnoid injection, and anesthetic systemic toxicity, the latter attributable to the high doses of local anesthetic required for the epidural anesthetic. Additional potential complications include epidural hematoma and epidural abscess, particularly in patients with preexisting coagulopathy or infection. Although postdural puncture headache is not an issue if the dura is not pierced, when dural puncture does occur inadvertently, the risk of headache is far greater than with spinal anesthesia owing to the larger diameter needles used for the epidural technique. (279)

120. Accidental dural puncture may be managed by converting to single-injection or continuous spinal anesthesia, or epidural anesthesia can be attempted at a different lumbar interspace. Either placement of an epidural catheter at another interspace or passage of a subarachnoid catheter may decrease the risk for postdural puncture headache. (279)

121. Accidental subarachnoid injection of large volumes of local anesthetic solution used for epidural anesthesia may produce rapid progression to total spinal anesthesia. Immediate treatment is focused on supporting ventilation and restoring or maintaining hemodynamics. However, in contrast to an excessive block produced during spinal anesthesia, the large epidural doses of local anesthetics injected into the subarachnoid space can result in permanent neurologic deficits because of the neurotoxic effects of these agents. Consequently, consideration should be given to irrigation of the subarachnoid space by removal of small volumes of CSF and repetitive injections of saline. This maneuver may circumvent or minimize neurologic injury. (280)

122. Because the onset of sympathetic nervous system block is slower in epidural versus spinal anesthesia, excessive decreases in systemic blood pressure do not usually accompany epidural anesthesia administered to normovolemic patients. (280)

123. The high doses of local anesthetics required for epidural anesthesia along with the presence of numerous venous plexuses in the epidural space create a risk of substantial systemic absorption of local anesthetic. Additionally, accidental intravascular injection of local anesthetic will produce high blood levels and predictable toxicity ranging from mild central nervous system symptoms (restlessness, slurred speech, tinnitus) to loss of consciousness, seizures, and cardiovascular collapse. (280)

124. The subdural space is difficult to enter deliberately because the arachnoid is generally closely adherent to the overlying dura. The rare occurrence of subdural

injection is difficult to detect because CSF cannot be aspirated through the catheter and the usual test dose is negative. Subdural injection of a local anesthetic solution can produce an unusual block characterized by patchy sensory anesthesia and often unilateral dominance. (280)

125. Neural injury after an epidural anesthetic is very rare but seems to be more likely if a paresthesia occurs during performance of this technique. The development of paresthesia as a result of the advancing epidural needle reflects stimulation of a nerve root and is a signal to the anesthetist that the needle is not in the midline and needs to be redirected. As with spinal anesthesia, injection of local anesthetic solution in the presence of a paresthesia is contraindicated because nerve damage may be induced or enhanced by the injection. (280)

126. Combined spinal-epidural anesthesia is a technique in which a spinal anesthetic and an epidural catheter are placed concurrently. This approach combines the rapid onset and intense sensory anesthesia of a spinal anesthetic with the ability to supplement and extend the duration of the block afforded by an epidural catheter. The technique is commonly used in obstetric anesthesia, as well as orthopedic procedures such as hip and knee replacement. (280, Figure 17-21)

127. Advantages of epidural block during general anesthesia include less need for opioids, pain-free emergence from anesthesia, and block of the stress response that is nearly complete for most surgical procedures performed below the umbilicus. However, use of this technique demands heightened attention to fluid management and blood pressure. (281)

Chapter

15 PERIPHERAL NERVE BLOCKS

Adam Collins

1. Name some types of peripheral nerve blocks.
2. Other than as anesthesia for a surgical procedure, what are some uses for peripheral nerve blocks?
3. What are some special considerations that should be made in the preoperative evaluation of a patient who is to undergo a peripheral nerve block?

PREPARATION FOR NERVE BLOCKS

4. What is the benefit of preoperative medication for patients who are to undergo a peripheral nerve block?
5. Where should a peripheral nerve block be performed?
6. What are the expected onset times and durations of some commonly used local anesthetics?

SPECIFIC BLOCK TECHNIQUES

7. What are some of the advantages of ultrasound-guided peripheral nerve blocks?
8. Describe the macroscopic cross-sectional appearance of peripheral nerves.
9. When using high-resolution ultrasound, what percent of the fascicles within a peripheral nerve are able to be visualized?
10. Describe the sonographic appearance of a proximal nerve.
11. What are the image characteristics of high-frequency ultrasound compared with low frequency?
12. What factors affect ultrasound visibility of needles?
13. Describe the short axis and long axis scanning orientations.
14. Describe the in-plane and out-of-plane needle approaches.
15. What is the significance of a paresthesia during block performance?
16. Describe cathodal stimulation and the significance of electrode reversal in evoking a motor response from a peripheral nerve.
17. What is an optimal stimulating threshold for nerve stimulator technique before injection of local anesthetic?

PERIPHERAL NERVE CATHETERS

18. What are some of the clinical uses of peripheral nerve catheters?
19. Describe the technique by which peripheral nerve catheters are placed.

CERVICAL PLEXUS BLOCK

20. For what surgical procedures is a cervical plexus block most often performed? What areas become anesthetized by a cervical plexus block?
21. What nerves form the cervical plexus?
22. How is blockade of the superficial cervical plexus achieved?

BRACHIAL PLEXUS BLOCK

23. For what surgical procedures is a brachial plexus block useful? What areas become anesthetized by a brachial plexus block?
24. What nerve roots form the brachial plexus?
25. What landmarks are used to locate the brachial plexus for blockade?
26. What are four different approaches to blockade of the brachial plexus?
27. How is a brachial plexus block via the interscalene approach achieved? What volume of local anesthetic is deposited with this approach to brachial plexus blockade?
28. What are some advantages of brachial plexus blockade via the interscalene approach?
29. What is a disadvantage of brachial plexus blockade via the interscalene approach?
30. What are some potential complications of brachial plexus blockade via the interscalene approach?
31. How is a brachial plexus block via the supraclavicular approach achieved? What volume of local anesthetic is deposited with this approach to brachial plexus blockade?
32. What are some advantages of brachial plexus blockade via the supraclavicular approach?
33. What are some potential complications of brachial plexus blockade via the supraclavicular approach?
34. Describe the in-plane ultrasound-guided technique for blockade of the brachial plexus via the axillary approach. What volume of local anesthetic is deposited with this approach to brachial plexus blockade?
35. Axillary block provides anesthesia for surgery in which regions of the upper extremity?
36. What nerves are blocked by injection superficial to the axillary sheath during the axillary brachial plexus block? How is this achieved?
37. What are some advantages of brachial plexus blockade via the axillary approach?
38. What are some potential complications of brachial plexus blockade via the axillary approach?

DISTAL NERVE BLOCKS OF THE UPPER EXTREMITY

39. What is the sensory distribution of the median nerve? How is it blocked at the forearm with ultrasound guidance?
40. What is the sensory distribution of the ulnar nerve? How is it blocked at the forearm with ultrasound guidance?
41. What is the sensory distribution of the radial nerve? What is the typical course of the superficial radial nerve through the forearm, and how is it blocked at the forearm with ultrasound guidance?

BLOCKS OF THE LOWER EXTREMITY

42. What are the challenges of lower extremity blocks relative to those of the upper extremity?
43. What are the four major nerves of the lower extremity?
44. What nerves form the sciatic nerve, and what are its approximate dimensions in the pelvis?
45. What area is anesthetized by sciatic nerve blockade and what additional blocks are usually necessary to provide lower extremity anesthesia?
46. How is sciatic nerve blockade achieved? What volume of local anesthetic should be deposited for sciatic nerve blockade?
47. What nerves form the femoral nerve? How does it reach the thigh? What is the terminal branch of the femoral nerve?
48. For what procedure is femoral nerve blockade a definitive anesthetic?
49. How is femoral nerve blockade achieved? What volume of local anesthetic should be deposited for femoral nerve blockade?
50. What nerve forms the saphenous nerve?
51. How is blockade of the saphenous nerve performed at the level of the thigh?
52. Where along the course of the sciatic nerve is the popliteal nerve block performed? What surgical sites are best covered by this block?

53. What supplemental blocks may need to be combined with popliteal nerve blockade?
54. What are the five nerves that supply the foot? What areas do each supply?
55. How is an ankle block achieved? What is the total volume of local anesthetic that is typically deposited in an ankle block?

INTRAVENOUS REGIONAL NEURAL ANESTHESIA

56. For what procedure types is intravenous regional neural anesthesia (Bier block) commonly used?
57. What are some contraindications for intravenous regional anesthesia?
58. How is a Bier block achieved? What volume of local anesthetic is used in a Bier block?
59. What local anesthetics are typically used for a Bier block?
60. What are some advantages of a Bier block?
61. What are some disadvantages of a Bier block?
62. What is a potential complication of a Bier block? How can this risk be minimized?

ANSWERS*

1. Types of peripheral nerve blocks include blocks of the cervical plexus, brachial plexus, median nerve, ulnar nerve, radial nerve, sciatic nerve, femoral nerve, saphenous nerve, and ankle block. (285)
2. In addition to surgical anesthesia, peripheral nerve blocks may be used for postoperative analgesia and for the diagnosis and management of chronic pain syndromes. (284)
3. Considerations that should be made in the preoperative evaluation of a patient who is to undergo a peripheral nerve block include the patient's coagulation status, the presence of any neuropathy in the involved nerves, the presence of any skin infection overlying the area where the needle will be inserted, and the presence of any anatomic abnormalities or difficulties with the usual landmarks for the performance of the nerve block. In addition, the patient should be evaluated in the usual manner with regard to history, physical examination, and laboratory analysis. The anesthesiologist must be prepared to administer another anesthetic in the event that the peripheral nerve block is not sufficient for surgical anesthesia and the surgery must proceed. (284-285)

PREPARATION FOR NERVE BLOCKS

4. Preoperative medication for patients who are to undergo a peripheral nerve block may reduce their level of anxiety. Patients are often more receptive to receiving a peripheral nerve block if they are assured they will be made comfortable during the anesthetic and surgical procedures. (284)
5. Peripheral nerve blocks that are not performed in the operating room should be performed in a block room with the appropriate monitors, drugs, equipment, and oxygen should their use become urgently necessary. (284-285)
6. The choice of local anesthetic agent for peripheral nerve blockade depends on a number of factors, including the desired onset, duration, and degree of conduction block (see Chapter 11). Lidocaine and mepivacaine, 1% to 1.5%, produce surgical anesthesia in 10 to 20 minutes that lasts 2 to 3 hours. Ropivacaine, 0.5%, and bupivacaine, 0.375% to 0.5%, have a slower onset and produce less motor blockade, but the effect lasts for at least 6 to 8 hours. (285)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

SPECIFIC BLOCK TECHNIQUES

7. High-resolution ultrasound imaging allows direct visualization of peripheral nerves, block needle placement, and the distribution of local anesthetic solution and thereby improves block success and minimizes local anesthetic volume (see Figure 15-1). In addition, ultrasound can also be used to visualize adjacent structures, such as blood vessels or pleurae, and may therefore reduce the risk for complications from peripheral nerve blocks. A major advantage of ultrasound imaging is that variability in surface landmarks, body habitus, and patient positioning can be appreciated. (285)
8. Peripheral nerves can be round, oval, or triangular in transverse cross section (short axis view) and can change shape along their nerve path.
9. About a third of the fascicles within a peripheral nerve can be seen with high-resolution ultrasound. (285)
10. Proximal nerves such as the roots and ventral rami of the brachial plexus appear dark, or hypoechoic, in their core but bright, or hyperechoic, in their outer mantle (Figure 15-1). This distinction occurs because incident sound waves reflect strongly off the connective tissue encasing nerve fascicles but pass through the inner portions of the fascicles undisturbed. (285-286)
11. High-frequency ultrasound provides better resolution but poor penetration into deeper tissue because of attenuation of the sound beam. (286)
12. Ultrasound visibility of needles for a regional block primarily depends on the gauge and insertion angle, such that larger needles parallel to the ultrasound transducer are seen most easily. (286)
13. In short axis imaging, cylindrical structures such as nerves appear as circles. Long axis imaging is achieved by placing the transducer longitudinally, or parallel to the course of a nerve, such that it appears as a linear structure. (286)
14. With the in-plane approach, the block needle is introduced within the plane of imaging, such that the entire needle and bevel are seen as a linear structure. The out-of-plane needle approach involves passing the needle from outside the plane of imaging so that it intersects the scan plane as an echogenic dot. (286, Figure 15-2)
15. A paresthesia is a radiating electric shocklike sensation that can occur during the performance of a peripheral nerve block, which indicates that the nerve has been localized by the needle tip. Local anesthetic solution should not be injected in the presence of persistent paresthesia because intraneural injection accompanied by intense pain increases the likelihood of permanent nerve injury. (286)
16. For nerve stimulation, the block needle is used as a stimulating cathode and another lead on the body serves as the anode to complete the electrical circuit (Figure 15-3). Cathodal stimulation is more efficient than anodal stimulation, so it is important to not reverse the leads during nerve stimulation–guided block procedures. The location of the surface anode (usually an electrocardiographic pad) on the patient does not alter the stimulation. (286)
17. A motor response evoked with currents of 0.3 to 0.5 mA indicates sufficient proximity of the block needle to the nerve for success of the block after the injection of local anesthetic solution. A motor response at a current of less than 0.2 mA may suggest an intraneural needle position. (286-287)

PERIPHERAL NERVE CATHETERS

18. Continuous peripheral nerve blocks can be used in the hospital setting to facilitate vigorous early joint mobilization following orthopedic surgery. They can also be used to provide potent analgesia for outpatient surgery (also see Chapter 37). (287)

19. For placement of these catheters, the peripheral nerve should be first located in a fashion similar to that for single-injection blocks (typically nerve stimulation or ultrasound guidance with a large-bore needle), and then the catheter is threaded. Initially injecting a local anesthetic or dextrose solution to create more space adjacent to the nerve before catheter placement is useful. (287)

CERVICAL PLEXUS BLOCK

20. The anesthesia produced by a cervical plexus block includes the area from the inferior surface of the mandible to the level of the clavicle. A cervical plexus block is used most often to provide anesthesia in conscious patients undergoing carotid endarterectomy. Although combined superficial and deep cervical plexus blocks have traditionally been used for this surgical procedure, studies have demonstrated that a superficial block alone is sufficient. (287)

21. The cervical plexus is derived from nerves C1 to C4. (287)

22. Blockade of the superficial cervical plexus can be achieved by infiltrating local anesthetic along the posterior border of the sternocleidomastoid muscle. (287)

BRACHIAL PLEXUS BLOCK

23. Brachial plexus blocks are useful for surgery on the shoulder or upper extremity. Areas anesthetized by a brachial plexus block include all the muscles and most of the sensation of the upper extremity. (287-288)

24. The brachial plexus is derived from the anterior rami of C5 to T1. (287-288)

25. Landmarks that may be used to locate the brachial plexus for blockade include the anterior and middle scalene muscles, the interscalene groove, the transverse process of C6, the clavicle, the axillary artery, and the subclavian artery pulse. With ultrasound use, these landmarks are the starting point for scanning. (287-292)

26. The four different approaches to blockade of the brachial plexus are the interscalene, supraclavicular, infraclavicular, and axillary approaches. (287-292)

27. An interscalene block of the brachial plexus is achieved by injecting local anesthetic solution into the interscalene groove adjacent to the transverse process of C6 (the external jugular vein often overlies this area) (Figure 15-7). An interscalene block of the brachial plexus should be performed with the arm at the patient's side to relax the shoulder. High-frequency ultrasound can be used to image the brachial plexus within the posterior triangle of the neck. In this location, the nerves of the brachial plexus do not contain an abundance of connective tissue. Therefore, the nerves appear hypoechoic on ultrasound scans (see Figure 15-7). Using an in-plane technique, local anesthetic can be deposited adjacent to the brachial plexus between the anterior and middle scalene muscles. Injection of 20 to 30 mL of local anesthetic solution will anesthetize the cervical plexus and brachial plexus, and thus permit surgery on the shoulder and more distal upper extremity, although fibers that innervate the ulnar side of the forearm and hand (C8-T1, inferior trunk) may be spared (Figure 15-6). (288-289)

28. Advantages of brachial plexus blockade via the interscalene approach include a relatively low risk of pneumothorax, ease of palpation of necessary landmarks, and ease of nerve imaging with ultrasound. Additionally, it is possible to perform the block with the patient's arm at his or her side. (288)

29. A disadvantage of brachial plexus blockade via the interscalene approach is the inconsistency with which the inferior trunk of the brachial plexus is blocked, making it possible that surgery involving the C8-T1 dermatomes will have inadequate anesthesia. (288)

30. Complications of brachial plexus blockade via the interscalene approach include phrenic and recurrent laryngeal nerve blocks; epidural, intrathecal, and intravascular injections; and nerve damage. (288-289)

31. Supraclavicular block of the brachial plexus is achieved by injecting 20 to 30 mL of local anesthetic solution around the brachial plexus where it is usually tightly bundled and adjacent to the subclavian artery, just cephalad to the clavicle. The supraclavicular block can be performed with a similar technique to interscalene blocks. The ultrasound probe is moved closer to the clavicle and faces caudally to facilitate imaging of the brachial plexus adjacent to the subclavian artery and over the first rib. In this location, almost all practitioners use the in-plane technique because of the proximity of the pleura. (289)

32. Advantages of a supraclavicular block are rapid onset and ability to perform the block with the arm in any position. Additionally the nerves are tightly bundled in this location. (289)

33. Complications of brachial plexus blockade via the supraclavicular approach include its relatively increased risk of a pneumothorax. In fact, the incidence of a pneumothorax with this technique is about 1%, making it a poor choice for patients with respiratory compromise. Other complications include phrenic nerve block, Horner syndrome, and nerve injury. (289)

34. An axillary brachial plexus block is achieved by injecting 30 to 40 mL of local anesthetic solution around the nerves that lie in close proximity to the axillary artery (Figure 15-9). At the level of the axilla, the terminal branches of the brachial plexus reside within the axillary sheath and in the tissue that immediately surrounds it (see Figure 15-9). The patient is positioned supine with the arm abducted to 90 degrees and externally rotated to gain access to the axilla. A high-frequency ultrasound transducer is placed in the axilla, showing the brachial artery and the surrounding nerves of the brachial plexus. A needle is advanced from superior to inferior within the plane of imaging so that the tip lies within the axillary sheath. Multiple injections of local anesthetic surround each of the nerves, including the musculocutaneous nerve, which lies lateral to the brachial plexus in the Five muscle. (290-292)

35. An axillary block can be used for anesthesia of the hand, forearm, and elbow. (290)

36. Five milliliters of local anesthetic solution is infiltrated into the subcutaneous tissue immediately superficial to the axillary artery to block the intercostobrachial, medial brachial cutaneous, and medial antebrachial cutaneous nerves. (292)

37. An axillary perivascular block has the advantage of being remote from the lung and neuraxis, and can therefore be performed with relative safety. (292)

38. Potential complications of brachial plexus blockade via the axillary approach include systemic local anesthetic toxicity as a result of intravascular injection and nerve injury from needle trauma, intraneural injection, and hematoma. (292)

DISTAL NERVE BLOCKS OF THE UPPER EXTREMITY

39. The median nerve provides most of the sensory innervation to the palm of the hand. The forearm is scanned in short axis with high-frequency ultrasound showing the median nerve with a fine fascicular appearance that is distinct from the surrounding muscles and tendons. Under continuous visualization, 3 to 5 mL of local anesthetic is injected around the median nerve. (292)

40. The ulnar nerve provides sensation to the dorsal and palmar sides of the ulnar aspect of the hand. The ulnar nerve is blocked by injecting 3 to 5 mL of local anesthetic solution around the ulnar nerve in the forearm, usually at a level in the forearm where the ulnar nerve is not in direct contact with the ulnar artery. (292)

41. Most patients have radial dominance of sensation on the dorsal aspect of the hand. The superficial radial nerve is the distal sensory branch of the radial nerve that follows the radial artery along its course through the forearm. It can be blocked by

ultrasound-guided infiltration of 3 to 5 mL of local anesthetic solution anywhere along its course deep to the brachioradialis muscle or in a subcutaneous ring at the level of the anatomic snuffbox. (292-293)

BLOCKS OF THE LOWER EXTREMITY

42. Unlike the compactness of the brachial plexus, the lower extremity is supplied by nerves that are widely separated from each other as they enter the thigh. For many operations, it is easier to perform an epidural or spinal anesthetic than to attempt the same extent of anesthesia with multiple peripheral nerve blocks. (293)

43. The four major nerves of the lower extremity are the sciatic, femoral, lateral femoral cutaneous, and obturator nerves. (293)

44. The sacral plexus (L4-5, S1-3) gives rise to the sciatic nerve, which is nearly 2 cm wide as it leaves the pelvis. (294-296)

45. Sciatic nerve blockade provides nearly complete anesthesia of the foot and lower part of the leg. More often, a sciatic nerve block is combined with a femoral nerve block to provide more extensive anesthesia of the lower extremity. (294-296)

46. The classic approach to sciatic nerve blockade is with the patient lying on the side opposite the nerve to be blocked (Figure 15-14). A line is drawn between the posterior superior iliac spine and the greater trochanter of the femur. Using a peripheral nerve stimulator, the needle is inserted about 5 cm caudad from the midpoint of this line. Foot movement evoked by nerve stimulation is a satisfactory end point for needle placement before the injection of local anesthetic solution (about 25 to 30 mL is typically used). (294-296)

47. The femoral nerve is derived from L2, L3, and L4. The femoral nerve reaches the thigh by passing underneath the inguinal ligament just lateral to the femoral artery and vein, and separated from them by the iliopectineal ligament. The femoral nerve lies deep to the fascia iliaca, which invests the iliopsoas muscle. Along its course, the femoral nerve divides into multiple anterior cutaneous branches of the thigh and gives rise to the saphenous nerve of the medial aspect of the leg. (293-294)

48. Femoral nerve blockade is most often used together with other nerve blocks for surgery in the leg. Alone, femoral nerve blockade provides anesthesia of the anterior thigh and may be used for muscle biopsies in that area. (293)

49. Femoral nerve blockade is performed with the patient in the supine position and the thigh slightly abducted and externally rotated to improve access. The femoral nerve is appreciated on sonograms as a flattened bundle of fascicles lying between the hypoechoic subcutaneous tissue and the hyperechoic iliopsoas muscle (Figure 15-12). The block needle is advanced within the plane of imaging from lateral to medial until it punctures the fascia iliaca, with a distinct pop. The needle position is optimized to create the circumferential spread of 20 to 30 mL of local anesthetic around the femoral nerve. (294)

50. The saphenous nerve is a branch of the femoral nerve that contributes to innervation below the knee. (294)

51. The saphenous nerve is blocked at the midthigh level, where it lies anterior to the femoral artery (Figure 15-13). The femoral artery is a landmark for the saphenous nerve, both of which lie just deep to the sartorius muscle (see Figure 15-13). The block needle is advanced within the plane of imaging and 5 to 10 mL of local anesthetic is deposited deep to the sartorius muscle, adjacent to the femoral artery. (294-295)

52. Popliteal nerve blockade provides sciatic nerve anesthesia near the point where the sciatic nerve divides into its common peroneal and tibial nerve components in the popliteal fossa. It is most commonly used for foot and ankle surgery. (296)

53. Femoral or saphenous nerve blockade can be performed in addition to a popliteal nerve block to improve tourniquet tolerance and for surgery that involves the medial aspect of the leg. (296)

54. The tibial, sural, deep peroneal, superficial peroneal, and saphenous nerves supply the entire innervation to the foot. The tibial nerve innervates the sole of the foot, heel, and plantar portion of the toes. The sural nerve innervates the lateral portion of the foot and ankle. The deep peroneal nerve innervates primarily between the first two digits of the foot. The superficial peroneal nerve innervates the majority of the dorsum of the foot. The saphenous nerve innervates the medial foot and ankle. (296-297)

55. The tibial nerve lies on the heel side of the posterior tibial artery and can be blocked by infiltrating 3 to 5 mL of local anesthetic solution in a fanning pattern around this artery. The sural nerve can be blocked by injecting 5 mL of local anesthetic solution in the groove between the lateral malleolus and the calcaneus near the small saphenous vein. The saphenous nerve is blocked by infiltration of 5 mL of local anesthetic solution anterior to the medial malleolus near the great saphenous. The deep peroneal is blocked by injecting 5 mL of local anesthetic solution adjacent to the anterior tibial artery. Alternatively, if arterial pulsation is absent, the deep peroneal nerve can also be blocked deep to the extensor hallucis longus tendon and extensor retinaculum. The superficial peroneal nerve's terminal branches are blocked by injecting a subcutaneous ridge of local anesthetic between the medial and lateral malleoli over the anterior surface of the foot. (296-297)

INTRAVENOUS REGIONAL NEURAL ANESTHESIA

56. Intravenous regional neural anesthesia (Bier block) is commonly used for anesthesia for short surgical procedures on an extremity, particularly those in which postoperative pain is not expected to be significant. (297)

57. Contraindications to a Bier block are essentially contraindications to tourniquet application (sickle cell disease, infection, ischemic vascular disease). Pain limits the effectiveness of exsanguination of extremities with fractures. Traumatic lacerations may allow escape of local anesthetic from the extremity. (297)

58. A Bier block is achieved by first placing an intravenous catheter distal in the extremity to be anesthetized. The extremity is then exsanguinated, a double tourniquet is placed proximal in the extremity, and the more proximal cuff is inflated. A dose of local anesthetic based on the patient's weight is administered slowly. The volume of local anesthetic is 40 to 50 mL in the upper extremity. If the patient starts to develop tourniquet pain during the procedure, the distal cuff may be inflated and the proximal cuff deflated. (297)

59. Commonly used local anesthetic solutions for intravenous regional neural anesthesia are 0.5% lidocaine or prilocaine (plain solutions without epinephrine). Bupivacaine is avoided because of potential systemic toxicity, most notably malignant ventricular cardiac dysrhythmias leading to refractory cardiac arrest. (297)

60. Technically, a regional intravenous neural block is easier and faster to perform than a brachial plexus block or lower extremity block and is readily applicable to all age groups, including pediatric patients. (297-298)

61. Severe tourniquet pain and the maximum allowable tourniquet time limit the practical duration of the block. Because the duration of postoperative analgesia is also limited, this procedure is not usually performed when postoperative pain is a significant issue. (297-298)

62. A complication of a Bier block includes the risk of excessive, toxic doses of local anesthetic reaching the systemic circulation with accidental deflation of the tourniquet. This risk can be minimized at the conclusion of cases 20 to 40 minutes in duration by deflating the tourniquet in increments over time. This allows the local anesthetic to enter the systemic circulation over a greater period of time. (298)

Chapter

16 PATIENT POSITIONING AND ASSOCIATED RISKS

Jae-Woo Lee, Lydia Cassorla

1. Whose responsibility is the intraoperative position of the anesthetized patient?
2. How does the lack of response to pain affect the positions that are tolerated by patients under general anesthesia? What is the clinical implication of this?
3. What are potential injuries to the patient that can be sustained during mask ventilation of the airway?
4. What areas of skin are especially prone to ischemic damage during surgery? How can this risk be minimized?

SPECIFIC POSITIONS

5. What are the cardiovascular effects of placing the patient in the supine position for a surgical procedure?
6. How does the supine position affect lung perfusion?
7. How does the functional residual capacity change when a patient's position is changed from standing to supine?
8. How should the patient's legs be ideally positioned during surgery in the supine position?
9. Why might focal alopecia result following surgery?
10. Why might backache result from surgery in the supine position?
11. What are some potential positions the patient's arms may be placed in while the patient is in the supine position for surgery?
12. Describe how the patient's arms should be positioned when the patient is supine and the arms are abducted.
13. Describe how the patient's arms should be positioned when the patient is supine and the arms are adducted.
14. What are the cardiovascular effects of placing the patient in the head-down position, or Trendelenburg position, for a surgical procedure?
15. What are the pulmonary effects of placing the patient in the Trendelenburg position for a surgical procedure?
16. How does the Trendelenburg position affect the patient's intracranial pressure?
17. What is a potential complication of the use of shoulder braces to prevent the patient from sliding off the table while in a steep Trendelenburg position?
18. How does the prone position affect the patient's ventilatory mechanics? How can this effect be offset?
19. What are the cardiovascular effects of placing the patient in the prone position for a surgical procedure? How can this potential problem be minimized?
20. What are the potential problems with turning the prone patient's head laterally?
21. What is a potential problem with placing the prone patient's head in a neutral forward-facing position, as in a Mayfield headrest? How can this potential problem be minimized?

22. How should the patient's arms be positioned while in the prone position?
23. How can venous pooling in the lower extremities be offset while the patient is in the prone position, as during a laminectomy?
24. How does the lateral decubitus position affect the patient's ventilatory mechanics and ventilation-perfusion ratio during mechanical ventilation of the lungs? How might these effects of the lateral decubitus position be manifest clinically?
25. What are the cardiovascular effects of placing the patient in the lateral decubitus position for a surgical procedure?
26. What is the purpose of the axillary roll for patients who are placed in the lateral decubitus position? What monitoring may be helpful?
27. How should the patient's head and neck be positioned when in the lateral decubitus position?
28. How should the patient's legs be positioned when in the lateral decubitus position?
29. How should the patient's nondependent arm be positioned when in the lateral decubitus position?
30. For what types of surgery is the sitting position most often used?
31. What are the cardiovascular effects of placing the patient in the sitting position for a surgical procedure?
32. What is the principal potential intraoperative complication of positioning a patient in the sitting position for surgery?
33. Which patients are most likely to manifest cardiopulmonary effects from being placed in the lithotomy position for a surgical procedure?
34. How should a patient with a history of low back pain be positioned in the lithotomy position for surgery?
35. What is the principal potential intraoperative complication of positioning a patient in the lithotomy position for surgery? How can this potential problem be minimized?
36. What is a potential problem that can result from placing a patient in the lithotomy position for more than 4 hours during a surgical procedure?
37. How can the patient's digits of the fingers or toes be injured during moving of operating table parts?

PERIPHERAL NERVE INJURY

38. How important are peripheral nerve injuries? During what types of anesthetics do peripheral nerve injuries occur? What is the mechanism of a peripheral nerve injury during surgery? How can this risk be minimized?
39. What are some coexisting medical conditions that place a patient at an increased risk for a peripheral nerve injury?
40. What is the usual recovery time from a peripheral nerve injury?
41. Which peripheral nerve is most likely to manifest a postoperative neuropathy?
42. What are some ways in which the ulnar nerve may be injured intraoperatively? What position should a patient's arm be placed in to minimize this risk?
43. Are males or females more prone to ulnar nerve injury during surgery?
44. How does injury to the ulnar nerve manifest clinically?
45. What is the second most common peripheral nerve injured during surgery?
46. Why is the brachial plexus especially susceptible to nerve injury during surgery?
47. What are some ways in which the brachial plexus may be injured intraoperatively?
48. How does injury to the brachial plexus manifest clinically?
49. What are some ways in which the radial nerve may be injured intraoperatively?
50. How does injury to the radial nerve manifest clinically?
51. What are some ways in which the median nerve may be injured intraoperatively?
52. How does injury to the median nerve manifest clinically?
53. What are some ways in which the sciatic nerve may be injured intraoperatively?
54. How does injury to the sciatic nerve manifest clinically?
55. Which peripheral nerve of the lower extremity is most likely to manifest a postoperative neuropathy?

56. What are some ways in which the common peroneal nerve may be injured intraoperatively?
57. How does injury to the common peroneal nerve manifest clinically?
58. What are some ways in which the anterior tibial nerve may be injured intraoperatively?
59. How does injury to the anterior tibial nerve manifest clinically?
60. What are some ways in which the femoral nerve may be injured intraoperatively?
61. How does injury to the femoral nerve manifest clinically?
62. What are some ways in which the saphenous nerve may be injured intraoperatively?
63. What are some ways in which the obturator nerve may be injured intraoperatively?
64. How does injury to the obturator nerve manifest clinically?
65. Can the intraoperative use of a tourniquet result in nerve injury?

PERIOPERATIVE EYE INJURY AND VISUAL LOSS

66. How common are perioperative eye injuries?
67. How does postoperative visual loss occur?
68. What risk factors are associated with postoperative visual loss?
69. What is the ASA Postoperative Visual Loss Registry?

EVALUATION AND TREATMENT OF PERIOPERATIVE NEUROPATHIES

70. Why is it important to seek early neurologic consultation when a peripheral nerve injury is manifest in the postoperative period?

ANSWERS*

1. The position the patient is placed in intraoperatively while under general anesthesia is the responsibility of the anesthesiologist, surgeon, and nurses. The responsibility is shared among these operating room personnel. During the course of surgery the responsibility becomes primarily that of the anesthesiologist, who must be aware of any changes in the patient's position. (300)
2. An awake patient will typically respond to pain, numbness, or tingling associated with nerve injury. However, positions that would not be tolerated by an awake patient can be assumed for hours while under anesthesia care, especially when combined with drug-induced skeletal muscle relaxation. Therefore, the anesthesiologist must share responsibility for the proper positioning of the patient during anesthesia, for appropriate padding of the pressure points, and must be aware of potential injuries associated with various positions. A description of the positioning and padding should also be documented in the anesthesia record. (300)
3. Potential injuries to the patient that can be sustained during mask ventilation of the airway include damage to the facial nerve and necrosis to the bridge of the nose. Facial nerve injury can be caused by the face strap on the anesthetic mask compressing the buccal branch of the nerve or by the anesthesiologist's fingers on the ascending ramus of the patient's mandible. Both of these risks are rare, however.

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

4. Skin that is subject to excessive or prolonged pressure is at risk for ischemic damage. Areas of skin that are especially prone to ischemic damage during surgery include the heels, supraorbital ridge, and the skin at the corner of the mouth in contact with the endotracheal tube. The risk of skin ischemia can be minimized with adequate padding at potential pressure points.

SPECIFIC POSITIONS

5. Placement of a patient in the supine position may modestly increase cardiac output secondary to an increase in venous return. This causes a slight, reflex mediated decrease in heart rate that results in minimal changes to the blood pressure. (301)

6. The supine position produces a relatively even distribution of blood flow throughout the lung. (301)

7. The functional residual capacity decreases when a patient's position is changed from standing to supine, largely because of cephalad displacement of the diaphragm by the abdominal contents. (301)

8. While undergoing surgery in the supine position, the patient's legs should be positioned with slight flexion at both the hips and knees. Not only does this facilitate venous drainage from the lower extremities, it also decreases the amount of anterior abdominal wall tension during surgical closure of the abdomen. (303, Figure 19-1)

9. Focal alopecia may result from continued pressure on one area of the scalp. This risk may be minimized by padding and by periodically moving the patient's head during long procedures if possible. (303)

10. Backache may result from surgery in the supine position because of the loss of the normal lordotic curvature of the lumbar spine that can occur, particularly with skeletal muscle relaxation. (303)

11. One or both arms may be placed in the abducted or adducted (tucked) positions while a patient is in the supine position for surgery. (302-303, Figure 19-1, *A* and *C*)

12. When the supine patient's arms are abducted, they should be placed on well-padded armboards. The arms should be extended less than 90 degrees at the shoulder. Some debate exists regarding the position of the hand when the arm is abducted. It is believed that supination of the forearm may result in greater protection of the ulnar nerve from compression. However, supination of the hand may result in greater stretching of the brachial plexus. In addition, supination of the forearm in awake patients is uncomfortable. An alternative is leaving the forearm in the neutral position. The neutral position is the spontaneous position of an awake, supine patient. (302-303)

13. When the supine patient's arms are adducted, or tucked in to the patient's side, care should be taken to avoid placing any portion of the arm or fingers against any metal surfaces or hard edges of the operating table. This can be accomplished by padding the arm circumferentially before securing it. Most often the arms are allowed to remain in the neutral position, with the palms facing the patient's side. (302-303)

14. Placement of a patient in the head-down position, or Trendelenburg position, for a surgical procedure results in increases in central venous, intracranial, and intraocular pressures. The Trendelenburg position is often used to increase venous return during hypotension, to improve exposure during abdominal and laparoscopic surgery, and during central line placement. (303)

15. Placement of a patient in the head-down position for a surgical procedure results in an increase in pulmonary venous pressure and a decrease in pulmonary

compliance and functional residual capacity. This occurs secondary to an increase in central venous pressure and from the cephalad displacement of the abdominal contents against the diaphragm. This may manifest as increased peak inspiratory pressure with mechanical ventilation. (303)

16. Placement of a patient in the head-down position for a surgical procedure results in an increase in the intracranial pressure. (303)

17. Brachial plexus injury can occur when shoulder braces are used to prevent the patient from sliding down the table when in the Trendelenburg position. The injury is due to both direct compression and stretching of the brachial plexus. (313)

18. Placement of a patient in the prone position results in cephalad displacement of the diaphragm because of pressure from the abdominal contents against the operating room table. This can lead to a decrease in the functional residual capacity and impairment of diaphragmatic movement manifesting as increased peak inspiratory pressures with mechanical ventilation. This effect of the prone position may be offset by allowing space for the abdomen and chest to move with minimum pressure during respiration. Examples are special tables such as the Jackson table with support only under bony areas, additions to a standard operating room bed such as the Wilson frame, and firm rolls or bolsters placed under each side from the clavicle to the iliac crest. (307-308, Figure 19-4)

19. Placement of a patient in the prone position may result in compression of the inferior vena cava, leading to impaired venous return to the heart and decreased cardiac output. This effect of the prone position may be offset by techniques that reduce compression of the abdomen, as outlined above. Examples include special tables, frames, and bolsters. (308, Figure 19-4, *A*)

20. Turning the prone patient's head laterally can result in jugular venous outflow obstruction, as well as obstruction to vertebral artery blood flow and, rarely, thrombosis. In addition, this position can result in postoperative neck pain, especially in patients with a history of cervical arthritis. The brachial plexus is also stretched on the contralateral side. These potential problems can be avoided by placing the patient's head neutral in a forward-facing position on a padded rest. The padded rest typically supports the patient's head around the periphery of the face, leaving the center of the face and eyes without contact with the padding. (308, Figure 19-4, *D*)

21. A potential problem with placing the prone patient's head in a neutral forward-facing position, as in a Mayfield headrest, is the risk of compression of the face on the table or padding. This can be especially hazardous with unrecognized movement of the patient during the surgery. Of particular concern is pressure on the globes of the eye, which can result in retinal ischemia and blindness. This potential problem can be minimized by frequently checking the patient's eyes, nose, and ears during the course of the surgical procedure. (308)

22. While in the prone position the patient's arms should be positioned such that abduction of the arms at the shoulder is limited to less than 90 degrees. The patient's arms may be placed at the patient's sides or above the head. This helps to minimize the risk of injury to the brachial plexus. (308)

23. Venous pooling in the lower extremities while the patient is in the prone position can be offset with the placement of fitted elastic stockings or sequential compression devices. (308)

24. Placement of a patient in the lateral decubitus position can result in significant mismatching of pulmonary ventilation-to-perfusion during mechanical ventilation of the lungs for a number of reasons. First, while in the lateral position the mechanically ventilated patient has relatively better ventilation of the nondependent lung as compared to the dependent lung. The reasons for the dependent lung being

ventilated less are secondary to the loss of lung volume from compression by abdominal contents and mediastinal contents. The patient concurrently has better perfusion of the dependent lung, primarily secondary to the effects of gravity. Together, these factors result in greater mismatching of ventilation and perfusion of the lungs during mechanical ventilation in a patient in the lateral decubitus position. Clinically, this may manifest as arterial hypoxemia. (306, Figure 19-3)

25. Placement of a patient in the lateral decubitus position can result in compression of the inferior vena cava from the pressure of a kidney rest. This can lead to a decrease in venous return to the heart. (305-306)

26. In the lateral position, the dependent brachial plexus may be injured should the axilla be compressed sufficiently to compress the brachial plexus. An axillary roll properly placed under the thorax caudal to the axilla supports the patient's chest and minimizes the risk of compression of the nerves and vessels in the axilla. Arterial or pulse oximetry monitoring of the dependent arm may help detect axillary compression. Alternatively, the radial pulse may be checked periodically to ensure complete compression of the artery has not occurred. (306, Figure 19-3, *C*)

27. The patient's head and neck while in the lateral decubitus position should be positioned such that the cervical vertebrae of the neck are in line with the thoracic vertebrae. This can be accomplished by placing the patient's head on a pillow of the correct height. Insufficient padding under the head of the patient in the lateral decubitus position can result in compression and stretching to the brachial plexus and direct compression to the dependent ear and eye. (305-306)

28. The patient's legs while in the lateral decubitus position should be positioned such that the dependent leg is flexed at the knee and there is a pillow between the two legs. This helps to minimize stretch of the nerves of the dependent leg and distributes more evenly the weight of the legs, such that discrete pressure points are avoided. Indeed, there have been case reports of arterial insufficiency of the dependent leg of patients undergoing hip arthroplasty in the lateral position. (305-306)

29. The patient's nondependent arm while in the lateral decubitus position should be supported by a holder or padding above and in front of the patient's face. Alternatively, the arm may be suspended from a support bar that is well padded. Both positions should limit the extension of the arm to less than 90 degrees at the shoulder. (305-306, Figure 19-3, *B*)

30. The sitting position is most often used for neurosurgical procedures, especially in the posterior fossa, and for orthopedic surgeries on the shoulder. The advantages of the sitting position for posterior fossa craniotomies are improved surgical exposure and facilitated jugular venous drainage leading to less bleeding. (309, Figure 19-5)

31. Patients placed in the sitting position for a surgical procedure may become hypotensive, especially if hypovolemic. Additionally, patients may have decreases in cardiac output and cerebral perfusion pressures. Hypotension can be avoided by positioning the patient in gradual steps to allow for accommodation, by ensuring adequate hydration, and through the temporary administration of small doses of vasopressors. (309)

32. The principal potential intraoperative complication of positioning a patient in the sitting position for neurosurgery is a venous air embolus. Placing the surgical site above the level of the heart during the procedure facilitates the entrainment of air. Patients undergoing craniotomies are especially at risk, given that veins in the bony cranium do not collapse after being transected. (310)

33. Patients with a large abdominal mass, pregnant, or obese patients are most likely to manifest cardiovascular effects when placed in the lithotomy position for a

surgical procedure. These patients are more likely to have obstruction of the inferior vena cava in this position. In addition, the lithotomy position leads to the cephalad displacement of the diaphragm by the abdominal viscera, potentially impairing spontaneous ventilation. (305, Figure 19-2)

34. Patients with a history of low back pain may suffer from exacerbation of their pain after being placed in the lithotomy position for surgery. These patients may benefit from assuming the position themselves when awake and choosing the position that is most comfortable for them. An alternative position for surgery may also be considered. (305)

35. The principal potential intraoperative complication of positioning a patient in the lithotomy position for surgery is peripheral nerve injury. Injury can occur to the sciatic, common peroneal, femoral, saphenous, or obturator nerves in this position. This potential problem can be minimized by ensuring that the patient's legs are well padded in areas where they could potentially be compressed such as against metal braces. While positioning the patient, the legs should be lifted simultaneously, flexed no more than 90 degrees at the hip, and then simultaneously rotated for placement into the stirrups. (305, Figure 19-2, *B* and *C*)

36. Compartment syndrome secondary to inadequate circulation can result from placing a patient in the lithotomy position for more than 4 hours during a surgical procedure. The common initiating event is probably direct local muscle pressure. This can occur from inadequate padding, tight leg straps, or the surgeon leaning on the leg for a prolonged period of time. The direct pressure may lead to arterial insufficiency, tissue necrosis and edema, and rhabdomyolysis. (305)

37. A patient's digits of the fingers or toes can be injured intraoperatively during moving of operating table parts. Movement of the table into a space where the fingers or toes lie could lead to crushing of the digit. (304-305, Figure 19-2, *D*)

PERIPHERAL NERVE INJURY

38. Peripheral nerve injuries are responsible for 18% of closed claims in the ASA Closed Claims Project, second only to death (22%). Peripheral nerve injuries have occurred in patients after regional anesthesia, monitored anesthesia care, and general anesthesia. The causes of a peripheral nerve injury are often multifactorial. However, injury occurring to a nerve intraoperatively is felt to be due to ischemia from compression or stretching of the nerve. The injury usually sustained to the nerve is neurapraxic, which is a loss of function without corresponding anatomic injury. The risk of sustaining an intraoperative nerve injury can be minimized by carefully positioning patients and by using padding when and where appropriate. There is evidence to suggest that patients who experience intraoperative nerve injury may have preexisting conditions that made the injury unavoidable, even with proper positioning and padding. (310-311, Tables 19-1 through 19-3)

39. Risk factors for peripheral nerve injury include extreme positions, male sex for ulnar nerve injury, extremes of weight, hypotension, prolonged tourniquet time, and central venous or arterial catheter placements. The prone "superman" and lateral decubitus positions appear to be risk factors for upper extremity nerve injuries. (312-313)

40. The usual recovery time from an intraoperative peripheral nerve injury is 3 to 12 months. In rare cases, injury can be permanent, particularly with a stretch injury that results in disrupted axons. (315)

41. The most common peripheral nerve to manifest a postoperative neuropathy is the ulnar nerve. The mechanism of ulnar neuropathy is felt to be multifactorial and remains poorly understood, and therefore is not completely preventable. (311-313)

42. The ulnar nerve may be injured intraoperatively secondary to compression of the nerve against the posterior aspect of the medial epicondyle of the humerus or in the cubital tunnel. There also appears to be an increased incidence of ulnar nerve injury associated with sternal retraction during cardiac surgery. The ulnar nerve may be at a greater risk of injury when the elbow is hyperflexed or the forearm is pronated. Supination of the forearm intraoperatively may provide some protection to the ulnar nerve, although this may increase the risk to the brachial plexus. (311-313)

43. Males are five times more likely to acquire an ulnar neuropathy than females, possibly due to anatomic differences. (313)

44. Ulnar nerve injury manifests clinically as decreased sensation over the ventral and dorsal portions of the medial 1½ fingers, and an inability to abduct or oppose the fifth finger. Over time, ulnar nerve injury results in the appearance of a "claw hand" secondary to atrophy of the intrinsic muscles. (311-313)

45. The second most common peripheral nerve injured during surgery is the brachial plexus. (310)

46. The brachial plexus is especially susceptible to nerve injury during surgery because its course is superficial and fixed between two points: the vertebra and the axillary fascia. In addition, it lies close to the clavicle and humerus, which are very mobile, and slings under the clavicle and the pectoralis muscles. (313)

47. The brachial plexus may be injured intraoperatively through both stretching and compression of the plexus. Stretching of the brachial plexus can occur with neck extension, with turning the head to the opposite side, or with the patient in the lateral decubitus position with inadequate padding to support the neck in the midline position. It can also occur in any position when the arm is abducted more than 90 degrees. Compression of the brachial plexus may occur with inappropriately placed shoulder braces or during spreading of the sternum during cardiac surgery. (313)

48. Injury to the brachial plexus manifests as a limply hanging arm at the side, rotated medially, with a pronated forearm. This position of the arm is commonly referred to as "waiter's tip." (313)

49. The radial nerve may be injured intraoperatively if the arm slips off the surgical table or if pressure is applied to the humerus where the radial nerve runs in the spiral groove. A rare cause of radial nerve injury is the mechanical effects of an automated blood pressure cuff. (313)

50. Injury to the radial nerve manifests as decreased sensation over the dorsal surface of the lateral three fingers and an inability to extend the metacarpophalangeal joints or abduct the thumb. It is also characterized by wristdrop. (313)

51. The median nerve may be injured intraoperatively by the insertion of an intravenous catheter into the antecubital fossa or by the extravasation of injected medications. (313)

52. Injury to the median nerve manifests as decreased sensation on the palmar surface of the lateral three fingers and an inability to oppose the first and fifth digits. (313)

53. The sciatic nerve may be injured intraoperatively by direct compression of the nerve or during intramuscular injections in the upper, outer quadrant of the buttocks. Injury may also occur by stretching with external rotation of the leg, which most often occurs while in the lithotomy position. The risk of sciatic nerve stretching can be minimized by the avoidance of excessive rotation of the legs at the hip while in the lithotomy position. Injury of the sciatic nerve may be mistaken as injury to the peroneal nerve, because the peroneal nerve is a branch of the sciatic nerve. (313-314)

54. Injury to the sciatic nerve manifests as decreased sensation over the lateral leg and foot, and weakness of all the skeletal muscles below the knee. (313-314)

55. The most common peripheral nerve in the lower extremity to manifest a postoperative neuropathy is the common peroneal nerve. (313-314)

56. The common peroneal nerve may be injured intraoperatively by compression between the patient's fibula and leg support for the lithotomy position. The risk of this nerve injury can be minimized with appropriate padding, limiting the length of cradle leg rests to avoid pressure on the fibular head, and strict attention to candy cane leg holders to avoid contact with the leg. (313-314)

57. Injury to the common peroneal nerve manifests as a loss of dorsal extension of the toes, inability to evert the foot, and footdrop. (313-314)

58. The anterior tibial nerve may be injured intraoperatively with prolonged plantar flexion of the feet. This risk can be avoided by placing a roll under the ankles of patients in the prone position.

59. Injury to the anterior tibial nerve manifests as footdrop.

60. The femoral nerve may be injured intraoperatively by compression from a pelvic retractor against the pelvic brim during abdominal surgery. It may also occur with excessive flexing and external rotation at the groin while in the lithotomy position. (314)

61. Injury to the femoral nerve manifests as a decreased sensation over the superior aspect of the thigh, as well as on the medial and anteromedial side of the leg. (314)

62. The saphenous nerve may be injured intraoperatively by compression against the medial tibial condyle and a metal support for the lithotomy position when the brace is placed medial to the patient's leg. The risk of a saphenous nerve injury may be minimized with the appropriate use of padding.

63. The obturator nerve may be injured intraoperatively during a difficult forceps-assisted vaginal delivery or by excessive flexion of the thigh to the abdomen, as during vaginal delivery.

64. Injury to the obturator nerve manifests as decreased sensation over the medial thigh and an inability to adduct the leg.

65. The intraoperative use of a tourniquet can result in nerve injury, particularly if the inflation time of the tourniquet exceeds 2 hours or with the application of excessive tourniquet pressures. For this reason, after about 2 hours if there is a continued need for the tourniquet, it may be prudent to deflate it for 15 minutes and reinflate it. (314)

PERIOPERATIVE EYE INJURY AND VISUAL LOSS

66. Although quite rare, eye complications accounted for 3% of all claims (ASA Closed Claims Project Database) and were associated with greater monetary settlements as compared with nonocular injuries. Corneal abrasion continues to be the most common type of perioperative eye injury. (314)

67. Postoperative visual loss is a rare devastating complication associated with patients undergoing spine surgery in the prone position and in cardiac surgery with cardiopulmonary bypass. Ischemic optic neuropathy (ION) and to a lesser extent central retinal arterial occlusion (CRAO) from direct eye compression are the conditions most commonly cited as potential causes. (314)

68. The causes of postoperative visual loss appear to be multifactorial in nature. However, patient risk factors include hypertension, diabetes, atherosclerosis, morbid obesity, and smoking. Perioperative risk factors for patients undergoing spine surgery in the prone position include prolonged hypotension, long duration of surgery, large volumes of blood loss, large crystalloid use, anemia or hemodilution, and increased intraocular or venous pressure. (314)

69. The ASA Committee on Professional Liability established the ASA Postoperative Visual Loss (POVL) registry to study the complication. By 2005, 131 cases were reported to the registry of which 73% of the cases occurred during spine surgeries and 9% involved cardiac surgery. Of patients with POVL undergoing spine surgery, 89% of patients were diagnosed with ION, predominantly posterior, and 11% with CRAO. (314)

EVALUATION AND TREATMENT OF PERIOPERATIVE NEUROPATHIES

70. Neurologic consultation obtained early after a peripheral nerve injury manifests in the postoperative period may be useful in detecting between acute and chronic injury. This can be accomplished through nerve conduction velocity and electromyographic studies. Signs of denervation from acute nerve injury are detected by an electromyogram 18 to 21 days after the injury, emphasizing the importance of obtaining neurologic consultation before this time. It may also be useful to test the same nerve in the limb opposite the symptomatic one to exclude any preexisting nerve injury that is asymptomatic. When the injury is reversible, recovery often takes place within 3 to 12 months. (315)

Chapter

17 ANESTHETIC MONITORING

Anil de Silva

1. What is the purpose of intraoperative patient monitoring?
2. What are some monitors that have been mandated for use by the American Society of Anesthesiologists? How frequently is it mandated that intraoperative blood pressure be measured?

ELECTROCARDIOGRAPHIC MONITORING

3. What are some potential intraoperative problems during anesthesia that can be detected by an anesthesiologist through the use of an electrocardiogram?
4. Which lead is selected on the electrocardiogram for continuous tracing on the monitor to best detect cardiac dysrhythmias? Why?
5. Which lead is selected on the electrocardiogram for continuous tracing on the monitor to best detect inferior wall myocardial ischemia? Which lead is selected for continuous tracing on the monitor to best detect anterior or lateral wall myocardial ischemia?

SYSTEMIC BLOOD PRESSURE MONITORING

6. How does an automated oscillometric blood pressure measuring device, such as the Dinamap, work?
7. What is the appropriate-sized cuff for use with an automated oscillometric blood pressure measuring device?
8. When using an automated oscillometric blood pressure measuring device, will the blood pressure be falsely high or low with a cuff that is too small? When using an automated oscillometric blood pressure measuring device, will the blood pressure be falsely high or low with a cuff that is too loose?
9. What is a potential problem that can result from too frequent cycling of an automated oscillometric blood pressure measuring device?
10. What are some possible indications for intraarterial blood pressure monitoring?
11. What are some arteries that may be used for intraarterial blood pressure monitoring? Which of these is most commonly selected?
12. How does the intraarterial blood pressure waveform change with increasing distance from the heart?

CENTRAL VENOUS PRESSURE MONITORING

13. What are some indications for the placement of a central venous catheter?
14. What veins are used for central venous access? What are some potential complications of the cannulation of veins for central access?
15. Which is the preferred jugular vein for cannulation? Why?
16. What are some advantages and disadvantages of cannulation of the internal jugular vein over other central veins?

17. What are some advantages and disadvantages of cannulation of the subclavian vein over other central veins?
18. What does the central venous waveform look like? What do each of the peaks and descents represent relative to the cardiac cycle?
19. Why is the central venous pressure able to be used to estimate a patient's intravascular fluid volume status?
20. Under which circumstances does central venous pressure not estimate a patient's intravascular fluid volume status? What invasive monitor can be used instead of a central venous catheter under these conditions?

PULMONARY ARTERY CATHETER MONITORING

21. Name six possible indications for the placement of a pulmonary artery catheter. What information can be obtained regarding the patient's status with the use of a pulmonary artery catheter?
22. Of what is the pulmonary capillary wedge pressure a reflection? What other measurement derived by the pulmonary artery catheter can also be used in lieu of the pulmonary capillary wedge pressure?
23. How is estimation of the cardiac output accomplished through the use of a pulmonary artery catheter?
24. What are some potential complications of pulmonary artery catheterization?
25. Please complete the following table illustrating the usefulness of central venous catheters and pulmonary artery catheters in the evaluation of various hemodynamic disorders (*PAEDP*, pulmonary artery end-diastolic pressure; *PAOP*, pulmonary artery occlusion pressure).

	Central Venous Pressure ↑ or ↓	***PAOP ↑ or ↓***	***PAEDP Relation to PAOP***
Hypovolemia			
Left ventricular failure			
Right ventricular failure			
Pulmonary embolism			
Cardiac tamponade			

ECHOCARDIOGRAPHIC MONITORING

26. What is some information that can be derived intraoperatively through the use of a transesophageal echocardiogram?
27. What is the difference between M-mode and B-mode echocardiography?
28. When would one use continuous-wave Doppler as opposed to using pulsed-wave Doppler? What is the Nyquist limit?

PULSE OXIMETRY MONITORING

29. How does a pulse oximeter work?
30. Enumerate five factors that influence the accuracy of pulse oximetry.
31. Is the Spo_2 read by the pulse oximeter falsely high or falsely low in the presence of carboxyhemoglobin?
32. What is the Spo_2 read by the pulse oximeter in the presence of methemoglobinemia?
33. What is the Spo_2 read by the pulse oximeter in the presence of intravenous dyes?

ELECTROPHYSIOLOGIC MONITORING

34. What is an evoked potential? What are some evoked potentials that can be monitored?
35. What are some intraoperative uses of evoked potentials? What is the most common procedure for which evoked potentials are monitored intraoperatively?

36. How do evoked potentials appear when the patient is under general anesthesia? What is the potential problem with this?
37. What are some factors that may limit the usefulness of evoked potentials in the intraoperative period?
38. The integrity of which spinal cord neurologic tissue is monitored by somatosensory evoked potentials and motor evoked potentials?

CAPNOGRAPHY MONITORING

39. What is a capnograph?
40. Please refer to Figure 20-10. What portion of the ventilatory cycle is represented by each letter in the figure?
41. What does the absence of carbon dioxide in a patient's exhaled gases indicate during endotracheal intubation? What does the absence of carbon dioxide in a person's exhaled gases indicate after proper and confirmed endotracheal intubation?
42. What are some possible causes of a decrease in the concentration of carbon dioxide in a patient's exhaled gases?
43. What are some possible causes of an increase in the concentration of carbon dioxide in a patient's exhaled gases?
44. How does the end-tidal carbon dioxide concentration measured on a capnogram compare with the arterial carbon dioxide concentration? Why?

ELECTROENCEPHALOGRAPHIC MONITORING

45. What are some intraoperative uses of an electroencephalogram?
46. What factors may influence the tracings obtained by an intraoperative electroencephalogram?
47. What is the bispectral index monitor?
48. What are some potential clinical uses of a bispectral index monitor? What are its limitations?

TEMPERATURE MONITORING

49. How does a patient's body temperature usually change under anesthesia?
50. What are some sites for measurement of a patient's body temperature?
51. What is the potential benefit of maintaining intraoperative normothermia?

INHALED GAS MONITORING

52. What are some methods by which the exhaled concentrations of multiple gases, including respiratory and anesthetic gases, may be measured?
53. What are some advantages and disadvantages of mass spectrometry techniques for measuring a patient's exhaled gases?
54. What are some advantages and disadvantages of Raman spectrometry techniques for measuring a patient's exhaled gases?

ANSWERS*

1. The primary purpose of intraoperative patient monitoring is to gather data regarding the physiologic status of the patient. Monitoring provides the anesthesiologist with the information to respond appropriately to any salutary or adverse physiologic changes. In addition, the patient's response to the therapeutic interventions can be assessed. (320)

2. The American Society of Anesthesiologists has mandated that qualified anesthesia personnel shall be present in the room to administer anesthesia and monitor the patient throughout the conduct of all general anesthetics, regional anesthetics, and monitored anesthesia care. The standard adopted by the American Society of Anesthesiologists is that during all anesthetics the patient's oxygenation,

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

ventilation, circulation, and temperature shall be continually evaluated. The full description of these standards (Appendix B) also provides an explanation of each of these objectives and specific methods by which they can be achieved. In brief, the use of pulse oximetry, capnography, an oxygen analyzer, a disconnect alarm, and a visual display of the electrocardiogram are all addressed. In addition, the blood pressure and heart rate are to be evaluated at least every 5 minutes during the course of anesthesia. (320)

ELECTROCARDIOGRAPHIC MONITORING

3. Potential intraoperative problems such as cardiac dysrhythmias, myocardial ischemia, and electrolyte abnormalities may all be detected through the use of an electrocardiogram. (321)
4. Lead II provides for the best visualization of the P wave on the electrocardiogram, making it the best lead for the detection of cardiac dysrhythmias on a continuous tracing. (321)
5. Lead II on the electrocardiogram provides for the best detection of inferior wall myocardial ischemia on a continuous tracing. The V5 precordial lead on the electrocardiogram provides for the best detection of anterior or lateral wall myocardial ischemia. (321)

SYSTEMIC BLOOD PRESSURE MONITORING

6. Automated oscillometric blood pressure monitoring devices work by inflating a pneumatic cuff encircling a limb until arterial blood flow through the limb is occluded. The cuff is then deflated until pressure oscillations are detected. The pressure at which oscillations are initially detected is considered to be the systolic blood pressure. The cuff continues to deflate and the oscillations increase for a time and then begin to decrease. The diastolic pressure is defined as the point at which further deflation of the cuff provides no further evidence of pressure oscillations. The most reliable blood pressure parameter measured by this noninvasive blood pressure monitoring device is the mean arterial blood pressure. (321-322, Figure 20-3)
7. The appropriate cuff size for use with a noninvasive blood pressure measuring device is one whose width is about 40% of the circumference of the patient's limb. (322)
8. When using an automated oscillometric blood pressure measuring device, the blood pressure will be falsely high when the blood pressure cuff is too small. Conversely, the blood pressure will be falsely low when the blood pressure cuff is too large. (322)
9. Cycling an automated oscillometric blood pressure measuring device too frequently can result in limited perfusion to the extremity distal to the cuff. Complications such as edema, nerve paresthesia, superficial thrombophlebitis, and compartment syndrome have all been reported as a result of noninvasive blood pressure devices that have been repeatedly cycled. These complications are rare. (321)
10. Possible indications for intraarterial blood pressure monitoring include the need for continuous blood pressure monitoring, access for frequent arterial blood gas samplings, need for monitoring intentional pharmacologic cardiovascular manipulation, and failure of indirect blood pressure measurement. (322)
11. Arteries that may be used for intraarterial blood pressure monitoring include the radial, ulnar, brachial, axillary, femoral, dorsalis pedis, and the superficial temporal arteries. Of these, the radial artery is the most frequently used artery for cannulation. (323, Table 20-3)
12. The waveform from an intraarterial catheter changes progressively with increasing distance from the heart. The waveform peak is higher and the trough lower at more distal arterial sites. The mean arterial pressure, however, remains approximately the same. (323, Figure 20-4)

CENTRAL VENOUS PRESSURE MONITORING

13. Indications for the placement of a central venous catheter include the measurement of central venous pressures, access through which to provide long-term intravenous feedings, access for the administration of large volumes of fluids, intravascular access when no peripheral access is available, the administration of vasoactive or caustic drugs, to initiate transvenous cardiac pacing, for temporary hemodialysis, and for the aspiration of air emboli. (324)

14. Veins that are cannulated for central venous access include the internal jugular, subclavian, femoral, and antecubital veins. Potential complications of cannulation of the central veins include arterial puncture, hematoma, hemothorax, pneumothorax, nerve injury, emboli, cardiac dysrhythmias, thrombosis, and infection. Accidental arterial puncture while attempting cannulation of the jugular vein can result in the need to surgically explore and repair the artery. A pneumothorax occurs more frequently after placement of a subclavian catheter. This is the basis for the recommendation that a chest radiograph be done after failed subclavian catheterization and before attempting catheterization on the other side. (323, Table 20-4)

15. The right internal jugular vein is preferred over the left jugular vein for cannulation because of its short, straight, valveless route to the superior vena cava. (323)

16. Advantages of cannulation of the internal jugular vein include its predictable anatomic location with palpable landmarks, its location at the head of the patient's bed allowing the anesthesiologist easy access to the catheter intraoperatively, and the relatively decreased complications associated with cannulation of this central vein. Disadvantages of cannulation of the internal jugular vein include the potential for puncture of the carotid artery and pleural cavity and trauma to the brachial plexus. (323)

17. Advantages of cannulation of the subclavian vein include its landmarks, its capacity to remain patent despite hypovolemia, easier nursing care, and the relative increase in patient comfort associated with cannulation of this central vein. Disadvantages of cannulation of the subclavian vein include the potential for puncture of the subclavian artery and pleural cavity and for thoracic duct damage on the left. (323)

18. The central venous pressure waveform has a typical trace in a normally functioning heart. The *a* wave correlates with atrial contraction, the *c* wave correlates with closure of the tricuspid valve and its bulging into the right atrium, and the *v* wave correlates with blood accumulation in the vena cava and right atrium against a closed tricuspid valve. The *x* descent correlates with atrial relaxation, and the *y* descent correlates with opening of the tricuspid valve and right ventricular filling. (324, Figure 20-5)

19. The central venous pressure parallels right atrial pressure in a patient with normal cardiovascular physiology. In these patients, the central venous pressure can be used to estimate the patient's intravascular fluid volume status. (324)

20. The central venous pressure does not estimate the patient's intravascular fluid volume status in the face of right-sided heart dysfunction, left ventricular dysfunction, or pulmonary hypertension. Under these conditions, a pulmonary artery catheter may be used for cardiovascular monitoring. (324)

PULMONARY ARTERY CATHETER MONITORING

21. Possible indications for the placement of a pulmonary artery catheter perioperatively include poor left ventricular function, valvular heart disease, recent myocardial infarction, adult respiratory distress syndrome or any pulmonary vascular disease process, massive trauma, and major vascular surgery. In general, the pulmonary artery catheter allows for more accurate assessment of cardiac filling pressure than a central venous monitor in the presence of pulmonary vascular disease, left-sided heart dysfunction, or potential left-sided heart dysfunction due to myocardial ischemia. The pulmonary artery catheter also measures cardiac output and calculates systemic and pulmonary vascular resistance. (324, Table 20-5)

22. The pulmonary capillary wedge pressure is a reflection of left atrial pressure. The pulmonary artery diastolic pressure may be used as an approximation of left atrial pressure in lieu of the pulmonary artery wedge pressure. This allows for continuous monitoring. The pulmonary artery diastolic pressure does not accurately reflect left atrial pressure in conditions in which pulmonary vascular resistance is increased, as with hypoxia, hypercarbia, hypothermia, and various forms of pulmonary disease. (324, Figure 20-6)

23. Cardiac output can be estimated through the use of a pulmonary artery catheter via the thermodilution method. To do this, cold saline is rapidly injected through the proximal central venous port. A thermistor located at the distal end of the pulmonary artery catheter senses the change in temperature. Because blood flow is the source of dilution of temperature, the flow, or cardiac output, can be calculated. It is the right ventricular cardiac output that is actually measured by this technique, whereas left ventricular cardiac output can only be estimated based on the results. (325)

24. Potential complications of pulmonary artery catheterization include pulmonary ischemia or infarction from prolonged wedging of the catheter, cardiac dysrhythmias, infection, catheter knotting, and, rarely, pulmonary artery rupture. (324)

25. (325, Table 20-6)

	Central Venous Pressure ↑ or ↓	***PAOP ↑ or ↓***	***PAEDP Relation to PAOP***
Hypovolemia	Decreased	Decreased	PAEDP = PAOP
Left ventricular failure	Increased	Increased	PAEDP = PAOP
Right ventricular failure	Increased	No change	PAEDP = PAOP
Pulmonary embolism	Increased	No change	PAEDP > PAOP
Cardiac tamponade	Increased	Increased	PAEDP = PAOP

ECHOCARDIOGRAPHIC MONITORING

26. Intraoperative cardiac imaging with a transesophageal echocardiogram is now widely accepted as a monitor for cardiac function during surgery, especially cardiac surgery. Information that can be derived from an intraoperative echocardiogram includes regional ventricular and atrial wall motion, ejection fraction, cardiac valve function, the presence of intracardiac air, and the effects of surgery and anesthesia on cardiac function. The use of a transesophageal echocardiogram requires advanced technical training. Complications associated with the use of transesophageal echocardiography include pharyngeal and esophageal injury and bleeding, but these occurrences are rare. (326, Table 20-7)

27. M-mode echocardiography provides a unidimensional view of the myocardium, while B-mode echocardiography provides a two-dimensional image of the myocardium. The M-mode is most useful for determining velocities, while the B-mode is most useful for evaluating changes in myocardium function. (326)

28. One would use continuous–wave Doppler when measuring velocities with high Doppler shifts. Pulsed-wave Doppler can only be used when the velocities measured are relatively slow. However an advantage is that the location of the moving object is also measurable. In pulsed-wave Doppler echocardiography, the maximal Doppler shift measurable by echocardiography is limited to half the pulse repetition frequency, also called the Nyquist limit. (326)

PULSE OXIMETRY MONITORING

29. A pulse oximeter works by emitting a light through a diode and sensing the light, usually on the opposite side of a digit. The wavelength of light that is absorbed by oxyhemoglobin relative to reduced hemoglobin in the pulsatile (and therefore arterial) vessel allows the device to calculate the saturation of oxygen in the peripheral artery. (327, Figure 20-8)

30. Factors that influence the accuracy of pulse oximetry include low flow conditions, motion artifact, nail polish, ambient light interference, dysfunctional hemoglobins, methylene blue, and a shift in the oxyhemoglobin dissociation curve. (327, Table 20-8)

31. The Spo_2 read by the pulse oximeter in the presence of carboxyhemoglobin is falsely high. This occurs because carboxyhemoglobin has an absorbance of light that is markedly similar to oxyhemoglobin. (327)

32. The Spo_2 read by the pulse oximeter in the presence of methemoglobinemia approaches 85% regardless of the true arterial hemoglobin oxygen saturation. (327)

33. The Spo_2 read by the pulse oximeter in the presence of intravenous dyes (methylene blue, indigo carmine) will be artificially low regardless of the true arterial hemoglobin oxygen saturation. (326)

ELECTRO-PHYSIOLOGIC MONITORING

34. An evoked potential is a measured low amplitude signal from the central nervous system that occurs in response to sensory or motor nerve stimulation. Evoked potentials that can be monitored include visual, auditory, sensory, and motor. (328)

35. Evoked potentials can be used intraoperatively to assess the integrity of the neural pathways during anesthesia. The most common evoked potentials monitored intraoperatively are somatosensory evoked potentials from the spinal cord during surgery on the spinal cord or vertebral column. (328)

36. Evoked potentials may undergo changes in the latency period and amplitude while patients are under general anesthesia. These changes are similar to the changes that are seen with neural ischemia, which can complicate interpretation of the evoked potential values. Limiting the minimum alveolar concentration (MAC) of volatile anesthetics to 0.5 to 0.75 facilitates monitoring of evoked potentials. Opioids and propofol have less of an effect on evoked potentials, and muscle relaxants do not affect somatosensory evoked potentials at all. (328)

37. Factors that may limit the intraoperative usefulness of evoked potentials because of their influence on the results include age and gender of the patient, arterial blood gas tensions, and body temperature. In addition, the cost and complexity of performing evoked potentials may limit their use. (328)

38. Somatosensory evoked potentials of the lower extremities monitor the integrity of the dorsal column of the spinal cord. Motor evoked potentials monitor the corticospinal tract. Unlike somatosensory evoked potentials, motor evoked potentials are sensitive to muscle relaxants. (328)

CAPNOGRAPHY MONITORING

39. A capnograph is a waveform display that illustrates the patient's inhaled and exhaled concentrations of carbon dioxide. (328-329)

40. In the capnogram, the point A designates the exhalation of anatomic dead space gas just before the exhalation of alveolar gas. Point B designates the beginning of exhalation of alveolar gas that contains carbon dioxide. Phase C-D designates the exhalation of alveolar gas, while point D designates the end-tidal carbon dioxide concentration. Phase D-E designates the beginning of inspiration and the entrainment of inspired gases. (329, Figure 20-10)

41. The absence of carbon dioxide in a patient's exhaled gases just after attempted endotracheal intubation with properly functioning equipment provides evidence

that the patient's lungs are not being ventilated. That is, the endotracheal tube may not be in the trachea. The absence of carbon dioxide in a patient's exhaled gases after intubation of the trachea has been confirmed may indicate that there is either a malfunction of equipment, a malfunction in the interface between the patient and the equipment (as in disconnection from the anesthesia circuit), movement or dislodgment of the endotracheal tube from its previously proper position, or a physiologic patient problem such as a cardiac arrest. (328)

42. Possible causes of a decrease in the patient's exhaled concentration of carbon dioxide include hyperventilation, hypothermia, low cardiac output, pulmonary embolism, accidental disconnection, tracheal extubation, or cardiac arrest. (328, Table 20-9)

43. Possible causes of an increase in the patient's exhaled concentration of carbon dioxide include hypoventilation, hyperthermia, sepsis, rebreathing, the administration of bicarbonate, and the insufflation of carbon dioxide during laparoscopy. (328, Table 20-9)

44. The end-tidal carbon dioxide concentration measured on a capnogram is less than the true arterial concentration of carbon dioxide, typically by a 2- to 5-mm Hg gradient. This occurs as a result of the alveolar-to-arterial difference for carbon dioxide concentrations secondary to dead space ventilation. (328)

ELECTROENCEPHALOGRAPHIC MONITORING

45. Intraoperative uses of an electroencephalogram include monitoring for cerebral ischemia and monitoring the depth of anesthesia. (329)

46. Among the factors that influence the tracings obtained by an electroencephalogram and limit its usefulness intraoperatively are anesthetics, changes in body temperature, and alterations in the arterial carbon dioxide concentration. (329)

47. The bispectral index monitor performs a bispectral analysis of the electroencephalogram and provides the clinician with a processed evaluation of its analysis through its display of a number between 0 to 100. The analysis is done through superficial scalp electrodes typically on the forehead of the patient. The number provided by the bispectral index monitor reflects the state of wakefulness of the central nervous system. (329, Figure 20-11)

48. The bispectral index monitor may be used clinically to predict loss of consciousness and lack of recall during anesthesia. A bispectral index numerical value of 0 is consistent with an isoelectric encephalogram. A numerical value of 60 or less corresponds to a low probability of recall or awareness. Thus the use of the bispectral index monitor for the titration of medicines to achieve adequate but not excessive loss of consciousness may result in more rapid awakening at the end of the procedure. The bispectral index has not been shown to be well correlated with the hemodynamic or movement responses to noxious stimuli. In addition, a recent study has shown that the use of a bispectral index monitor showed no decrease in the incidence of awareness when using volatile anesthetics. (329)

TEMPERATURE MONITORING

49. Patients will typically have a passive decrease in body temperature by 1° C to 4° C during anesthesia. Intraoperative passive cooling occurs because of anesthesia-induced vasodilation, environmental temperature, and surgical exposure. The mechanism for core heat loss is through redistribution, and for peripheral heat loss is through radiation, convection, conduction, and evaporation. (330)

50. Sites for body temperature monitoring include the esophagus, nasopharynx, rectum, bladder, and tympanic membrane. Axillary and skin temperature monitors are less reliable. (330)

51. Maintaining intraoperative normothermia may decrease risks associated with hypothermia, namely coagulopathies, impaired wound healing, and potentially increased myocardial oxygen requirements as from shivering. (330)

INHALED GAS MONITORING

52. Multiple gas analysis can be achieved by infrared absorption, mass spectrometry, and Raman spectroscopy. (330)

53. Advantages of mass spectrometry techniques for measuring a patient's exhaled gases are that it can measure the gases continuously, it can measure all gases including inhaled anesthetics, oxygen, and nitrogen, and it can measure the inspired gas concentrations as well as the exhaled concentrations. A disadvantage of the mass spectrometry technique is that it has traditionally used large and expensive monitors. (330)

54. Advantages of Raman spectrometry techniques for measuring a patient's exhaled gases are that they can measure all gases including inhaled anesthetics, oxygen, and nitrogen and they do not alter the gas molecule so that it can be returned to the anesthetic delivery system. A disadvantage of Raman spectrometry techniques is that they require a very high intensity light source to work, such as a laser. (330)

Chapter

18 ACID-BASE BALANCE AND BLOOD GAS ANALYSIS

Linda Liu

GENERAL DEFINITIONS

1. What is the importance of maintaining a physiologic acid-base status?
2. What is the definition of an acid or a base?
3. How are acidemia and alkalemia defined?
4. How are acidosis and alkalosis defined?
5. What is the definition of base excess?

REGULATION OF THE HYDROGEN ION CONCENTRATION

6. What is the normal plasma H^+ concentration, the normal plasma HCO_3^- concentration, and the normal arterial pH of blood?
7. How is normal arterial pH maintained?
8. What are the buffering systems, and which system has the greatest contribution to the total buffering capacity of blood?
9. How does the bicarbonate buffering system work? What enzyme facilitates this reaction?
10. How does hemoglobin act as a buffer?
11. How does the ventilatory response work?
12. How does the renal response work?
13. How quickly can the buffering system, ventilation changes, and the renal response work?

MEASUREMENT OF ARTERIAL BLOOD GASES

14. What is the relationship between a venous and arterial blood gas drawn from the same patient concurrently?
15. What errors can occur if heparin or air is present in an arterial blood gas sample?
16. What happens if there is a delay in analysis of the blood sample?
17. How does temperature affect the arterial blood gas (ABG)?
18. What does an anesthesia provider using alpha stat during cardiopulmonary bypass do to the ABG?
19. What does an anesthesia provider using pH stat during cardiopulmonary bypass do to the ABG?

DIFFERENTIAL DIAGNOSIS OF ACID-BASE DISTURBANCES

20. What is the difference between a primary disturbance and a compensatory disturbance in acid-base status?
21. What adverse responses are associated with severe acidemia?
22. What adverse responses are associated with severe alkalemia?
23. What defines a primary respiratory acidosis or alkalosis?
24. What are the causes of a respiratory acidosis?
25. What is the compensatory response for a respiratory acidosis?
26. What is the treatment for a respiratory acidosis?

27. What are the causes of a respiratory alkalosis?
28. What is the compensatory response for a respiratory alkalosis?
29. What is the treatment for a respiratory alkalosis?
30. What defines a primary metabolic acidosis or alkalosis?
31. How is the anion gap calculated?
32. What are the causes of a metabolic acidosis?
33. What is the compensatory response for a metabolic acidosis?
34. Describe how the Stewart strong ion difference approach works.
35. What is the treatment for a metabolic acidosis?
36. What are the causes of a metabolic alkalosis?
37. What is the compensatory response for a metabolic alkalosis?
38. What is the treatment for a metabolic alkalosis?
39. How can an acute respiratory process be distinguished from a chronic process?
40. How is the Δgap determined?
41. How is the Winter's formula used?
42. Diagram the algorithm for diagnosing an acid-base disorder.

OTHER INFORMATION PROVIDED BY THE ARTERIAL BLOOD GAS

43. Define dead space to tidal volume (V_D/V_T) ratio.
44. What are the causes of arterial hypoxemia?
45. What does the alveolar gas equation calculate?
46. How is the alveolar-arterial (A-a) gradient calculated? And what is the significance of the gradient?
47. What is the $Pa_{O_2}/F_{I_{O_2}}$ (P/F) ratio?

CARDIAC OUTPUT ESTIMATES

48. What is the normal mixed venous P_{O_2}?
49. What is the Fick equation used for?
50. What is the arteriovenous difference used for?

ANSWERS*

GENERAL DEFINITIONS

1. A physiologic acid-base status optimizes enzyme function, myocardial contractility, and saturation of hemoglobin with oxygen. (334)
2. Bronsted defined an acid as a molecule that can act as a proton [H^+] donor, and a base as a molecule that can act as a proton acceptor. In biologic molecules, weak acids or bases are molecules that can reversibly donate H^+ or reversibly bind H^+. (334)
3. Acidemia is defined as an arterial pH less than 7.35 and alkalemia is defined as an arterial pH greater than 7.45. (334)
4. An acidosis is the underlying process that lowers the pH, whereas an alkalosis is the process that raises the pH. A patient can have a mixed disorder with both an acidosis and an alkalosis, but can only be either acidemic or alkalemic. (334)
5. Base excess is usually defined as the amount of strong acid or strong base required to return 1 L of whole blood exposed in vitro to a P_{CO_2} of 40 mm Hg to a pH of 7.4. The number is supposed to refer to the metabolic component of an acid-base disorder. It is most often used in the operating room as a surrogate marker for lactic acidosis to help determine the adequacy of volume resuscitation. (335)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

REGULATION OF THE HYDROGEN ION CONCENTRATION

6. At 37° C, the normal plasma H^+ concentration is 35 to 45 nmol/L. The normal plasma HCO_3^- concentration is 24 ± 2 mEq/L, and the normal arterial pH of blood is between 7.36 and 7.44. (335)
7. Normal arterial pH is maintained through three systems: buffers, ventilation changes, and renal response. The ventilatory response involves changes in alveolar ventilation and CO_2 concentrations. The renal response involves reabsorption of bicarbonate ions or secretion of hydrogen ions. (335)
8. The buffering systems in blood include bicarbonate, hemoglobin, phosphate, and plasma proteins. The bicarbonate buffering system is the largest contributor and provides 50% of the total buffering capacity of the body. Hemoglobin is responsible for about 35% of the total buffering capacity, and phosphate and plasma proteins account for the remainder. (335)
9. Carbonic anhydrase facilitates the hydration of carbon dioxide in the plasma and in the erythrocytes into H_2CO_3, which spontaneously dissociates to H^+ and HCO_3^-. The HCO_3^- that is formed then enters the plasma to function as a buffer, and the H^+ that is generated is buffered by hemoglobin. (335)
10. In plasma, hemoglobin exists as a weak acid. It acts as a buffer by binding H^+ generated by the bicarbonate buffering system. Carbon dioxide can also be transported by hemoglobin as carbaminohemoglobin. Deoxyhemoglobin has a greater affinity for carbon dioxide, so venous blood carries more carbon dioxide than arterial blood. (335-336)
11. Carbon dioxide diffuses across the blood-brain barrier to change CSF pH. Central chemoreceptors lie on the anterolateral surface of the medulla and respond to changes in CSF pH. Minute ventilation increases 1 to 4 L/min for every 1 mm Hg increase in P_{CO_2}. Peripheral chemoreceptors are at the bifurcation of the common carotid arteries and aortic arch. The peripheral chemoreceptors are sensitive to changes in P_{O_2}, P_{CO_2}, pH, and arterial perfusion pressure. They communicate with the central respiratory centers via the glossopharyngeal nerves. The stimulus from central and peripheral chemoreceptors to either increase or decrease alveolar ventilation diminishes as the pH approaches 7.4 such that complete correction or overcorrection is not possible. (336)
12. The kidneys correct for pH changes by reabsorbing filtered HCO_3^-, excreting titratable acids, and producing ammonia. (336-337)
13. The buffering system of the blood responds to changes in arterial pH almost instantly. Compensatory changes in alveolar ventilation in response to changes in arterial pH occur within minutes. Compensatory changes by the kidneys in response to changes in arterial pH require 12 to 48 hours and may not be maximal for up to 5 days. (335)

MEASUREMENT OF ARTERIAL BLOOD GASES

14. Venous P_{CO_2} is 4 to 6 mm Hg higher and pH 0.03 to 0.04 lower than arterial values. Venous blood cannot be used for estimation of oxygenation because venous P_{O_2} is significantly lower than arterial P_{O_2} and the relationship is not linear. (338)
15. Because heparin is acidic, excessive amounts of heparin in the syringe containing blood for arterial blood gas and pH analysis may result in a falsely decreased arterial pH reading. Air bubbles in the syringe containing blood for an arterial blood gas sample could result in the diffusion of oxygen and carbon dioxide between the air bubble and the blood in the syringe. Typically, this results in a decrease in the carbon dioxide tensions in the blood sample. The change in oxygen tension (either falsely higher or lower) depends on the patient's P_{O_2}. (338)
16. A delay in analysis of the blood sample can lead to oxygen consumption and carbon dioxide production by the metabolically active white blood cells. Usually this error is small and can be reduced by placing the sample on ice. In some leukemia

patients with markedly elevated white blood cell counts, this error can become significant. This is known as leukocyte larceny. (338)

17. Decreases in temperature decrease the partial pressure of a gas in solution even though the total gas content does not change. A blood gas with a pH of 7.4 and P_{CO_2} of 40 mm Hg at 37° C will have a pH of 7.58 and P_{CO_2} of 23 mm Hg at 25° C. The change in P_{O_2} with respect to temperature depends on the degree that hemoglobin is saturated with oxygen, but as a guideline, the P_{O_2} is decreased approximately 6% for every 1° C that the patient's body temperature is below 37° C. (338)

18. The term alpha stat developed because as the patient's pH was allowed to drift with temperature, the protonation state of histidine residues remained "static." During cardiopulmonary bypass, an anesthesia provider using alpha stat would manage the patient based on an ABG measured at 37° C and strive to keep that pH at 7.4, while the patient's true pH would be higher. (338)

19. pH stat requires keeping a patient's pH static at 7.4 based on the core temperature. During cardiopulmonary bypass, an anesthesia provider using pH stat would manage the patient based on an ABG that is corrected for the patient's temperature. This usually means adding carbon dioxide so that the patient's temperature-corrected blood gas has a pH of 7.4. (338)

DIFFERENTIAL DIAGNOSIS OF ACID-BASE DISTURBANCES

20. A primary disturbance in acid-base status is the initial deviation in the arterial pH secondary to either respiratory or metabolic causes. A compensatory response occurs in an attempt to reverse the alteration in the arterial pH. Typically the compensatory response is not able to completely reverse the deviation in arterial pH. (339)

21. Acidemia usually leads to decreased myocardial contractility. Respiratory acidosis may produce more rapid and profound myocardial dysfunction than metabolic acidosis because of the rapid entry of carbon dioxide into the cardiac cells. In the brain, this rapid rise in carbon dioxide can lead to confusion, loss of consciousness, or seizures. (339)

22. Severe alkalemia can lead to decreased cerebral and coronary blood flow due to arteriolar vasoconstriction. The consequences are more prominent with respiratory than with metabolic causes because of the rapid movement of carbon dioxide across cell membranes. Acute hyperventilation can produce confusion, myoclonus, asterixis, depressed consciousness, and seizures. (339)

23. A primary respiratory acidosis is accompanied by a P_{CO_2} above normal, usually greater than 43 mm Hg. A primary respiratory alkalosis is accompanied by a P_{CO_2} below normal, usually lower than 37 mm Hg. (339-340)

24. Respiratory acidosis may occur secondary to increased carbon dioxide production, decreased carbon dioxide elimination, or from rebreathing or absorption. Causes of increased carbon dioxide production include: malignant hyperthermia, sepsis, or overfeeding. Causes of decreased carbon dioxide elimination include: CNS depressants, decreased skeletal muscle strength, or intrinsic pulmonary disease. Causes of rebreathing or absorption include: exhausted soda lime, incompetent one-way valves, or laparoscopic surgery. (339)

25. Over the course of hours to days, the kidneys will compensate for the acidosis by increased hydrogen ion secretion and bicarbonate reabsorption. The hallmark of a chronic respiratory acidosis is an elevated P_{CO_2} with a near normal pH. (339-340)

26. The treatment for a respiratory acidosis is treatment of the underlying disorder. The use of mechanical ventilation to decrease an acutely increased P_{CO_2} may be necessary if the pH is less than 7.2. (340)

27. Respiratory alkalosis may occur with increased minute ventilation or decreased carbon dioxide production. Causes of increased minute ventilation relative to carbon dioxide production include: CNS disease, pain and anxiety, sepsis, liver disease, pregnancy, or hypoxemia. Causes of decreased carbon dioxide production include: hypothermia and skeletal muscle paralysis. (340)

28. Respiratory alkalosis is compensated for by decreased reabsorption of bicarbonate ions from the renal tubules and increased urinary excretion of bicarbonate. (340)

29. Treatment for a respiratory alkalosis should be directed at correcting the underlying cause. Mild alkalemia usually does not require treatment. During general anesthesia, the minute ventilation may be decreased in order to decrease the elimination of carbon dioxide. (340)

30. A metabolic acidosis is present when accumulation of any acid other than carbon dioxide results in a pH lower than 7.35. The HCO_3^- concentration is usually less than 22 mEq/L. A metabolic alkalosis is present when the pH is higher than 7.45 due to gain of bicarbonate ions or loss of hydrogen ions. The HCO_3^- concentration is usually greater than 26 mEq/L. (340-342)

31. The anion gap is the difference between the measured cations (sodium) and measured anions (chloride and bicarbonate). A normal gap value is 8 to 12 mEq/L and is mostly composed of albumin. A patient with a low serum albumin will have a lower anion gap. Each 1 g/dL decrease in serum albumin below 4.4 g/dL will lower the actual concentration of unmeasured anions by 2.3 to 2.5 mEq/L. (341)

32. The causes of a metabolic acidosis are divided into anion gap and nonanion gap causes. An increase in the anion gap occurs when the anion replacing bicarbonate is not one that is routinely measured. The most common unmeasured anions are lactic and keto-acids. Other common anions include: methanol, ethylene glycol, uremia, paraldehyde, and aspirin. Metabolic acidosis with a normal anion gap occurs when chloride replaces the lost bicarbonate, such as with bicarbonate-wasting processes in the kidney (renal tubular acidosis) or gastrointestinal tract (diarrhea). Aggressive fluid resuscitation with normal saline will induce a nongap metabolic acidosis because the chloride administration impairs bicarbonate reabsorption in the kidneys. (341)

33. Compensatory responses for a metabolic acidosis include increased alveolar ventilation from carotid body stimulation and renal tubule secretion of hydrogen ions into urine. Chronic metabolic acidosis is associated with loss of bone mass because buffers present in bone are used to neutralize the nonvolatile acids. (341)

34. The strong ion approach distinguished six primary acid-base disturbances (strong ion acidosis and alkalosis, nonvolatile buffer acidosis and alkalosis, and respiratory acidosis and alkalosis) as opposed to the four differentiated by the Henderson-Hasselbalch equation (metabolic acidosis and alkalosis, and respiratory acidosis and alkalosis). The more complex Stewart approach may be similar to the traditional Henderson-Hasselbalch approach if changes in albumin concentration are accounted for in the measurement of the anion gap. (341)

35. Treatment for metabolic acidosis is based on whether an anion gap is present or not. Intravenous administration of sodium bicarbonate can be given for a nongap acidosis because the problem is bicarbonate loss. Management of an anion gap acidosis should be guided by diagnosis and treatment of the underlying cause in order to remove the nonvolatile acids in the circulation. (342)

36. Causes of a metabolic alkalosis are based on whether the underlying cause is chloride responsive or chloride resistant. Chloride responsive causes include: renal loss from diuretics, GI loss from vomiting, or alkali administration. Chloride resistant causes include: hyperaldosteronism, refeeding syndrome, and profound hypokalemia. (342)

37. Compensatory responses for a metabolic alkalosis include increased reabsorption of hydrogen ions and decreased secretion of hydrogen ions by renal tubule cells, and alveolar hypoventilation. (342)

38. Treatment of a metabolic alkalosis should be aimed at reducing the acid loss by stopping gastric drainage or fluid repletion with saline and potassium chloride, which allows the kidneys to excrete excess bicarbonate ions. Occasionally, a trial of acetazolamide may be useful in causing a bicarbonaturia. (342)

39. Acute respiratory acidosis can be distinguished from a chronic respiratory acidosis by the degree of elevation of HCO_3^-. The renal effects to compensate for a respiratory acidosis take 12 to 48 hours to take effect and are reflected by a more marked increase in the plasma HCO_3^- concentration. During an acute process, the pH changes 0.08 for every 10 mm Hg change in P_{CO_2} from 40 mm Hg. During a chronic process, the pH changes 0.03 for every 10 mm Hg change in P_{CO_2} from 40 mm Hg. (342-343)

40. If an anion gap is present, then a Δgap should be determined. The Δgap is the excess anion gap added back to the serum bicarbonate level. It is used to determine if another concurrent metabolic process is present along with an anion gap metabolic acidosis. If the Δgap is less than 22 mEq/L, then a concurrent nongap metabolic acidosis exists. If the Δgap is greater than 26 mEq/L, then a concurrent metabolic alkalosis exits. (342-343)

41. The Winter's formula is used to determine whether an appropriate respiratory compensation is present for the metabolic acidosis. If measured P_{CO_2} is greater than calculated from the Winter's formula, then the compensation is not adequate and respiratory acidosis is also present. If the measured P_{CO_2} is less than calculated, then a respiratory alkalosis is present. For a metabolic acidosis, the calculated P_{CO_2} equals the serum HCO_3^- concentration multiplied by 1.5 plus 8. For a metabolic alkalosis, the calculated P_{CO_2} equals the serum HCO_3^- concentration multiplied by 0.7 plus 21. (342-343)

42. Step 1: Determine oxygenation
Step 2: Determine acidemia (pH $<$ 7.35) or alkalemia (pH $>$ 7.45)
Step 3: Determine whether the etiology is from a respiratory (P_{CO_2} change from 40) or metabolic (HCO_3^- – change from 24 mEq/L) process
Step 4: If there is a respiratory abnormality, then assess whether the process is acute or chronic. If there is a metabolic acidosis, then skip to step 5. If there is a metabolic alkalosis, then skip to step 7.
Step 5: If there is a metabolic abnormality, determine the anion gap
Step 6: Determine the Δgap.
Step 7: Determine whether there is adequate respiratory compensation for the metabolic process. (342-343)

OTHER INFORMATION PROVIDED BY THE ARTERIAL BLOOD GAS

43. The dead space to tidal volume (V_D/V_T) ratio is the fraction of each tidal volume that is involved in dead space ventilation. Normal V_D/V_T is less than 0.3 and is mostly due to anatomic dead space. An increased dead space will decrease the efficiency of ventilation. Patients with a pulmonary embolus or chronic obstructive pulmonary disease are examples of patients who may have an increased V_D/V_T ratio. (343)

44. Arterial hypoxemia is caused by a low P_{O_2} in the inhaled gases, hypoventilation, or venous admixture with or without a decreased mixed venous oxygen content. An increase in the venous admixture involves blood that passes from the pulmonary circulation to the systemic circulation without passing by ventilated alveoli. These right-to-left shunts can be intrapulmonary (atelectasis, pneumonia, one-lung ventilation) or intracardiac (congenital heart disease). (344)

45. The alveolar gas equation estimates the partial pressure of alveolar oxygen (P_{AO_2}) by using barometric pressure, water vapor pressure, the inspired oxygen content, and P_{CO_2}. (344-345)

46. The A-a gradient formula calculates the difference in oxygen partial pressure between alveolar (P_{AO_2}) and arterial (Pa_{O_2}) blood. Calculation of the gradient provides an estimate of venous admixture as the cause of hypoxia. Normally, the A-a gradient is less than 15 mm Hg while breathing room air due to shunting via the thebesian and bronchial veins. Increased inspired F_{IO_2} can lead to a larger gradient: up to 60 mm Hg while breathing F_{IO_2} of 1.0 in healthy patients. The A-a gradient can also provide an assessment of the patient's shunt fraction. To estimate the amount of shunt present, the shunt fraction is approximately 1% of cardiac output for every 20 mm Hg difference in the A-a gradient when the Pa_{O_2} is higher than 150 mm Hg. (344-345)

47. The Pa_{O_2}/F_{IO_2} (P/F) ratio is an alternative to the A-a gradient to communicate the degree of hypoxia. Patients with acute respiratory distress syndrome (ARDS) should have a P/F ratio below 200. (345)

CARDIAC OUTPUT ESTIMATES

48. Normal mixed venous P_{O_2} (Pv_{O_2}) is 40 mm Hg. A true mixed venous P_{O_2} should reflect blood from the superior and inferior vena cava. It is usually obtained from the distal port of an unwedged pulmonary artery catheter. Many physicians use the trend from a venous P_{O_2} obtained from the superior vena cava as a surrogate number. If tissue oxygen consumption is unchanged, then changes in Pv_{O_2} will reflect direct changes in cardiac output. (345)

49. The Fick equation is used to calculate cardiac output if Pa_{O_2}, Pv_{O_2}, and hemoglobin are known. It basically states that the delivery of oxygen in the veins must equal the delivery of oxygen in the arteries minus the oxygen that is consumed (V_{O_2}). (345-346)

50. The arteriovenous difference is the difference between the arterial and mixed venous oxygen content. The number is a good estimate of the adequacy of oxygen delivery. The normal arteriovenous difference is 4 to 6 mL of O_2/dL of blood. When tissue oxygen consumption is constant, an increased arteriovenous difference means that there is higher oxygen extraction, which can be seen with decreased cardiac output or congestive heart failure. A lower arteriovenous difference means there is lower extraction or higher cardiac output, which can occur during cyanide poisoning or sepsis. (346)

Chapter

19 HEMOSTASIS

Greg Stratmann

COAGULATION

1. What is the mechanism of coagulation?
2. What activates platelets to form the initial platelet plug at the site of vascular injury?
3. What is the role of activated platelets in the formation of a blood clot?
4. Where is tissue factor located? What is its role in coagulation at the site of vascular injury?
5. What physiologic event leads to the secretion of tissue plasminogen activator and eventually fibrinolysis?
6. How is fibrinolysis affected normally by surgery or massive trauma?
7. What is the potential clinical effect of systemic fibrinolysis? What can be used for the treatment of systemic fibrinolysis?

COMMON LABORATORY TESTS OF HEMOSTASIS

8. Name some laboratory tests of platelet function.
9. How can a difficult blood draw result in an artificially low platelet count number?
10. Which test of platelet function is the single best predictor of functional platelet disorders?
11. How is a bleeding time test of platelet function performed?
12. What is a normal bleeding time?
13. What are some limitations of the bleeding time test of platelet function?
14. What function of platelets is evaluated by the platelet function analysis test?
15. What are some common causes of platelet dysfunction that can be detected by the platelet function analysis test?
16. What are platelet aggregation studies of platelet function?
17. What are a benefit and a drawback of platelet aggregation studies over other platelet function tests?
18. Name some laboratory tests of coagulation.
19. Low levels of which factors will result in a prolonged prothrombin time?
20. What is the international normalized ratio (INR)? What is it useful for?
21. Low levels of which factors will result in a prolonged partial thromboplastin time?
22. What drug therapy can be monitored by the partial thromboplastin time?
23. A low level of which factor will result in a prolonged prothrombin time and a normal partial thromboplastin time?
24. What is evaluated by the thrombin time test?
25. What is the relationship between the results of the thrombin time test and the results of the prothrombin time and partial thromboplastin time tests?
26. What is tested by the activated clotting time (ACT)? What is its clinical use?
27. What elements of blood clot formation, consolidation, and lysis are measured by thromboelastography?
28. Name some laboratory tests of fibrinolysis.

29. What is suggested by elevated levels of fibrinopeptide or fibrin monomer?
30. What is suggested by elevated levels of fibrin degradation products?
31. What is suggested by elevated D-dimer levels?

DISORDERS ASSOCIATED WITH ALTERED HEMOSTASIS DURING SURGERY

32. In general, what laboratory values of platelet counts are associated with uncontrolled intraoperative bleeding?
33. In general, what percent of coagulation factors must be present to prevent uncontrolled intraoperative bleeding?
34. Name some diseases associated with an increased incidence of bleeding during surgery.
35. Name some diseases or conditions associated with an increased incidence of thrombosis during surgery.
36. Name some diseases that are associated with initiating disseminated intravascular coagulation during surgery.
37. What are some hereditary coagulation and platelet disorders? Which of these is the most common?
38. How are hereditary coagulation disorders treated?
39. Where is von Willebrand factor stored?
40. Name three important hemostatic functions of von Willebrand factor.
41. How does von Willebrand disease inhibit the formation of fibrin?
42. What are the clinical effects of von Willebrand disease?
43. How can von Willebrand disease be distinguished from factor VIII deficiency?
44. How many types of von Willebrand disease are there? What are they and how are they inherited?
45. What is the anesthetic management of a patient with von Willebrand disease when undergoing a surgical procedure?
46. What disease or condition is a contraindication to the administration of desmopressin acetate tablets (DDAVP)?
47. What are alternative perioperative treatment options of patients with von Willebrand disease if DDAVP is not available?
48. How does vitamin K support coagulation?
49. Which coagulation factors are vitamin K dependent?
50. How could a patient become vitamin K deficient without fasting?
51. Which coagulation factor is not synthesized in the liver? Where, instead, is this factor made?
52. Name three reasons for the increased risk of bleeding caused by severe liver disease.
53. What diseases or conditions are associated with acquired antibodies to coagulation factor VIII? What is the clinical relevance of this?
54. What are some causes of peripheral platelet destruction?
55. What are some causes of thrombocytopenia that can occur during pregnancy?
56. What percent of platelets are normally sequestered in the spleen? What happens during pathologic splenic sequestration of platelets?
57. Name some causes of an impaired quality of platelet function despite the adequate number of circulating platelets.
58. What are some intraoperative conditions that may facilitate bleeding?
59. At what body temperature can hypothermia begin to contribute to intraoperative bleeding?
60. How can anemia and hemodilution cause a coagulopathy?

DISORDERS FAVORING THROMBOSIS

61. What are some inherited factor deficiencies that can lead to a hypercoagulable state?
62. What is factor V Leiden?
63. What is antiphospholipid syndrome?

64. What percent of patients with systemic lupus erythematosus have circulating lupus anticoagulant? What is the clinical implication of this?
65. What laboratory analysis values for partial thromboplastin time and prothrombin time are associated with lupus anticoagulant?
66. What is the classic set of circumstances, sometimes referred to as Virchow triad, that predisposes patients to perioperative thrombosis?
67. What is disseminated intravascular coagulation (DIC)?
68. What coagulation test results would you expect in a patient with DIC?
69. Which conditions have similar laboratory findings as those of DIC? Which lab finding might help distinguish between DIC and these conditions?
70. What is the treatment for DIC?

ANTICOAGULANTS, THROMBOLYTICS, AND ANTIPLATELET DRUGS

71. What are some common clinical complications associated with perioperative thrombosis?
72. What categories of drugs are available to prevent and treat perioperative thrombotic complications?
73. What are some clinically used anticoagulants?
74. What is the mechanism of action of warfarin (Coumadin)?
75. Which of the coagulation factors has the shortest half-life? Why is knowledge of this factor's plasma half-life important for warfarin therapy?
76. Why is it necessary to coadminister heparin in the early phases of warfarin treatment?
77. What laboratory test monitors warfarin therapy? Why is it necessary to monitor warfarin therapy and not therapy with oral direct thrombin inhibitors?
78. What are some advantages of unfractionated heparin therapy over low-molecular-weight heparin (LMWH) or pentasaccharide (fondaparinux) drugs?
79. Why does unfractionated heparin therapy need to be closely monitored?
80. Why is it necessary to monitor unfractionated heparin therapy and not therapy with LMWH or pentasaccharide drugs?
81. What laboratory test is used to monitor unfractionated heparin therapy?
82. What are some procedures in which heparin is administered to prevent blood clotting? What laboratory test value is the usual end point for heparin therapy in these procedures?
83. How is heparin anticoagulation during surgery reversed? What is the dose? What is its mechanism of action?
84. What are some potential negative effects of the administration of protamine to reverse the anticoagulation effects of heparin?
85. What are some potential disadvantages and/or side effects of the administration of heparin?
86. What is heparin-induced thrombocytopenia? How many types are there?
87. How is the diagnosis of heparin-induced thrombocytopenia (HIT) type 2 made? What is its incidence among patients who receive heparin therapy? What is the mortality rate of patients with HIT type 2?
88. What is the incidence of HIT type 2 among patients who receive heparin therapy? What is the mortality rate of patients with HIT type 2?
89. What is the management of heparin-induced thrombocytopenia once the diagnosis is made?
90. What is heparin resistance and what causes it?
91. How is heparin resistance treated?
92. How does heparin differ from both LMWH and pentasaccharide drugs regarding its effect on thrombin?
93. What is the mechanism of action of LMWH and pentasaccharide drugs for anticoagulation?
94. What are some advantages and disadvantages of LMWH and pentasaccharide drugs over heparin for anticoagulation therapy?
95. What are some direct thrombin inhibitor drugs that are in current clinical use?

96. What are the drawbacks of direct thrombin inhibitor drugs for intraoperative anticoagulation?
97. A patient with a recent history of HIT type 2 is scheduled for a semielective coronary artery bypass graft surgery. If the risk of bleeding associated with intraoperative direct thrombin inhibitor therapy is considered excessive, what other management options exist to meet the need for systemic anticoagulation for cardiopulmonary bypass?
98. What are some thrombolytic drugs currently used in clinical practice?
99. What is the mechanism of action of thrombolytic drugs?
100. How long is surgery contraindicated after thrombolytic therapy?
101. What are some classes of antiplatelet drugs currently used in clinical practice? What are some examples of drugs in each of these classes?
102. How is platelet function affected by aspirin, nonsteroidal antiinflammatory drugs, and COX-2 inhibitors?
103. How is platelet function affected by thienopyridine derivatives?
104. What is the duration of the effects of the thienopyridine derivatives clopidogrel and ticlopidine on platelets after their discontinuation?
105. How is platelet function affected by GPIIb/IIIa antagonists?
106. What is the duration of the effects of GPIIb/IIIa drugs after their discontinuation?

AN APPROACH TO PATIENTS WHO ARE ANTICOAGULATED

107. When a patient on warfarin presents for surgery, what are the conflicting risks?
108. Which surgeries are generally associated with high risks of perioperative thrombosis?
109. Which baseline medical conditions place patients on chronic warfarin therapy at a high risk of perioperative thrombosis regardless of the type of surgery?
110. Which baseline medical conditions place patients on chronic warfarin therapy at an intermediate risk of perioperative thrombosis regardless of the type of surgery?
111. Which baseline medical conditions place patients on chronic warfarin therapy at a low risk of perioperative thrombosis regardless of the type of surgery?
112. Why is it important to stratify the risk of perioperative thrombosis for patients on chronic warfarin therapy?
113. In what way does the management of patients on chronic warfarin therapy at high risk for perioperative thrombosis differ from those at intermediate or low risk?
114. In a patient receiving perioperative heparin bridging therapy for warfarin treatment, when should the intravenous heparin infusion be stopped prior to surgery and when is it restarted?
115. In a patient receiving perioperative LMWH bridging therapy for warfarin treatment, when is the last dose of LMWH administered and when is it restarted?
116. In which patients should the administration of perioperative heparin likely be avoided?
117. How should a patient on chronic warfarin therapy who needs emergency surgery be managed?
118. Why should the administration of oral vitamin K be considered for the emergency patient on chronic warfarin therapy who is receiving fresh frozen plasma or prothrombin complex to reverse the effects of warfarin?
119. How should vitamin K be administered for emergency surgery in patients on chronic warfarin therapy? Why is this route preferred over the others?

AN APPROACH TO PATIENTS RECEIVING ANTIPLATELET THERAPY

120. How long do patients with bare metal coronary stents require antiplatelet therapy?
121. How long do patients with drug-eluting coronary stents require antiplatelet therapy?
122. Why do patients with drug-eluting coronary stents require antiplatelet therapy much longer than patients with bare metal coronary stents?
123. How should patients with coronary stents that require antiplatelet therapy be managed in the perioperative period?

NEURAXIAL INTERVENTIONS IN PATIENTS BEING TREATED WITH ANTICOAGULANT DRUGS

124. What is the risk of neuraxial interventions in patients who are concomitantly being treated with anticoagulant drugs? How should these patients be managed?

AN INTRAOPERATIVE APPROACH TO UNCONTROLLED BLEEDING

125. In the event of the massive transfusion of blood, and when laboratory testing is not available, at what volume of blood loss does the dilution of coagulation factors and platelets warrant the transfusion of fresh frozen plasma or platelets, respectively?
126. During ongoing blood loss, what laboratory value would indicate the need for the replacement of coagulation factors with fresh frozen plasma?
127. During ongoing blood loss, what laboratory value would indicate the need for the replacement of platelets with a transfusion of concentrated platelets?
128. During ongoing blood loss, what laboratory value of fibrinogen would indicate the need for a transfusion of cryoprecipitate?
129. What are some indications for the transfusion of cryoprecipitate?
130. What is the role of recombinant factor VIIa in perioperative hemorrhage?
131. List some adjuvant hemostatic agents and their mechanism of action.
132. What are some of the indications for DDAVP as an adjuvant hemostatic agent?

ANSWERS*

COAGULATION

1. The traditional thinking regarding the mechanism of coagulation was that there were two independent pathways, which could independently activate a common pathway leading to the generation of thrombin, which converts fibrinogen to fibrin. These two pathways were termed intravascular (intrinsic) and extravascular (extrinsic). It is now believed that this thinking is flawed; it appears the intrinsic pathway is not important in physiologic coagulation *per se*. Instead, the current understanding is that coagulation is a cell-based process that occurs on the surface of subendothelial cells and platelets, and that it involves elements of both the intrinsic and extrinsic systems. Specifically the extrinsic system generates a small amount of thrombin, which then activates parts of the intrinsic system. The extrinsic system also activates the intrinsic system directly via a recently discovered link between the two systems. This then leads to the overwhelming generation of thrombin (thrombin burst), which causes blood to clot. (349, Figure 22-1)
2. Platelets are activated at the site of vascular injury to form the initial platelet plug by adhering to collagen or von Willebrand factor. (349)
3. Platelets, once activated, degranulate and release large amounts of calcium and factors V and VIII. This activates a series of events that eventually leads to a cross-linked fibrin meshwork that traps activated platelets and red blood cells to form a blood clot. (349)
4. Tissue factor is located on subendothelial cells. Tissue factor located on the surface of perivascular subendothelial cells at the site of vascular injury binds with circulating factor VII to form a complex that leads to coagulation. (349)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

5. The secretion of tissue plasminogen activator occurs when the endothelium is activated by injury. This results in the activation of plasminogen to plasmin, which degrades fibrin to soluble products such as D-dimers. This normally remains localized to areas of thrombus. (350)
6. In general, surgery and/or massive trauma results in an elevation of acute phase reactants that induces both a hypercoagulable state and inhibits the normal process of fibrinolysis. (350)
7. The potential clinical effect of systemic fibrinolysis is the inability to dissolve thrombus, or clots, and for continued bleeding. This can occur by unknown mechanisms in the setting of surgery, cardiopulmonary bypass, or massive trauma. Systemic antifibrinolytics such as ε-aminocaproic acid and tranexamic acid have been used to treat systemic fibrinolysis in this setting. (350-351)

COMMON LABORATORY TESTS OF HEMOSTASIS

8. Laboratory tests of platelet function include the platelet count, bleeding time, platelet function analysis, and platelet aggregation studies. (351)
9. Platelet counts are quantified by automated instruments. Minimal platelet clumping, as can occur with a difficult blood draw, can result in an artificially low platelet count number. To confirm that an automated instrument-measured low platelet count is valid, the platelet count can be examined visually for clumping. Most clinical laboratories visually inspect platelet samples when the results of a platelet count are less than 100,000 cells/μL. (351)
10. The bleeding time is the test of platelet function that is the single best predictor of functional platelet disorders. (351)
11. The bleeding time test is a standardized test that involves making an incision 9 mm long and 1 mm deep on the volar surface of the forearm. A blood pressure cuff is placed on the upper arm insufflated to a pressure of 40 mm Hg. Excess blood is blotted away every 30 seconds with filter paper while not touching the edge of the incision. The time is calculated from incision to the end of bleeding, and this time is the result of the test. (351)
12. A normal bleeding time is less than 11 minutes. (351, Table 22-1)
13. Some limitations of the bleeding time test of platelet function are its required specific standard for performance, the difficulty with controlling the environment in which it is performed, the potential for scar formation at the test site, and that it is not readily available. (351)
14. The platelet function analysis test evaluates for the presence of dysfunctional platelet adhesion. Platelet adhesion is the sticking of platelets to other surfaces. Platelet aggregation, or the sticking of platelets to each other, is not evaluated by this test. (351)
15. Some common causes of platelet dysfunction that can be detected by the platelet function analysis test include uremia, hereditary platelet disorders such as von Willebrand disease, postcardiopulmonary bypass platelet dysfunction, and the presence of antiplatelet medications. (351)
16. Platelet aggregation studies of platelet function test the response of platelets to aggregating agents such as collagen, adenosine diphosphate (ADP), epinephrine, and ristocetin. (351)
17. A benefit of platelet aggregation studies over other platelet function tests is the ability of the test to differentiate between different causes of platelet aggregation dysfunction. A drawback of platelet aggregation studies over other platelet function tests is that it cannot be performed intraoperatively and is rarely performed perioperatively. (351)

18. Laboratory tests of coagulation include the prothrombin time, partial thromboplastin time, thrombin time, fibrinogen levels, ACT, and thromboelastography. (352)

19. Low levels of factors VII, X, V; prothrombin; and fibrinogen prolong the prothrombin time. (352)

20. The international normalized ratio (INR) is a number that standardizes reagent differences between prothrombin time results across different laboratories. The INR is useful for monitoring oral anticoagulant drug therapy with warfarin. (352)

21. Low levels of factors VIII, IX, XI, and XII will result in a prolonged partial thromboplastin time. Adequate levels of factors X and V; prothrombin; and fibrinogen must also be present. (352)

22. Heparin therapy can be monitored by the partial thromboplastin time. (352)

23. A low level of factor VII is the only cause of a prolonged prothrombin time and a normal partial thromboplastin time. (352)

24. The thrombin time test evaluates the thrombin-fibrinogen interaction and is prolonged with low levels of fibrinogen, abnormal fibrinogen, and in the presence of circulating anticoagulants such as heparin. (352)

25. The prothrombin time test and the partial thromboplastin time tests will both be prolonged if the thrombin time test is prolonged. Adequate fibrinogen levels are necessary for all three of these tests of coagulation. (352)

26. The ACT measures the amount of time required for whole blood to clot in a test tube. The ACT test is used clinically to monitor heparin therapy intraoperatively. (352)

27. Thromboelastography measures the time until initial clot formation (clotting factor concentrations and possible anticoagulant medicine), the time until clot formation (fibrinogen and platelets), the absolute clot strength (platelet quantity and aggregation), and the degree of clot lysis (excessive fibrinolysis or antifibrinolytic therapy). Note that thromboelastography does not measure platelet adhesion, only platelet aggregation. (352)

28. Laboratory tests of fibrinolysis include fibrinopeptide and fibrin monomer levels, fibrin degradation products, and D-dimer levels. (352)

29. Elevated levels of fibrinopeptide or fibrin monomer are suggestive of intravascular coagulation. (352)

30. Elevated levels of fibrin degradation products are suggestive of conditions of intravascular fibrin deposition with resultant secondary fibrinolysis, such as disseminated intravascular coagulation. (352)

31. D-dimers are essentially a specific fibrin degradation product and are generated by the fibrinolytic activity of plasmin. Plasmin cleaves cross-linked fibrin. Fibrin monomers are cross-linked by factor XIII to form D-dimers. Elevated D-dimer levels are suggestive of some prior formation of cross-linked fibrin (i.e., clot) such as that caused by thrombotic or thromboembolic disorders. (352)

DISORDERS ASSOCIATED WITH ALTERED HEMOSTASIS DURING SURGERY

32. Platelet counts of 50,000 cells/μL can be associated with uncontrolled intraoperative bleeding. (353)

33. In general, 20% to 30% of coagulation factors must be present to prevent uncontrolled intraoperative bleeding. (353)

34. Some diseases associated with an increased incidence of bleeding during surgery include hereditary and spontaneous coagulation factor deficiencies, hereditary and spontaneous platelet disorders, liver disease, renal disease, HELLP syndrome,

acute immune thrombocytopenia, elevated plasma proteins, multiple myeloma, dysproteinurias, myeloproliferative disorders, coagulation factor inhibitors, and drugs. Examples of drugs include warfarin, heparin, aspirin, nonsteroidal antiinflammatory drugs, digitalis, thiazide diuretics, and ethyl alcohol. (353, Table 22-2)

35. Some diseases or conditions associated with an increased incidence of thrombosis during surgery include hereditary or spontaneous hypercoagulable states, anticoagulant or factor mutations, factor V Leiden, homocystinemia, dysfibrinogenemia, increased platelet turnover, prosthetic heart valves, antiphospholipid antibody, lupus anticoagulant, anticardiolipin antibody, and blood stasis and vascular damage. (353, Table 22-2)

36. Some diseases that are associated with initiating disseminated intravascular coagulation during surgery include crush injury, acute hemolytic transfusion reaction, abruption placentae, cardiopulmonary bypass, intravascular emboli, sepsis, liver disease, arterial hypoxemia acidosis, pancreatitis, immune complex disease, allergic reactions, transplant rejection, and cancer. (353, Table 22-2)

37. Some hereditary coagulation and platelet disorders include von Willebrand disease and deficiencies in factor VIII (hemophilia A), factor IX (hemophilia B or Christmas disease), factor XII, and factor XI. Of these, von Willebrand disease is the most common with a prevalence of 1% to 2% in some populations. (353, Table 22-3)

38. Hereditary coagulation disorders are treated with a specific factor concentrate or cryoprecipitate, as needed. Replacement therapy should aim to achieve 50% to 100% of normal factor levels perioperatively until wound healing is complete. (353-354)

39. Von Willebrand factor is stored in platelets. (354)

40. Von Willebrand factor has three important hemostatic functions. First, it mediates adhesion of platelets to the damaged vessel wall, or the subendothelium. Second, it is important in the adhesion of platelets to each other (platelet aggregation). Finally, it protects factor VIII from inactivation and clearance. (354)

41. Fibrin formation requires sufficient levels of factor VIII. If factor VIII levels are low (e.g., hemophilia A), fibrin formation is impaired. Von Willebrand factor protects factor VIII levels from clearance and thus factor VIII levels are low in certain forms of von Willebrand disease. (354)

42. Quantitative or qualitative deficits in von Willebrand factor results in dysfunctional platelet adhesion, dysfunctional platelet aggregation, and insufficient levels of factor VIII. The clinical effects of von Willebrand disease therefore are defective platelet plug formation and defective fibrin formation. (354)

43. Von Willebrand disease can be distinguished from factor VIII deficiency through the evaluation of the results of a bleeding time electrophoresis of von Willebrand antigens, ristocetin cofactor, or platelet function analysis tests. (355)

44. There are three types of von Willebrand disease. Type 1 is an insufficient quantity of von Willebrand factor. This type of von Willebrand disease is the most common, accounting for 70% to 80% of von Willebrands disease. Type 1 von Willebrand disease is associated with a decrease in factor VIII levels by 5% to 30%. Type 2 applies when there is a defect in the quality of von Willebrand factor. Type 3, which is rare, is when von Willebrand factor is absent entirely. Types 1 and 2 are autosomal dominant, while type 3 is autosomal recessive. (354, Table 22-4)

45. To most appropriately manage a surgical patient with von Willebrand disease, the type of disease must be determined. If necessary, a hematology consult should be obtained. Bleeding in the presence of von Willebrand disease can be treated with DDAVP, with the exception of type 3 and type 2B. Type 3 von Willebrand disease requires von Willebrand factor and factor VIII concentrates, as well as a platelet transfusion. In type 2B von Willebrand disease, DDAVP is actually contraindicated

because of transient thrombocytopenia after its administration. If the patient has a type of von Willebrand disease that should respond to DDAVP, the dose that should be administered is 0.3 μg/kg 1 hour before incision. (355)

46. DDAVP should be administered very cautiously or not at all to patients with unstable coronary artery disease. When DDAVP is administered, there can be an increase in platelet aggregation at sites of high shear stress, such as at coronary narrowing. This can precipitate platelet plug formation and thus increase the risk for myocardial infarction in these patients. (355)

47. There are alternative treatment options of patients with von Willebrand disease if DDAVP is not available. These include cryoprecipitate and intermediate purity concentrates of factor VIII. Cryoprecipitate contains large amounts of von Willebrand factor and factor VIII, both of which are low in patients with von Willebrand disease. Intermediate purity concentrates of factor VIII used for the treatment of hemophilia A should also work, since these contain large amounts of von Willebrand factor. High purity (recombinant) factor VIII preparations that do not contain von Willebrand factor are not useful. (355)

48. Vitamin K is a cofactor in an enzymatic reaction necessary for the production of certain coagulation factors. (355)

49. Factors II, VII, IX, and X, as well as protein C and protein S are vitamin K dependent coagulation factors. (355)

50. If intestinal absorption is impaired (ileitis, celiac disease, etc.) or bacterial production of vitamin K is decreased (antibiotic therapy), or both of these circumstances are present, vitamin K deficiency could develop. (355)

51. Factor VIII is made in lung endothelial cells. All other coagulation factors are synthesized in the liver. (355)

52. Decreased coagulation factor levels, increased fibrinolysis (liver degrades plasmin), and splenic platelet sequestration in patients with portal hypertension can all contribute to the increased risk of bleeding in patients with severe liver disease. (355)

53. There are several diseases or conditions that are associated with acquired antibodies to coagulation factor VIII. Patients with hemophilia A (factor VIII deficiency), who have undergone longstanding factor VIII replacement, occasionally develop antibodies against that factor. Also, rheumatoid arthritis, ulcerative colitis, and old age have all been associated with antibodies against factor VIII. Clinically, these patients may have severe bleeding after minor injury. (355)

54. Some causes of peripheral platelet destruction include viral infections, chronic lymphocytic leukemia, lymphoma, colon cancer, collagen vascular disease, multiple blood transfusions, and drugs such as heparin, quinine, quinidine, digitoxin, and thiazides. (355, Table 22-5)

55. Some causes of thrombocytopenia that can occur during pregnancy include gestational thrombocytopenia, preeclampsia, and HELLP syndrome. (355)

56. Normally about one third of platelets are sequestered in the spleen, where they remain until times of vascular stress when they are released into the circulation. During pathologic splenic sequestration states, the spleen does not release platelets into the circulation, and splenomegaly and thrombocytopenia result. (355-356)

57. There are a number of situations in which the number of platelets may be adequate, but they are defective such that there is an increased risk of bleeding. Impaired platelet function can be seen in uremia, and in the presence of some drugs such as aspirin, nonsteroidal antiinflammatory agents, and alcohol. Platelet function is also impaired when there are high levels of circulating fibrin-fibrinogen split products, as can occur with severe liver disease, in disseminated intravascular coagulation, and with therapeutically induced fibrinolysis such as with the

treatment with urokinase. Platelet dysfunction also occurs in conditions in which there are high levels of abnormal serum proteins, such as multiple myeloma, dysproteinemias, or transfused dextran infusions. (356)

58. Some intraoperative conditions that may facilitate bleeding include hypothermia, acidosis, anemia, and hemodilution. (356)

59. Hypothermia with temperatures of 34° C or less is associated with poor platelet function and decreased procoagulant activity. (356)

60. Anemia and hemodilution can both cause a coagulopathy. Increasing anemia results in decreasing plasma viscosity. The formation and strength of hemostatic plugs are impaired in the presence of low plasma viscosity. Aggressive intravenous fluid resuscitation can dilute plasma coagulation factors and platelet numbers below amounts needed for effective hemostasis. (355)

DISORDERS FAVORING THROMBOSIS

61. Some factor deficiencies that are inherited can lead to a hypercoagulable state. These may include antithrombin, protein C, protein S, or factor V. Inheritance of these deficiencies may lead to deep vein thrombosis and pulmonary embolism. (356)

62. Factor V Leiden is a disease in which factor V has qualitative abnormalities. The patients are resistant to activated protein C. Normally protein C activated by thrombin, in the presence of thrombomodulin, inactivates factor V, limiting thrombin production. Therefore patients with factor V Leiden are somewhat hypercoagulable and are prone to thrombosis. (356)

63. Antiphospholipid syndrome is a heterogeneous group of syndromes that manifests as venous and arterial microvascular thromboses. Antiphospholipid syndrome describes an autoimmune production of antibodies against phospholipids in cell membranes. When antiphospholipid syndrome occurs in isolation, it is called primary antiphospholipid syndrome. Antiphospholipid syndrome most commonly occurs in conjunction with another autoimmune disease. (356)

64. Lupus anticoagulant is a type of phospholipids antibody. About 5% to 10% of patients with systemic lupus erythematosus have lupus anticoagulant. These patients are at an increased risk for perioperative thromboses. (356)

65. In patients with lupus anticoagulant the partial thromboplastin time is prolonged and the prothrombin time is normal to slightly prolonged. This would suggest that a bleeding disorder is present (lupus anticoagulant) when, in fact, the patient is prone to thrombosis. (356)

66. Virchow triad is the combination of venous stasis, hypercoagulability, and vascular damage. All of these conditions are typically present in the perioperative period. (356)

67. Disseminated intravascular coagulation (DIC) is an acquired disorder characterized by uncontrolled intravascular coagulation and fibrinolysis with bleeding and thrombosis. Generalized intravascular thrombin generation and fibrin deposition in small blood vessels lead to the formation of microvascular thrombi. Tissue hypoxia and multiorgan failure follow. Normal regulatory control of thrombin and plasmin is impaired, thereby allowing these proteolytic enzymes to activate and consume circulating coagulation factors, fibrinogen, and platelets. (356)

68. The laboratory findings in DIC reflect the pathophysiology of the condition, which is the concurrence of thrombus formation and fibrinolysis with consumption of coagulation factors. The combination of a decreased platelet count, decreased fibrinogen, prolonged PT and PTT, and elevated fibrin degradation products or D-dimers is present in DIC. Once elevated, D-dimers remain increased for days, thus making serial test measurements more sensitive and specific than single measurements. (356)

69. Both fibrin degradation products and D-dimers are elevated with trauma or recent surgery, and with liver and kidney disease. Coagulation test results in patients with severe liver disease may be similar to those in patients with DIC, although D-dimer levels may not be as high and platelet counts not as low. Factor VIII activity is helpful in discriminating between these conditions because factor VIII is consumed in DIC and factor VIII levels are normal or elevated in liver disease. (356-357)

70. The most definitive treatment of DIC is removal of the stimulus causing DIC. Other treatment of DIC is a matter of controversy. Generally, treatment is supportive with replacement of factors and platelets as needed. This has previously been contested as "fueling the fire" but there is no evidence that factor replacement worsens DIC and common sense dictates that replacement of consumed products is necessary to minimize bleeding complications. Heparin has been suggested as a treatment option with the rationale that DIC, when primarily caused by uncontrolled coagulation, may be halted when coagulation is inhibited. This approach is also currently not supported by clinical evidence. (357)

ANTICOAGULANTS, THROMBOLYTICS, AND ANTIPLATELET DRUGS

71. Perioperative thrombotic events include deep vein thrombosis, pulmonary embolism, stroke, and myocardial infarction. (357)

72. Generally, drugs against perioperative thrombotic complications either prevent (anticoagulants, antiplatelet drugs) or treat (thrombolytics) thrombus formation. Since venous thrombosis starts with activation of the coagulation cascade, it seems logical to aim to prevent thrombus formation by inhibiting some aspect of the coagulation system with anticoagulants. Since arterial thrombus formation starts with platelet adhesion, it seems logical to primarily target that process with antiplatelet drugs. (357)

73. Anticoagulants in clinical use include heparin, LMWH parin, fondaparinux, warfarin, direct thrombin inhibitors, and a recently FDA-approved oral direct thrombin inhibitor. These drugs could potentially replace warfarin as oral anticoagulants. (357)

74. Warfarin is a vitamin K antagonist. Warfarin exerts its effect through the inhibition of an enzyme that recycles vitamin K (vitamin K epoxide reductase). Warfarin thus causes a state similar to vitamin K deficiency. (357)

75. Initiation of the anticoagulant and antithrombotic effects of warfarin depends on the plasma factor VII concentration because factor VII has the shortest half-life (3 to 6 hours). Several factor half-lives are required to deplete factor VII to the 20% to 30% level needed for effective anticoagulation. Therefore, despite oral warfarin reaching effective plasma concentrations in 90 minutes, full anticoagulant efficacy does not develop until several days later. (357)

76. Heparin coadministration during the first 5 days of warfarin therapy is necessary for two reasons. First, the anticoagulant activity of warfarin does not develop for several days. Second, since the plasma half-life of protein C is only 6 to 10 hours, a hypercoagulable state due to uninhibited thrombin formation can initially develop when warfarin therapy is commenced. This is prevented by heparin coadministration. (357)

77. Warfarin therapy is monitored with the measurement of the prothrombin time (INR). Warfarin has a very narrow therapeutic window between bleeding and the prevention or treatment of thrombosis. In addition, drugs, foods, and alcohol can profoundly alter the pharmacokinetic profile of warfarin. Therefore, it is necessary to monitor warfarin therapy. This is in contrast to the more modern anticoagulants such as oral direct thrombin inhibitors, which require no monitoring. (357)

78. Some advantages of unfractionated heparin therapy over low LMWH or pentasaccharide (fondaparinux) drugs include its immediate onset, efficacy against

thrombin, short half-time of 30 to 60 minutes, and reversibility with protamine. These characteristics of heparin therapy make it more useful for administration intraoperatively than LMWH or fondaparinux. (357)

79. Unfractionated heparin therapy needs to be closely monitored because of its unpredictable pharmacokinetics. Heparin binds to plasma proteins, macrophages, endothelial cells, and proteins released from activated platelets and endothelial cells. This variation in the available free heparin in plasma makes its necessary to monitor heparin therapy with laboratory tests. (357)

80. Unfractionated heparin has unpredictable pharmacokinetics caused by heparin binding to plasma proteins, macrophages, endothelial cells, and proteins released from activated platelets and endothelial cells. These properties are a function of the saccharide chain length, which is greater for unfractionated heparin than for LMWH or pentasaccharide drugs. Therefore these shorter drug preparations do not require monitoring with partial thromboplastin time. (357)

81. The efficacy of unfractionated heparin is monitored using the partial thromboplastin time. Heparin given intraoperatively can be monitored through measurement of the ACT. (357)

82. Cardiac surgery, vascular surgery, and percutaneous interventional procedures such as neuroangiography and cardiac arrhythmic tract ablations are some procedures in which heparin is administered to prevent clotting. The degree of anticoagulation required with heparin varies in these procedures. In cardiac surgery, heparin is administered to achieve a level of anticoagulation that would allow cannulation for cardiopulmonary bypass without risking clot formation in the bypass circuit. To achieve this level of anticoagulation 300 to 400 U/kg of unfractionated heparin is usually required, and the goal for treatment usually requires an ACT of greater than 400 seconds. Most vascular and percutaneous procedures require lower levels of heparin anticoagulation; for these procedures the goal is to achieve an ACT of twice baseline or less. (357)

83. Heparin anticoagulation during surgery is reversed through the administration of protamine. The dose of protamine for this purpose is 1 mg for every 100 units of heparin that has been administered. Protamine binds to heparin and reverses its effect. (357)

84. A negative effect of protamine is its potential to cause a significant histamine release manifested as bronchoconstriction, and a decrease in systemic vascular resistance resulting in hypotension. Protamine administration can also cause pulmonary hypertension. The pulmonary hypertension that can result from the administration of protamine can be severe in rare cases. (357-358)

85. Heparin-induced thrombocytopenia and osteopenia are two potential side effects of the administration of heparin that are directly related to the number of saccharide residues and therefore occur with lower frequency or not at all with LMWH or pentasaccharide drugs. (358)

86. HIT is characterized by a decrease in platelet count after initiation of heparin therapy. HIT type 1 is not mediated by immunoglobulin G (IgG), is self-limited, and does not require intervention. HIT type 2 is the most feared nonhemorrhagic complication of heparin treatment and is usually due to antiplatelet factor 4 antibodies causing platelet aggregation. (358, Table 22-6)

87. HIT type 2 is a clinical diagnosis, which requires a decrease in the platelet count to less than 100,000 cells/μL or less than 50% of baseline 5 to 10 days after the initiation of heparin therapy. There is a recovery of the platelet count after discontinuation of heparin. Heparin-platelet factor 4 antibody testing confirms the diagnosis. (358)

88. HIT type 2 occurs with an incidence of 1% to 3% among patients treated with heparin. The mortality rate for patients with HIT type 2 is 20% to 30%. (358)

89. Heparin-induced thrombocytopenia type 1 does not require any special therapeutic intervention, since the condition is self-limiting. Heparin-induced thrombocytopenia type 2 requires cessation of all heparin, including heparin flushes or heparin-coated central venous catheters. An alternative form of anticoagulation must be sought (e.g., direct thrombin inhibitors). (358)

90. Heparin resistance is present when the usual heparin doses do not result in adequate prolongation of the partial thromboplastin time or ACT. Insufficient antithrombin or excessive heparin-binding proteins (factor VIII, fibrinogen, and other acute-phase proteins) are thought to be the cause. (358)

91. Heparin resistance can be treated initially with additional doses of heparin. If insufficient anticoagulation persists after the administration of additional heparin, fresh frozen plasma may be used in an attempt to increase plasma concentrations of antithrombin. (358)

92. LMWH and pentasaccharide drugs, unlike unfractionated heparin, do not directly inhibit thrombin. Eighteen saccharide subunits (pentasaccharide plus 13 additional subunits) are required to bridge the gap between antithrombin and thrombin. LMWH, by definition, is any heparin molecule that does not have the sufficient saccharide chain length to inhibit thrombin. (358)

93. Any drug containing the pentasaccharide subunit that is shared by unfractionated heparin, LMWH, and pentasaccharide binds antithrombin. Antithrombin inhibits factor Xa, regardless of its activity against thrombin. This confers the anticoagulant efficacy of LMWH and pentasaccharide. (358)

94. LMWH and pentasaccharide drugs have a slower onset time (20 to 60 minutes) but a longer half-time than heparin. This allows for once or twice a day administration and it can be administered subcutaneously. In addition, the predictable pharmacokinetics of LMWH and pentasaccharide drugs makes laboratory monitoring of its efficacy unnecessary. Thus, these drugs are easier to manage on an outpatient basis. LMWH and pentasaccharide drugs also have lower to nonexistent risks of osteopenia and heparin-induced thrombocytopenia. One disadvantage of LMWH and pentasaccharide drugs is that they have an increased risk of bleeding complications when compared to unfractionated heparin. Another disadvantage is the inability to reverse the effects of these drugs with protamine. (358)

95. There are three intravenous direct thrombin inhibitor drugs in current clinical use. These are hirudin, argatroban, and bivalirudin. There is also one oral direct thrombin inhibitor drug, dabigatran, which was FDA approved in October of 2010 for the treatment of atrial fibrillation. (358)

96. Compared to unfractionated heparin at equipotent doses, direct thrombin inhibitors are associated with an exceedingly high risk of bleeding. In addition, no reversal agent exists for this group of drugs. (358-359)

97. If systemic anticoagulation is required in a patient with a recent history of HIT type 2, the surgery could be delayed until such time as the antiplatelet factor 4 antibodies, which are thought to be responsible for the thrombotic complications of HIT type 2, have disappeared. This will usually take 3 to 4 months. If that is considered unacceptably long, plasmapheresis can be used in an attempt to eliminate the antiplatelet factor 4 antibodies. (359)

98. Thrombolytic drugs currently used in clinical practice include streptokinase and urokinase, alteplase, and tenecteplase. Streptokinase and urokinase are native tissue plasminogen activators, while alteplase and tenecteplase are exogenous tissue plasma activators. (359)

99. The mechanism of action of thrombolytic drugs is through the activation of plasmin. Exogenous tissue plasminogen activators are more fibrin sensitive. All tissue plasminogen activators are both thrombolytics and anticoagulants since fibrinolysis generates increased amounts of circulating fibrin degradation products. This inhibits platelet aggregation. (359)

100. Surgery or puncture of noncompressible vessels is contraindicated within a 10-day period after the administration of thrombolytic drugs. (359)

101. Antiplatelet drugs are classified by their mechanism of action, such as cyclooxygenase inhibitors, thienopyridine derivates, and GPIIb/IIIa antagonists. Cyclooxygenase inhibitors include nonselective inhibitors such as aspirin or nonsteroidal antiinflammatory drugs, such as ibuprofen, diclofenac, and naproxen. Selective cyclooxygenase-2 inhibitors include valdecoxib and celecoxib. Examples of thienopyridine derivatives are ticlopidine and clopidogrel. Examples of GPIIb/IIIa antagonists are abciximab, eptifibatide, and tirofiban. (359)

102. Aspirin inhibits platelet granule release irreversibly for the life of the platelet. Platelet function recovers by means of replacing inhibited platelets with newly generated and thus functional platelets. Nonsteroidal antiinflammatory drugs reversibly inhibit platelets with return of normal platelet function within 3 days after drug administration. Cyclooxygenase-2 inhibitors do not affect platelet function. (359)

103. The thienopyridine derivatives clopidogrel and ticlopidine inhibit the binding of platelets to fibrinogen. This results in an inhibition of platelet aggregation. (359)

104. Platelet functions normalize 7 days after discontinuing clopidogrel, and 14 to 21 days after discontinuing ticlopidine. (359)

105. The platelet GPIIb/IIIa receptor mediates platelet aggregation by allowing the binding of platelets to fibrinogen or von Willebrand factor. GPIIb/IIIa antagonists are therefore potent inhibitors of platelet aggregation. (359)

106. Platelet aggregation normalizes 8 hours after discontinuing eptifibatide and tirofiban, and 24 to 48 hours after discontinuing abciximab. (359)

AN APPROACH TO PATIENTS WHO ARE ANTICOAGULATED

107. Patients on warfarin undergoing surgery are challenging to manage perioperatively. On the one hand, the anticoagulant could predispose to bleeding complications if it is not discontinued far enough in advance of the surgery. On the other hand, when the anticoagulant is discontinued, it adds to the overall risk of thrombotic complications, which can have devastating consequences. The risk of bleeding is a function of reversal of the drug effect with time, which is assessed by the INR. The risk for a thrombotic complication after stopping warfarin therapy depends on the surgical procedure, the original indication for warfarin therapy, and the degree of the rebound hypercoagulable state associated with warfarin cessation. This risk is assessed jointly by a multidisciplinary team. (359)

108. Major abdominal and cardiothoracic procedures generally carry the highest risk of perioperative thrombosis. (359)

109. Patients on chronic warfarin therapy who have had a venous thrombotic or arterial embolic event within a month before surgery, or who have mitral or cage valve prosthesis are at a high risk of perioperative thrombosis regardless of the type of surgery. (359, Figure 22-2)

110. Patients on chronic warfarin therapy who have had a venous thrombosis less than 2 to 3 months prior, with atrial fibrillation with a history of prior

embolism or with recurrent venous thrombosis, are at an intermediate risk of perioperative thrombosis regardless of the type of surgery. (360, Figure 22-2)

111. Patients on chronic warfarin therapy who have atrial fibrillation without a history of prior embolism, or who have a valve prosthesis other than mitral or cage prosthesis, are at a low risk of perioperative thrombosis regardless of the type of surgery. (360, Figure 22-2)

112. It is important to stratify the risk of perioperative thrombosis for patients on chronic warfarin therapy because patients must be managed differently with regard to anticoagulation in the perioperative period based on their risk of thrombosis. (359, Figure 22-2)

113. Patients on chronic warfarin therapy at high risk for a perioperative thrombosis should be managed differently with regard to anticoagulation in the perioperative period than those at a low or intermediate risk of thrombosis. In either case, the warfarin is discontinued 5 days before surgery. However, patients at a high risk for thrombosis receive an intravenous unfractionated heparin infusion that is closely monitored as an inpatient. All others can receive bridging therapy as an outpatient using either LMWH or pentasaccharide. Postoperative anticoagulation starts 12 hours after hemostasis has been achieved in either case, but high-risk patients receive either an intravenous infusion of unfractionated heparin or LMWH, or pentasaccharide for a full 5 days while warfarin therapy is reinitiated early and as an inpatient. Patients with intermediate or low risk for thrombosis can be treated with subcutaneously injected unfractionated heparin, LMWH, or pentasaccharide as an outpatient and warfarin can be recommenced electively. (359-360, Figure 22-2)

114. In a patient receiving perioperative heparin bridging therapy for warfarin treatment, the intravenous heparin infusion is discontinued 6 hours prior to surgery and should not be restarted before 12 hours after hemostasis is achieved. (359)

115. In a patient receiving perioperative LMWH bridging therapy for warfarin treatment, LMWH is discontinued 12 hours before surgery and restarted 12 hours after hemostasis is achieved. (359)

116. Patients with a high likelihood of perioperative bleeding should likely not be administered heparin in the perioperative period. This may include patients with thrombocytopenia or concurrent antiplatelet therapy, or patients with a history of bleeding in the gastrointestinal, genitourinary, or central nervous system. (359-360)

117. For the emergency surgical patient on chronic warfarin therapy, the administration of fresh frozen plasma or prothrombin complex concentrate will restore the concentration of vitamin K dependent coagulation factors, and thus reverse the effects of warfarin. Vitamin K dependent coagulation factors are quickly restored with these products. (360)

118. The administration of oral vitamin K should be considered for the emergency patient on chronic warfarin therapy who is receiving fresh frozen plasma or prothrombin complex to reverse the effects of warfarin because of the half-life of these products. The restoration of vitamin K dependent coagulation factors by transfusion of these products is immediate, but the duration of the effect is only 4 to 6 hours. Thus oral vitamin K at a dose of 1 mg should be administered concomitantly. (360)

119. Vitamin K is administered at 1 mg orally in addition to intravenous infusions of fresh frozen plasma or prothrombin complex concentrate in patients on warfarin that require emergency surgery. The subcutaneous or intramuscular

routes can have prolonged action and can make postoperative warfarin therapy challenging. Intravenous vitamin K is associated with a greater risk of anaphylaxis. (360)

AN APPROACH TO PATIENTS RECEIVING ANTIPLATELET THERAPY

120. Patients with bare metal coronary stents require antiplatelet therapy for at least 4 months after stent placement. (360)

121. Patients with drug-eluting coronary stents require antiplatelet therapy for at least 12 months after stent placement. (360)

122. Drug-eluting coronary stents are designed to retard intimal hyperplasia, but in so doing they also delay the formation of an antithrombotic intimal layer. The intimal layer forms very slowly in the area of the drug-eluting stent, and this intimal layer confers the anticoagulant property of the vessels. Hence patients with drug-eluting coronary stents are at much greater risk for perioperative myocardial infarctions when the antiplatelet therapy is stopped than those with bare metal coronary stents. (360-361)

123. Patients with coronary stents that require antiplatelet therapy should have their elective surgical procedure postponed until the antiplatelet therapy is no longer recommended. In cases in which the surgery cannot be postponed, the risks of bleeding and thrombosis need to be carefully weighed often by a multidisciplinary approach including the cardiologist, surgeon, and anesthesiologist. If the risk of thrombosis is high, bridging therapy with a short-acting antiplatelet agent may be indicated. (361, Figure 22-3)

NEURAXIAL INTERVENTIONS IN PATIENTS BEING TREATED WITH ANTICOAGULANT DRUGS

124. There is a risk of bleeding and neurologic injury in patients who are undergoing neuraxial interventions while receiving anticoagulant drug therapy. The management of these patients should be guided by the recommendations of the American Society of Regional Anesthesia, who have provided algorithms for management for each type of anticoagulant drug. (361, Table 22-7)

AN INTRAOPERATIVE APPROACH TO UNCONTROLLED BLEEDING

125. In the absence of laboratory testing during the massive transfusion of packed red blood cells, fresh frozen plasma is generally indicated after the replacement of about one blood volume. Platelets are generally indicated after the replacement of about two blood volumes. (361)

126. During ongoing blood loss, a prothrombin time of 1.5 times the normal range or greater would indicate the need for the replacement of coagulation factors with fresh frozen plasma. (361)

127. During ongoing blood loss, a platelet count lower than 50,000 to 80,000 cells/μL would indicate the need for the replacement of platelets with a transfusion of concentrated platelets. (361-362)

128. During ongoing blood loss, a fibrinogen level of less than 125 mg/dL would indicate the need for a transfusion of cryoprecipitate. Cryoprecipitate (one concentrate per 10 kg of body weight) can be used to augment fibrinogen. However, each fresh frozen plasma and platelet pheresis unit has approximately twice the amount of fibrinogen contained in one cryoprecipitate concentrate. (362)

129. An indication for the transfusion of cryoprecipitate would be to treat a low fibrinogen level in small children. Also, a cryoprecipitate transfusion is appropriate when factor VIII or von Willebrand factor needs to be replaced specifically. (362)

130. Recombinant factor VIIa has been designed and licensed for the treatment of bleeding in hemophilia patients. It has also been used off-label in patients with life-threatening, uncontrolled intraoperative bleeding unresponsive to conventional therapy. It is of unproven benefit and extremely expensive. (363)

131. Other hemostatic drugs used perioperatively include DDAVP and the lysine analogs antifibrinolytics, ε-aminocaproic acid and tranexamic acid. DDAVP (0.3 μg/kg IV) releases von Willebrand factor from endothelial cells and the lysine analogues inhibit fibrinolysis. (362)

132. DDAVP has proven useful for the prevention of bleeding in some forms of von Willebrand disease. It is also useful in mild forms of factor VIII deficiency and for bleeding associated with uremia. (362)

Chapter

20 FLUID MANAGEMENT

Charles J. Fox, Henry Liu, Alan David Kaye

OVERVIEW OF FLUID AND ELECTROLYTE PHYSIOLOGY

1. What is the goal of perioperative fluid management?
2. What percentage of body weight is represented by water?
3. In what two compartments is total body water found?
4. What percentage of extracellular fluid volume is occupied by plasma volume? What are the other constituents of extracellular fluid?
5. How does plasma differ from other components of extracellular fluid?
6. What are the major sources of daily water loss? How does temperature affect daily water loss?
7. What body compartment has the highest concentration of potassium? What electrolytes are found in plasma?
8. Which source produces the greatest volume of gastrointestinal fluid? Which source of gastrointestinal fluid contains the highest concentration of bicarbonate?

FLUID REPLACEMENT SOLUTIONS

9. What are the daily water, potassium, and sodium requirements for the average adult?
10. How are crystalloids grouped? How do crystalloid solutions distribute?
11. What is the composition of a balanced salt solution?
12. What occurs when normal saline is used in large volumes?
13. What group of patients routinely receives normal saline during surgery? Why?
14. What is the sodium concentration of hypertonic saline? What are the potential benefits of hypertonic saline?
15. What is the advantage of using 5% dextrose water instead of pure water? What are the clinical indications for use of 5% dextrose water?
16. What are colloids? How should colloids be used to correct blood loss in clinical practice?
17. What are the differences between 5% albumin and 25% albumin?
18. What is dextran? What is the indication for its intravenous administration?
19. What are hydroxyethyl starches?
20. What are some potential adverse effects of using hydroxyethyl starches or dextran for volume replacement?
21. What are the arguments for crystalloids versus colloids for perioperative fluid replacement?

PERIOPERATIVE FLUID STRATEGIES

22. What is the 4-2-1 rule of perioperative fluid management?
23. What is compensatory intravenous volume expansion?
24. How is fluid deficit corrected?
25. How is blood loss replaced clinically?

26. What is "third-space loss of fluid"? What is used to replace it?
27. Why might the traditional fluid management strategy cause problems? How might one restrict the fluid administration?

ANSWERS*

OVERVIEW OF FLUID AND ELECTROLYTE PHYSIOLOGY

1. Proper perioperative fluid management requires knowledge of the patients' surgical procedure, their preexisting disease states, and the physiologic effects of the anesthetic plan. Balancing these three factors will allow the anesthesiologist to maintain the patient's intravascular volume, cardiac preload, oxygen-carrying capacity, coagulation status, electrolyte balance, and acid-base homeostasis. (364)
2. Total body water represents approximately 60% of the body's total weight in the average adult. The relative percentage of body water can vary depending on age, gender, and adiposity. The average 70 kg man contains approximately 600 mL/kg or 40 L of total body water. (364)
3. Total body water is found in the intracellular and extracellular compartments. The intracellular fluid volume averages 400 to 450 mL/kg and the extracellular fluid volume averages 150 to 200 mL/kg. (364)
4. The two main components of the extracellular compartment are blood volume, which averages 60 to 65 mL/kg, and the interstitial fluid volume, which averages 120 to 165 mL/kg. The other constituents of extracellular fluid include pleural fluid, peritoneal fluid, aqueous humor, sweat, urine, lymph, and cerebrospinal fluid. (364-365)
5. The difference between plasma and other components of extracellular fluid is the protein count. Plasma contains a much higher concentration of protein, which results in a much higher plasma oncotic pressure. This oncotic gradient between the plasma and interstitial fluid helps maintain intravascular volume. (364-365)
6. The major sources of daily water loss under normal activity and temperature are urine, sweat, feces, and insensible losses. The average 70 kg man loses approximately 2300 mL of water per day. The majority of this water loss is from urine (1400 mL/day) and insensible losses (700 mL/day). However, when body temperature is increased, daily water loss increases to 3300 mL/day, largely due to the increase in water loss from sweating (1400 mL/day). (Table 23-1, 365)
7. Potassium concentration is highest in intracellular fluid, which contains 150 mEq/L. Plasma contains 4 mEq/L of electrolytes, while extracellular fluid is responsible for 4.5 mEq/L. (Table 23-2, 365)
8. A normal adult produces about 6000 to 8000 mL of gastrointestinal fluid per day. The stomach and ileum can each generate up to 2000 mL/day of gastrointestinal fluid; however, the jejunum may produce the greatest volume of gastrointestinal fluid (4000 mL/day). The gastrointestinal fluid generated by the pancreas contains the highest concentration of bicarbonate (95 to 120 mEq/L). (Table 23-3, 365)

FLUID REPLACEMENT SOLUTIONS

9. The average adult needs 1.5 to 2.5 L of water, 50 to 100 mEq of sodium, and 40 to 80 mEq of potassium daily. (365)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

10. Crystalloids are fluids that contain water and electrolytes. They are grouped as balanced, hypertonic, and hypotonic salt solutions. Crystalloid fluids distribute freely between the intravascular and interstitial compartments. Approximately one third of intravenously administered crystalloid remains intravascular. (365-366)

11. The most common balanced salt solutions used are lactated Ringer solution, Plasma-lyte, and Normosol. All balanced salt solutions have a composition similar to ECF. Their sodium concentrations are considered hypotonic and a buffer is present that takes the place of bicarbonate. (366)

12. Normal saline (0.9% NaCl) is isotonic, but contains more chloride than ECF. It contains no other electrolytes or buffer. Large scale fluid replacement with normal saline results in a nonanion gap metabolic acidosis. (366)

13. Normal saline is commonly used in patients with chronic renal failure. Their inability to excrete potassium makes normal saline a popular crystalloid choice. (366)

14. Hypertonic salt solutions contain 250 to 1200 mEq/L of sodium. The higher the sodium concentration, the less volume is needed for resuscitation because hypertonic salt solutions osmotically shift fluid from the intracellular space to the extracellular space. The reduced volume needed may reduce tissue edema. This may prove beneficial for those patients experiencing prolonged bowel surgery, burns, or brain injuries. (367)

15. Five percent dextrose water (D_5W) is considered a free water solution because the dextrose is metabolized. It is considered iso-osmotic and does not cause hemolysis. Hemolysis results when pure water is infused intravascularly. D_5W is commonly used to prevent hypoglycemia in diabetic patients taking insulin in the perioperative period. Also, it is used as a treatment for hypernatremia. (367)

16. Colloids are the fluids containing large molecules, which usually do not cross capillary membranes and remain in the intravascular space. Commonly used colloids are albumin, hydroxyethyl starch (hetastarch), and dextran. When used to correct the perioperative blood loss, colloids are generally administered in a volume equivalent to the volume of blood loss. Colloids are distributed entirely intravascularly, so the initial volume is equivalent to plasma volume. The half-life of albumin in circulation is 16 hours, but it can be as short as 2 to 3 hours. (367-368)

17. Albumin solutions are commercially available mostly in 5% and 25%. Five percent albumin is also called plasma protein fractions, which has an osmotic pressure around 20 mmHg (as plasma colloid osmotic pressure). Twenty-five percent albumin has five times the normal concentration and expands blood volume by five times after intravenous administration. Infectious agents are eliminated during the preparation process for all albumin solutions. (367)

18. Dextran is commercially available in Dextran 40 and Dextran 70, which indicate their mean molecule weight 40,000 Da and 70,000 Da, respectively. Dextran solutions are water-soluble glucose-polymers that are synthesized by certain bacteria and degraded enzymatically to glucose. Six percent Dextran 70 is administered for the same indications as 5% albumin (temporary volume expansion). However, Dextran 40 is administered for vascular surgery to prevent thrombosis and is rarely used to expand volume. (367)

19. Hydroxyethyl starches (HES) are synthetic colloid solutions and are characterized by their concentration, molar substitution, and molecular weight. Solutions with higher molar substitution and molecular weight hydroxyethyl starches usually have a more prolonged volume effect, but may experience more side effects. (367)

20. HES and dextran solutions are generally very safe. HES may produce coagulation disturbances and renal toxicity. HES interfere with von Willebrand factor, factor VIII, and platelet function. The effects on renal toxicity are controversial but appear

more common in older, higher-molecular-weight solutions. Dextran can potentially cause anaphylactic or anaphylactoid reactions in about 1 in every 3300 administrations, increased bleeding time caused by decreased platelet adhesiveness (at doses of 20 mL/kg/24 hours), Rouleaux formation, and noncardiogenic pulmonary edema in rare cases. (367)

21. Crystalloid solutions are effective plasma volume expanders, which are cheaper than current colloid preparations, and do not contain the transmission risks associated with colloid fluids. Also, some studies indicate that albumin enters the pulmonary interstitial compartment freely and only increases the amount of albumin cleared by lymphatics. Historically, colloids have shown no advantage over crystalloid when used for expansion on intravascular volume. Proponents of colloids argue that continued crystalloid use dilutes plasma proteins and lowers plasma oncotic pressure. This increase in interstitial fluid supports edema formation. Lastly, colloid is administered 1:1 for every milliliter of blood loss. This may lead to a more rapid restoration of filling pressure and arterial blood pressures. (367-368)

PERIOPERATIVE FLUID STRATEGIES

22. The 4-2-1 rule provides a very close approximation of the water requirement. This rule states that the first 10 kg of body weight needs 4 mL/kg/hr and the second 10 kg of body weight needs 2 mL/kg/hr. After the first 20 kg of body weight, the water requirement is 1 mL/kg/hr. For example, a 70 kg man requires 110 mL/hr of water, or 2640 mL/day.

23. Most general and regional anesthetics cause venous and arteriolar dilation, thus increasing the total vascular capacity. Fluids must be infused to fill the expanded intravascular space. If not, the patient will potentially have decreased venous return and decreased preload. This may lead to lower cardiac output and lower organ perfusion pressure. Perioperatively, administration of intravenous fluids can maintain venous return, cardiac preload, stroke volume, and cardiac output. The administration of intravenous fluids to fill the increased vascular capacity due to anesthesia is called compensatory intravenous volume expansion (CVE). CVE with 5 to 7 mL/kg of balanced salt solution is advised before or simultaneously with the onset of anesthesia. (369)

24. The fluid deficit equals the maintenance fluid requirement times the hours since last intake ("NPO deficit"), plus unreplaced preoperative external and third-space losses. If hypovolemia is present, sufficient fluid should be infused to restore filling pressures, heart rate, and arterial pressure to preinduction baseline values. Fluid deficit is corrected by infusing three to four times the maintenance rate until the calculated deficit has been corrected. Balanced salt solutions are usually the most commonly used replacement of fluid deficits. (369)

25. Each milliliter of blood loss is usually replaced with 3 mL of balanced salt solution or 0.9% sodium chloride solution, 1 mL of colloid solution, or 0.5 mL of packed red blood cells (PRBC) plus colloid or crystalloid solutions. The general principle for the replacement of external losses (e.g., blood, ascites) is to maintain normal blood volume and normal composition of the extracellular fluid volume. Hemoglobin levels of 7.5 g/dL or higher are usually well tolerated in patients with reasonable cardiac function and without compromised regional circulations. A formula used to calculate the red blood cell (RBC) volume is based on a patient's weight (kilograms), initial hematocrit, and desired hematocrit. The EBV is estimated blood volume, whose value is 55 mL/kg in an average adult woman and 70 mL/kg in an average adult man. (369)

$$\mathrm{PRBC}_{\mathrm{infused}} = (\mathrm{Hct}_{\mathrm{desired}} \times \mathrm{EBV} \times \mathrm{Weight} - \mathrm{Hct}_{\mathrm{observed}} \times \mathrm{EBV} \times \mathrm{Weight})/0.60$$

26. Third-space loss of fluid is the fluid redistributed to spaces inside the patient's body but functionally not participating in the intravascular blood circulation

(e.g., ascites, pleural effusion, and gastrointestinal tract fluid accumulation). The composition of third-space losses is usually equivalent to extracellular fluids (in regard to electrolytes) but contains a lower concentration of proteins. A balanced salt solution is the most appropriate replacement for third-space fluid losses. (369)

27. Certain surgical procedures or patient disease states may lend themselves to restricting fluid administration. For instance, in patients undergoing pulmonary surgery, the risk of postpneumonectomy pulmonary edema is directly related to the amount of fluids administered. Patients undergoing liver resection may benefit from a low central venous pressure to prevent bleeding. Patients with a history of end-stage renal disease or congestive heart failure may also benefit from restricted fluid administration. Restrictive fluid management strategies include: replacing blood loss on a milliliter per milliliter basis with colloid, not replacing urine or third-space loss during surgery, no fluid loading prior to anesthesia, colloid bolus for treatment of hypovolemia, postoperative restriction of fluids, and administration of diuretics for weight gain. (370)

Chapter

21 BLOOD THERAPY

Ronald D. Miller, Tula Gourdin

BLOOD THERAPY PROCEDURES

1. What is the recipient's blood tested for during the routine typing of blood? What is the risk of transfusing blood to patients without typing the recipient's blood?
2. How is the crossmatching of blood accomplished?
3. How does the transfusion of O-negative packed red blood cells in an emergency situation affect the patient's subsequent transfusions?
4. What does type-specific blood refer to? What is the chance of a significant hemolytic reaction with the transfusion of type-specific blood to a patient?
5. What does a type and screen refer to? When is a type and screen typically ordered? What is the chance of a significant hemolytic reaction with the transfusion of typed and screened blood to a patient?
6. What is contained in preservative solutions for the storage of blood? What is the benefit of adding adenine to the preservative solution?
7. How long can blood be stored?
8. What is the temperature at which blood is stored? Why?

DECISION TO TRANSFUSE

9. What are the considerations when deciding whether to do a blood transfusion?
10. What are the indications for the transfusion of blood?

BLOOD COMPONENTS

11. Name the components that can be derived from whole blood. What is the advantage of using components for blood therapy instead of whole blood?
12. What is the hematocrit and total volume in a unit of packed red blood cells?
13. How much will hemoglobin concentration increase with the transfusion of a single unit of packed red blood cells?
14. What is the indication for the administration of packed red blood cells?
15. What solutions may be used to reconstitute packed red blood cells for administration?
16. What potential complication associated with the administration of whole blood is less likely to occur with the administration of packed red blood cells?
17. What is the advantage of using whole blood for massive blood loss replacement?
18. What is the recommended ratio of packed red blood cells to fresh frozen plasma and platelets when transfusing for massive blood loss replacement?
19. When is the administration of platelets indicated during surgery?
20. How much will the platelet count increase after the administration of 1 unit of platelets?

21. What are some of the risks associated with the administration of platelets?
22. What is fresh frozen plasma? What is contained in fresh frozen plasma?
23. When is the administration of fresh frozen plasma indicated during surgery?
24. What is cryoprecipitate? What is contained in cryoprecipitate?
25. What is cryoprecipitate useful for treating?

COMPLICATIONS OF BLOOD THERAPY

26. Name some potential complications of blood therapy.
27. What is the risk of the transmission of infectious diseases with the transfusion of blood?
28. What are the various types of transfusion reactions that may occur with blood therapy?
29. Why are febrile transfusion reactions thought to occur? How do febrile transfusion reactions manifest?
30. How are febrile transfusion reactions treated?
31. Why are allergic transfusion reactions thought to occur? How do allergic transfusion reactions manifest?
32. How are allergic transfusion reactions treated? How are allergic transfusion reactions distinguished from hemolytic transfusion reactions?
33. Why are hemolytic transfusion reactions thought to occur?
34. What are the clinical signs that a hemolytic transfusion reaction has occurred? Which of these are masked by anesthesia?
35. What diagnostic tool provides evidence that a hemolytic transfusion reaction has occurred?
36. What are some consequences that can follow a hemolytic transfusion reaction?
37. What is the treatment for a hemolytic transfusion reaction?
38. What is transfusion-related acute lung injury (TRALI)?
39. Describe the immunosuppression that may accompany blood transfusions.
40. What are some metabolic abnormalities that may accompany blood transfusions?
41. How much does the serum potassium level increase in patients after the transfusion of blood?
42. How do concentrations of 2,3-diphosphoglycerate change with the prolonged storage of blood? How does this affect oxygen delivery to the tissues?
43. How does the administration of citrate in blood products affect the recipient's serum calcium concentration?
44. What is the potential risk of hypothermia with the administration of blood products?
45. What are some ways in which massive blood transfusions can result in coagulation disorders?
46. What is dilutional thrombocytopenia? What is the treatment of dilutional thrombocytopenia?
47. Which clotting factors may decrease in concentration in the patient's blood with massive transfusions? What percent of each of these clotting factors is necessary to maintain hemostasis during surgery? How can this clotting factor deficiency be treated?

AUTOLOGOUS BLOOD TRANSFUSIONS

48. What is the advantage of the administration of autologous blood over homologous blood for necessary blood transfusions?
49. What is an acceptable schedule for the collection of predeposited blood for autologous blood transfusion? How can anemia secondary to the donation of autologous blood be minimized?
50. What are some complications that can occur with autologous blood transfusions of predeposited blood?
51. How is the intraoperative salvage of blood for autologous blood transfusions accomplished? What are some relative contraindications to the intraoperative salvage of blood?

52. What are some complications that may accompany the intraoperative salvage of blood for autologous blood transfusions?
53. What is the hemodilution technique for autologous blood transfusions? What are some advantages of this technique?

CONCLUSIONS AND FUTURE DIRECTIONS

54. Describe some of the trends for transfusion of blood products.

ANSWERS*

BLOOD THERAPY PROCEDURES

1. Routine typing of the recipient's blood tests for the presence of A or B or both A and B antigens on the recipient's red blood cells and for the presence of anti-A or anti-B antibodies in their serum. It also tests for the presence or absence of Rh(D) antigen on the red blood cell. The purpose of typing the recipient's blood is to avoid the transfusion of incompatible blood to the recipient. This may occur if the patient has antibodies to A or B or to A and B in their serum and they are transfused red blood cells that have the corresponding antigen on the red blood cells. Likewise, if a recipient lacks the Rh(D) antigen, the transfusion of the Rh(D)+ blood would be incompatible. The risk of transfusing patients who have not had this typing done, or who have had it done incorrectly and the blood is incompatible, is a transfusion reaction. In this case, the transfusion would result in disastrous, rapid intravascular hemolysis. (372-373)
2. Crossmatching of blood is done to test for a serious transfusion reaction before the administration of the blood to the recipient. A crossmatch test is accomplished by incubating the recipient's plasma with the donor's red blood cells. There are three steps to the process, which in its entirety takes about 45 minutes to perform. The first phase is the immediate phase, in which the blood is tested for ABO compatibility at room temperature. It also tests for incompatibilities in the M, N, P, and Lewis groups. The second phase is the incubation phase, which tests for the presence of antibodies at 37° C. Albumin or a low ionic strength saline solution is added to the products of the first phase to cause the agglutination of weak or incomplete antibodies that are present. The last phase is the antiglobulin phase, in which antiglobulin is added to the products of the second phase. Incomplete antibodies in the Rh, Kell, Duffy, and Kidd systems will be detected by this step. In each phase, incompatible blood will result in agglutination during the crossmatch test. (372-373)
3. In emergency situations in which acute large blood loss requires rapid administration of blood, there may be inadequate time to perform a type-and-cross or even to wait for type-specific blood. In these situations, O-negative packed red blood cells are administered because they lack the A, B, and Rh(D) antigens. O-negative red blood cells cannot be hemolyzed by anti-A or anti-B antibodies that may be present in the patient's blood and is therefore termed the *universal donor*. After the administration of 2 units of O-negative packed red blood cells, subsequent blood transfusions may have to be continued with O-negative blood. The concern is that the transfusion of blood that is the patient's type may result in major intravascular hemolysis of donor red blood cells by increasing titers of transfused anti-A and anti-B antibodies. The risk of continued use of O-negative

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

packed red blood cells under these conditions is minor hemolysis of donor red blood cells and hyperbilirubinemia. In most centers, however, the need for O-negative blood is rare. Subsequent transfusions with the patient's own blood type is usually possible and preferred. (372-373)

4. Type-specific blood refers to blood that has only been typed for the A, B, and Rh antigens. Type-specific blood testing is merely the first phase, or the immediate phase, of the crossmatch. It requires only about 5 minutes to perform. The chance of a significant hemolytic reaction with the transfusion of type-specific blood to a patient is about 1 in 1000. Type-specific blood is most frequently transfused in emergent situations in which time does not allow for a formal crossmatch. (372-373)

5. A type and screen refers to a recipient's blood that, in addition to being typed for the A, B, and Rh antigens, has been screened for the most common antibodies. A type and screen is performed by incubating the recipient's plasma with commercially prepared type O red blood cells that contain all the antigens able to cause a hemolytic reaction. Agglutination would designate a positive antibody screen, and the recipient's serum is further tested for identification of the antibodies responsible for the agglutination. If, however, no agglutination results, the patient is said to be antibody screen negative. In a type and screen the patient's blood is not matched to a specific unit of donor blood. This allows for 1 unit of blood to be available for more than one patient. A type and screen is typically ordered for surgical procedures in which the risk of transfusion is remote. If the patient subsequently requires transfusion, the immediate phase of a crossmatch blood test is performed to exclude blood type incompatibilities before its administration to the patient. The chance of a significant hemolytic reaction with the transfusion of typed and screened blood to a patient is 1 in 10,000. (373)

6. Solutions used to preserve blood include phosphate, dextrose, and adenine. The addition of adenine to the preservative solution of blood allows red blood cells to resynthesize adenosine triphosphate. This allows red blood cells to continue to fuel their metabolic requirements and increases their survival time in storage. Phosphate acts as a buffer, and dextrose provides energy to the red blood cells. (373)

7. Blood can be stored for 21 to 35 days. The duration of the storage of blood is determined by the requirement that at least 70% of the red blood cells be viable for more than 24 hours after transfusion. (373)

8. Blood is stored at a temperature of 1° C to 6° C. This slows down the rate of glycolysis in red blood cells and increases their survival time in storage. (373)

DECISION TO TRANSFUSE

9. The decision to transfuse should be based on a combination of (1) monitoring for blood loss, (2) monitoring for inadequate perfusion and oxygenation of vital organs, and (3) monitoring for transfusion indicators, especially the hemoglobin concentration. (373)

10. The fundamental indication for the transfusion of blood is to increase the oxygen-carrying capacity of the blood. The key question is when hypovolemia exists, what type of fluid should be given? Measurement of actual blood loss and hemoglobin levels are important. Because there are no direct measures of the oxygen-carrying capacity, the hemoglobin concentration is usually the basis on which the decision to transfuse is made. Blood transfusion is almost always justified when the hemoglobin value is less than 6 g/dL and is rarely justified when the hemoglobin value is greater than 10 g/dL. Oxygen transport is maximized when the hemoglobin level is 10 g/dL, such that the transfusion of blood at hemoglobin levels above 10 g/dL may provide no further benefit to the patient. The threshold for the transfusion of blood between hemoglobin values of 6 g/dL and 10 g/dL is further modified by several factors. These include the patient's age and medical

status, the surgical procedure and the potential for ongoing losses, and the extent to which the patient's current anemia is chronic or is due to blood loss that is acute. For example, patients with coronary artery disease and who are at risk for myocardial ischemia may benefit from keeping the hemoglobin level no less than 10 g/dL, whereas a young healthy patient may not be transfused until the hemoglobin level is 6 to 7 g/dL. The decision to transfuse blood must therefore be made on an individual basis. (373-375)

BLOOD COMPONENTS

11. Components that can be derived from whole blood include packed red blood cells, platelet concentrates, fresh frozen plasma, cryoprecipitate, albumin, plasma protein fraction, leukocyte-poor blood, factor VIII, and antibody concentrates. The advantage of using components for blood therapy instead of whole blood is that a patient's specific deficiency can be directly corrected. It also allows for prolonged storage, the retention of unnecessary components for other patients who may need them, and the avoidance of transfusing unnecessary components that could potentially contain antigens or antibodies. (374-375)

12. In a given unit of packed red blood cells, the total volume is about 250 to 300 mL and the hematocrit is about 70% to 80%. (374)

13. A single unit of packed red blood cells will increase adult hemoglobin levels by about 1 g/dL. (374)

14. The administration of packed red blood cells is indicated for the treatment of anemia (i.e., hemoglobin $<$10.0 g/dL). The purpose of transfusing packed red blood cells is to augment the oxygen-carrying capacity of the blood by increasing the hemoglobin concentration. If available, whole blood may be preferred to also treat hypovolemia. (374-375)

15. Packed red blood cells can be administered either alone or reconstituted in crystalloid or colloid. Reconstitution with 50 to 100 mL of saline facilitates the administration of packed red blood cells. Crystalloid solutions that are hypotonic should not be used to reconstitute packed red blood cells. Hypotonic solutions can result in red blood cell swelling and lysis. Examples of hypotonic solutions include glucose-containing solutions and Plasmanate. The reconstitution of packed red blood cells in solutions containing calcium (e.g., lactated Ringer solution) may result in clotting. (374)

16. The potential for citrate toxicity that can result from the administration of whole blood is less likely to occur with the administration of packed red blood cells simply because there is less volume of citrate infused with each unit of packed red blood cells. (377)

17. Whole blood transfusion may be advantageous over packed red blood cell transfusion when blood losses are greater than 30% of the blood volume, or when massive, as in the case of trauma. Whole blood transfusion under these circumstances is associated with a decreased incidence of hypofibrinogenemia and possibly coagulopathies. (374-375)

18. When transfusing blood components to replace massive blood loss as in trauma, the recommended ratio is 1.5 units packed red blood cells to 1.0 unit of fresh frozen plasma, and 1.0 unit of platelets for every 6 units of packed red blood cells. (375)

19. The administration of platelets during surgery is usually indicated for platelet counts less than 50,000 cells/mm^3. Both laboratory analysis and the clinical situation must be taken into consideration. For instance, in cases of surgical trauma or in cases of bleeding in the brain, eye, or airway the transfusion of platelets at a higher number may be warranted. (375)

20. The platelet count will increase by 5000 to 10,000 cells/mm^3 after the administration of 1 unit of platelets to a 70-kg adult. (375)

21. Risks associated with the administration of platelets include the transmission of viral diseases and sensitization to the human leukocyte antigens present on the platelet cell membranes. Bacterial contamination is more likely than in any other blood product because they are stored at room temperature. Although the risk is small (1/5000 to 12,000), platelet-related sepsis should be considered in a patient who develops a fever a few hours after receiving platelet therapy. The proper diagnosis can be confused with transfusion-related lung therapy (TRALI). (375-376)

22. Fresh frozen plasma is the plasma portion of 1 unit of donated blood. The plasma is frozen within 6 hours of collection. All plasma proteins are contained in fresh frozen plasma. Included are all the coagulation factors except platelets. This includes factors V and VIII, which decrease in concentration during the storage of packed red blood cells. (375)

23. The administration of fresh frozen plasma is indicated during surgery when the prothrombin time and/or partial thromboplastin times are greater than 1.5 times normal and there is a clinical indication of the need to transfuse. Other indications include the need to reverse warfarin therapy or for the correction of known factor deficiencies. (375)

24. Cryoprecipitate is the plasma fraction that precipitates when fresh frozen plasma is thawed. Cryoprecipitate contains high concentrations of factor VIII, von Willebrand factor, factor XIII, fibrinogen, and fibronectin. (375-376)

25. Cryoprecipitate is useful for the treatment of factor VIII deficiency as in hemophilia A, von Willebrand factor deficiency, and fibrinogen deficiency (e.g., from fresh frozen plasma). The transfusion of cryoprecipitate should be considered when fibrinogen levels are less than 100 mg/dL. (375-376)

COMPLICATIONS OF BLOOD THERAPY

26. Complications of blood therapy include transfusion reactions, metabolic abnormalities, the transmission of infectious diseases, hypothermia, coagulation disorders, acute lung injury, and immunomodulation. (376-378)

27. Because of pre-transfusion interviews for identification of risky donors and the implementation of routine laboratory screening, as well as the use of volunteer instead of paid donors, the risk of transmission of infectious agents to recipients of blood is rare. For example, the risk of infectivity with hepatitis in 1980 was 1 in 10 transfusions, whereas now it is about 1 in 1.5 to 2.0 million transfusions. The risk of infectivity with HIV is now 1 in 1.8 million. Although the risk of transmission of these viruses is small, the potential for transmission still exists and must be discussed with the patient as part of informed consent for transfusion. (374-376, Table 24-2)

28. The types of transfusion reactions that may occur with blood therapy include febrile, allergic, and hemolytic transfusion reactions. (378)

29. Febrile transfusion reactions are thought to occur as a result of antibodies in the recipient's serum interacting with antigens from the donor's cells. Febrile transfusion reactions are the most frequently occurring transfusion reaction. A febrile transfusion reaction may manifest as fever, chills, headache, myalgias, nausea, and a nonproductive cough occurring after the initiation of the transfusion of blood. When a fever occurs after a transfusion has been started, a febrile transfusion reaction can be distinguished from a hemolytic transfusion reaction by evaluating the serum and the urine for hemolysis. (378)

30. Febrile transfusion reactions are treated by decreasing the rate of the infusion of blood and administering antipyretics. Persistent cases may require the termination of the blood transfusion. (378)

31. Allergic transfusion reactions are thought to occur as a result of the presence of incompatible plasma proteins in the donor blood. Allergic transfusion reactions manifest as urticaria, pruritus, and occasional facial swelling. (378)

32. The treatment of an allergic transfusion reaction is through the intravenous administration of antihistamines. There are more severe cases of allergic transfusion reactions that are anaphylactic without red blood cell destruction. Those cases are believed to be due to the transfusion of IgA to patients who are IgA deficient. In such situations the blood transfusion should be discontinued. The differentiation between allergic reactions and hemolytic reactions can be made by checking the urine and plasma for free hemoglobin. (378)

33. Hemolytic transfusion reactions are usually a result of the administration of an erroneous unit of blood to a patient. Transfused donor cells are attacked by the recipient's antibody and complement, resulting in intravascular hemolysis. As little as 10 mL of donor blood can result in a hemolytic transfusion reaction, which can be fatal. The severity of a transfusion reaction can be proportional to the volume of transfused blood. (378)

34. Clinical signs of a hemolytic transfusion reaction include fever, chills, chest pain, hypotension, nausea, flushing, dyspnea, and hemoglobinuria. All of these are masked by anesthesia except for hemoglobinuria and hypotension. (378)

35. The diagnosis of a hemolytic transfusion reaction can be made by a direct antiglobulin test and rechecking the labeling of the blood with the blood bank. Other laboratory analysis should be performed, including plasma and urine hemoglobin and bilirubin analysis. The plasma bilirubin concentration will peak at 3 to 6 hours after starting the blood transfusion. Hemoglobinuria or hemolysis in the presence of a transfusion and suspected hemolytic transfusion reaction should be treated as one until proven otherwise. (378)

36. Hemolytic transfusion reactions can result in renal failure and disseminated intravascular coagulation. (378)

37. The first step in the treatment of a hemolytic transfusion reaction is to stop the transfusion and notify the blood bank. Subsequent treatment interventions are geared toward preventing renal failure by maintaining urine output. It is believed that renal failure occurs as a result of precipitates in the renal tubules. The urine output is recommended to be maintained at about 100 mL/hr through the administration of lactated Ringer solution and mannitol and/or furosemide as necessary. The urine may also be alkalinized with bicarbonate. Laboratory analysis should be performed, including diagnostic tests of urine and plasma hemoglobin concentrations as well as baseline coagulation studies. Finally, unused blood should be sent to the blood bank along with a sample from the patient for a repeat type and crossmatch analysis. (378)

38. Transfusion-related acute lung injury (TRALI) is acute, noncardiogenic pulmonary edema associated with dyspnea and arterial hypoxemia that occurs within 6 hours of a transfusion. TRALI is the leading cause of transfusion-related deaths in the United States. If TRALI is suspected, the transfusion should be immediately stopped, the blood bank notified, and the exudative fluid from the patient's endotracheal tube can be evaluated for protein concentration. If platelets have been given, platelet-induced sepsis is part of the differential diagnosis. Standard supportive therapy is required. (376, Table 24-3)

39. A nonspecific immunosuppressive effect of homologous blood transfusions has been established. It appears that this effect is related to the volume of plasma transfused, because whole blood appears to have a greater immunosuppressive effect than packed red blood cells. Blood transfusions have a suggested correlation to an increased risk of the recurrence of tumor or decreased survival in cancer patients. Overall prognosis may be poorer and postoperative infections increased

in patients who have received blood transfusions. Removing the white blood cells from blood and platelets, or leukoreduction, is helpful. (376)

40. Metabolic abnormalities that may accompany blood transfusions include increased levels of serum hydrogen and potassium, decreased 2,3-diphosphoglycerate levels, metabolic alkalosis, and hypocalcemia. (376-377)

41. Potassium concentrations in blood stored for 21 days may be as high as 20 to 30 mEq/L. Even after the transfusion of large volumes of blood, serum potassium levels rarely increase with the transfusion of blood. This is in part because the high concentration of potassium exists in a small volume and the total potassium content is small. Nevertheless, hyperkalemia resulting from blood transfusions is occasionally reported. In most cases it was associated with large volumes of blood rapidly infused, typically given at rates greater than 120 mL/min. (377)

42. Concentrations of 2,3-diphosphoglycerate in erythrocytes decrease with the prolonged storage of blood. Decreased concentrations of 2,3-diphosphoglycerate are associated with a shift of the oxyhemoglobin dissociation curve to the left and an increase in the affinity of hemoglobin for oxygen. This could result in a decrease in the delivery of oxygen to the tissues. This effect of a decrease in 2,3-diphosphoglycerate could be further compounded by the presence of acidosis and hypothermia. Although of concern for the effect on oxygen delivery to the tissues, there appears to be little clinical consequence of the decreased level of 2,3-diphosphoglycerate. (377)

43. The infusion of citrate preservative during the transfusion of blood can result in a metabolic alkalosis and hypocalcemia. The theory is that the metabolic alkalosis results from the metabolism of citrate in the liver to bicarbonate. Hypocalcemia can result from the binding of citrate to calcium in the intravascular space but is usually attenuated by the mobilization of calcium stores in bone. Hypocalcemia can be augmented by hypothermia, liver disease, or hyperventilation because these will all decrease the rate of metabolism of citrate to bicarbonate. Under these circumstances, the infusion of large volumes of citrate combined with the decreased metabolism of citrate can result in hypocalcemia. Indeed, serum ionized calcium has been found to begin to decrease with a rate of infusion of 1 unit of blood every 10 minutes. This syndrome rarely occurs except where the rate of blood transfusion is more rapid than 50 mL/min, with patients with hypothermia or liver disease, or neonates with immature liver function. Supplemental calcium may be needed in these cases. (377)

44. Intraoperative hypothermia can lead to intraoperative cardiac irritability, especially in the presence of arterial pH abnormalities. Postoperative hypothermia can lead to shivering and increased myocardial oxygen demand. Because blood being stored for transfusion is stored at a temperature below 6° C, the administration of stored blood to a patient can result in decreases in the patient's body temperature. This risk can be minimized by administering the blood through warmers. It is prudent to confirm that the blood is being warmed to an appropriate temperature of 37° C to 38° C because red blood cells will hemolyze if overheated. Blood warmers are designed to make this concern not likely. (377)

45. Massive blood transfusions can result in two different coagulation disorders: a dilutional thrombocytopenia and a dilution of some of the coagulation factors necessary to clot blood. Either case may manifest clinically as continued frank bleeding without clotting in the surgical site. It may also manifest as hematuria, gingival bleeding, and spontaneous oozing from various puncture areas in both surgical and nonsurgical sites, such as sites of intravenous access. If this clinical situation is noted, disseminated intravascular coagulation and a hemolytic transfusion reaction should also be considered as a potential source for the bleeding abnormalities. (377-378)

46. Dilutional thrombocytopenia refers to the dilution of platelets from their baseline concentration to a decreased concentration by virtue of the loss of platelets during bleeding without subsequent replacement, as with the administration of crystalloid, colloid, or non–platelet-containing blood products. This occurs even with the transfusion of blood because platelet activity has decreased to about 5% of normal after just 2 days of blood storage. The risk of a dilutional thrombocytopenia is the loss of the ability of blood to clot. When platelet counts decrease to less than 75,000/mm^3, a bleeding disorder is likely to occur. This level of platelets has been seen to occur after the transfusion of 10 to 15 units of non–platelet-containing blood products to previously healthy patients with previously normal platelet counts. Of note is that patients with chronically decreased platelet counts appear to tolerate thrombocytopenia better than patients with an acute decrease in platelets. The treatment of a dilutional thrombocytopenia by transfusing platelets should be instituted when a combination of clinical status and laboratory analysis confirms suspicions of a bleeding disorder secondary to insufficient platelets. (377)

47. Factors V and VIII are necessary for normal blood clotting. For normal blood clotting to occur there must be 5% to 20% of the normal amount of factor V and 30% of the normal amount of factor VIII. When these factors decrease to below these levels, abnormal blood clotting may result. This is manifest on laboratory analysis as a prolongation of the prothrombin time and/or partial thromboplastin time. The importance of factors V and VIII during the transfusion of blood arises from the decrease in concentration of these factors in stored blood. After 21 days of blood storage, the concentration of factors V and VIII is 15% and 50% of their normal values, respectively. During times of massive transfusions, a decrease in these factors may contribute to bleeding disorders. This is particularly true if the blood being transfused has little plasma volume or has been stored for long periods of time. The treatment of bleeding disorders secondary to a dilution of factors V and VIII is the administration of fresh frozen plasma, which contains all clotting factors. The decision to administer fresh frozen plasma is determined by laboratory analysis and the clinical status of the patient. The administration of fresh frozen plasma is also indicated when laboratory analysis reveals a prolongation of the prothrombin time and/or partial thromboplastin time greater than 1.5 times normal, when normal platelet counts exclude thrombocytopenia as a cause of the bleeding disorder, and when there is uncontrolled bleeding in the surgical field. (377)

AUTOLOGOUS BLOOD TRANSFUSIONS

48. Autologous blood donation should be considered for procedures in which significant blood loss is likely to occur. An obvious advantage of the administration of autologous blood rather than homologous blood to patients requiring blood transfusions is the decreased risk of complications associated with homologous blood transfusions, including transfusion reactions and the transmission of blood-borne diseases. In addition, autologous blood donation reserves blood bank stores for other patients, thus decreasing the strain on blood bank resources. (378-379)

49. The collection of predeposited blood for autologous blood transfusion must be done in a manner that will not decrease the patient's hemoglobin level to unacceptable levels preoperatively. Because of the risk of preoperative anemia, patients selected for autologous blood donation probably should not have significant cardiac or neurologic disease. A collection schedule that can be employed is the donation of 1 unit of blood every 4 days. This can be done for up to 3 units. The final unit of blood must be donated 72 hours or more before the surgical procedure to ensure that the patient's plasma volume has been restored. Anemia secondary to the donation of autologous blood remains a concern. Patients scheduled to predeposit autologous blood for blood transfusions are typically prescribed ferrous sulfate. Studies have shown that the administration of erythropoietin to these patients may be beneficial as well but requires parenteral or subcutaneous administration and is expensive. (378-379)

50. A significant complication that can occur with autologous blood transfusions is the risk of clerical error leading to the erroneous blood being transfused to the patient. Blood should be checked just as meticulously whether autologous or homologous blood is being transfused. Other complications include sepsis from bacterial contamination or hypersensitivity to stabilizers. (379)

51. The intraoperative salvage of blood should be considered for surgical procedures that result in blood loss from a clean wound and will likely lead to the need to transfuse blood to the patient. Intraoperative blood salvaging is accomplished by semiautomated systems that collect, wash, and store red blood cells in a reservoir for their future administration. The hematocrit of blood prepared in this manner is 50% to 60%, and the pH is alkaline. Relative contraindications to the intraoperative salvage of blood include malignancy and the presence of blood-borne disease. Blood that has been contaminated with bowel contents should probably not be transfused. (379)

52. Complications of intraoperative blood salvaging include a dilutional coagulopathy, the reinfusion of blood treated with anticoagulants, hemolysis, air embolism, fat embolism, sepsis, and disseminated intravascular coagulation. (379)

53. Hemodilution for autologous blood transfusion should be considered for patients who are expected to lose more than 2 units of blood intraoperatively and who have an adequate preoperative hematocrit. It is probably not appropriate for patients with anemia or severe cardiac or neurologic disease. The hemodilution technique involves the removal of venous or arterial blood from the patient just before or after the induction of anesthesia and restoration of the plasma volume with crystalloid or colloid. The volume of blood that can be removed from the patient is dependent on the patient's preoperative hematocrit, estimated blood volume, and the lowest hematocrit acceptable for that patient. The blood is stored in the operating room at room temperature in a sterile container that contains anticoagulants, and it can be transfused to the patient when it is indicated or after major blood loss has ceased. The blood does not undergo any other biochemical transformations. There are several advantages to the hemodilution method of autologous blood transfusions. This method is less expensive than autologous blood donations and does not require the patient's cooperation or time that is required for the predepositing of autologous blood. In addition, the decreased viscosity and hematocrit of the blood result in a decrease in the concentration and number of red blood cells lost during the procedure. Finally, the blood that is transfused to the patient has platelet and coagulation factor activity that would have been lost in autologous blood that had been stored. (379)

CONCLUSIONS AND FUTURE DIRECTIONS

54. Transfusions have become increasingly safer primarily due to the decrease in the transmission of infectious diseases. There is an increased emphasis on defining ratios of blood products that should be given (e.g., 1:1 packed red blood cells with fresh frozen plasma or platelets). Consistent with the practice of medicine overall, well-designed protocols will increasingly be the basis upon which transfusion practice is based. (379)

Chapter

22 CARDIOVASCULAR DISEASE

Arthur W. Wallace

CORONARY ARTERY DISEASE

1. What percent of adult patients undergoing surgery are estimated to have, or be at risk for, coronary artery disease?
2. What are some components of a routine preoperative cardiac evaluation? What are some more specialized methods of cardiac evaluation? What is the ultimate purpose of a preoperative cardiac evaluation?
3. What are some important aspects of the preoperative history taken from patients with coronary artery disease with respect to their cardiac status?
4. What are some coexisting noncardiac diseases that are frequently present in patients with coronary artery disease?
5. By what percent can a major coronary artery be stenosed in an asymptomatic patient?
6. What is the best indicator for a patient's cardiac reserve?
7. When is angina pectoris considered "stable"?
8. When is angina pectoris considered "unstable"? What is the clinical implication of unstable angina?
9. What is it likely an indication of when dyspnea follows the onset of angina pectoris?
10. How does angina pectoris due to spasm of the coronary arteries differ from classic angina pectoris?
11. What is silent myocardial ischemia?
12. What is the most common symptom of angina in men and women?
13. Approximately what percent of myocardial ischemic episodes are not associated with angina pectoris? Approximately what percent of myocardial infarctions are not associated with angina pectoris?
14. Is hypertension or tachycardia more likely to result in myocardial ischemia in the patient with coronary artery disease? What is the physiologic explanation for this?
15. What is the basis for the common recommendation that elective surgery be delayed until 6 months or more after a prior myocardial infarction?
16. What is the approximate incidence of perioperative myocardial infarction 6 months after a myocardial infarction? What is the approximate incidence of perioperative myocardial infarction in patients who have not had a prior myocardial infarction?
17. What time period after surgery do most perioperative myocardial infarctions occur?
18. What are some cardiac medications that patients with coronary artery disease are likely to be taking? What is the recommendation regarding the patient's preoperative medicine regimen with regard to their regular cardiac medicines?
19. What information can be gained from a preoperative electrocardiogram?

20. How might myocardial ischemia appear on the electrocardiogram?
21. Complete the following table:

Electrocardiogram Lead	*Coronary Artery Responsible for Myocardial Ischemia*	*Area of Myocardium That May Be Involved*
II, III, Avf		
V_3-V_5		
I, aVL		

22. Name some determinants of myocardial oxygen requirements and delivery.
23. What are some intraoperative goals for the anesthesiologist in an attempt to decrease the risk of myocardial ischemia in patients at risk?
24. What is the difference between risk stratification and risk reduction?
25. What are the risks of recent percutaneous coronary angioplasty in surgical patients and how do they differ with bare metal versus drug eluting stents?
26. What are two potential benefits of administering premedication preoperatively to patients with coronary artery disease?
27. How should anesthesia be induced in patients at risk for myocardial ischemia?
28. Why is there an increased risk of myocardial ischemia during direct laryngoscopy? What are some things the anesthesiologist may do during this time to minimize this risk?
29. What are some methods of maintenance of anesthesia that may be employed by the anesthesiologist for the patient with coronary artery disease?
30. What is coronary artery steal syndrome? What is its clinical significance?
31. What is a concern regarding the administration of a regional anesthetic to patients with coronary artery disease?
32. What are some considerations an anesthesiologist should take when selecting a neuromuscular blocking drug for patients with coronary artery disease? What is unique about pancuronium in this situation?
33. How should neuromuscular blockade be reversed in patients with coronary artery disease?
34. What are some factors that influence the intensity of intraoperative monitoring by the anesthesiologist?
35. When might an intraoperative pulmonary artery catheter be useful? What information does it provide?
36. What is some information that may be provided by an intraoperative transesophageal echocardiogram?
37. What are some treatment options when myocardial ischemia is detected intraoperatively?
38. What is the problem with decreases in body temperature that may occur intraoperatively in patients with coronary artery disease?
39. Why is it important to monitor heart rate in the patient with coronary artery disease?

VALVULAR HEART DISEASE

40. What information can be gained from Doppler echocardiography in patients with valvular heart disease?
41. How should anesthetic drugs and neuromuscular blocking drugs be selected for the patient with valvular heart disease?
42. When is it important to administer antibiotics to patients with known valvular heart disease?
43. What is mitral stenosis? How does it affect left atrial and pulmonary venous pressures? At what chronic left atrial pressure is an increase in pulmonary vascular resistance likely to be seen?
44. What is the most common cause of mitral stenosis? How does it present?

45. Why are patients with mitral stenosis at an increased risk of atrial fibrillation?
46. Why are patients with mitral stenosis at an increased risk of thrombus formation in the left atrium?
47. What are some anesthetic considerations for patients with mitral stenosis?
48. How can the maintenance of anesthesia be achieved in patients with mitral stenosis?
49. How might the adequacy of intravascular fluid replacement be monitored in patients with mitral stenosis? Why is this important?
50. Why might the mechanical support of ventilation be required postoperatively in patients with mitral stenosis?
51. What is mitral regurgitation? How is mitral regurgitation reflected on the recording of pulmonary artery occlusion pressure tracings?
52. What is the most common cause of mitral regurgitation? What other pathologic process is often present under these circumstances? What are some other causes of mitral regurgitation?
53. What are some anesthetic considerations for patients with mitral regurgitation?
54. How can the maintenance of anesthesia be achieved in patients with mitral regurgitation?
55. What is aortic stenosis? How is the severity of aortic stenosis estimated? What is considered to be hemodynamically significant aortic stenosis?
56. Name at least two causes of aortic stenosis. What is the natural course of aortic stenosis?
57. Why might patients with aortic stenosis have angina pectoris despite the absence of coronary artery disease?
58. How is aortic stenosis diagnosed on cardiac auscultation? Why is it important for the anesthesiologist to rule out aortic stenosis by auscultation preoperatively?
59. What are some anesthetic considerations for the patient with aortic stenosis?
60. What would result from tachycardia, bradycardia, or decreases in systemic vascular resistance in the patient with aortic stenosis?
61. How can the maintenance of anesthesia be achieved in patients with aortic stenosis?
62. How should the intravascular fluid status be managed intraoperatively in patients with aortic stenosis?
63. In patients with chronic aortic stenosis, why might the pulmonary artery occlusion pressure not be reflective of the left ventricular end-diastolic volume?
64. How effective are external cardiac compressions in patients with aortic stenosis during cardiopulmonary arrest?
65. What is aortic regurgitation? What is the effect of chronic aortic regurgitation on the left ventricle?
66. What is acute aortic regurgitation most likely due to? What is chronic aortic regurgitation most likely due to?
67. Why might a patient with aortic regurgitation have angina pectoris despite the absence of coronary artery disease?
68. What are the goals for the anesthetic management of aortic regurgitation? The anesthetic management of aortic regurgitation resembles the anesthetic management for which other valvular disease?
69. What is mitral valve prolapse? What percent of the adult population is estimated to have mitral valve prolapse?
70. What are some other conditions associated with mitral valve prolapse?
71. What symptoms do most patients with mitral valve prolapse have?
72. What are some potential complications of mitral valve prolapse?
73. What is the goal of the maintenance of anesthesia in patients with mitral valve prolapse? How should the intravascular fluid volume status be managed in patients with mitral valve prolapse?
74. What is the potential problem with regional anesthesia in patients with mitral valve prolapse?

DISTURBANCES OF CARDIAC CONDUCTION AND RHYTHM

75. What are some tools available to the clinician for the diagnosis of disturbances in cardiac conduction and rhythm?
76. What are some types of conduction defects? Are conduction defects above or below the atrioventricular node usually permanent?
77. Is the placement of a prophylactic artificial cardiac pacemaker before surgery indicated in a patient with a bifascicular block? Why or why not? What is the theoretical concern?
78. How is third-degree atrioventricular heart block treated? What are the various methods by which this can be accomplished? How can third-degree heart block be treated pharmacologically?
79. What is sick sinus syndrome? How does it present? How is it treated?
80. What are ventricular premature beats? What are the hallmark features of a ventricular premature beat on an electrocardiogram?
81. When do premature ventricular beats warrant treatment? How are they treated under these circumstances?
82. What may be some causes of ventricular premature beats?
83. When is ventricular tachycardia diagnosed? How can it be treated?
84. What are preexcitation syndromes?
85. What is Wolff-Parkinson-White (WPW) syndrome? What is the incidence of WPW syndrome in the general population? How is it characterized on the electrocardiogram?
86. What is the most common cardiac dysrhythmia associated with WPW syndrome? How can it be treated?
87. What is the goal of the anesthetic management of a patient with WPW syndrome?
88. What are the various methods by which paroxysmal atrial tachycardia or fibrillation may be treated in the perioperative period in patients with WPW syndrome?
89. What is prolonged QT interval syndrome? What adverse events are associated with a prolonged QT interval? How can they be treated pharmacologically?
90. What is a congenital cause of prolonged QT interval syndrome? How is a stellate ganglion block thought to work for this?
91. What is the goal of the anesthetic management of a patient with a chronically prolonged QT interval?

ARTIFICIAL CARDIAC PACEMAKERS

92. What should be included in the preoperative evaluation of the patient with an artificial cardiac pacemaker?
93. How should the pacemaker be evaluated by the anesthesiologist preoperatively?
94. What intraoperative monitoring is important in a patient with an artificial cardiac pacemaker?
95. What can occur if the ground plate for electrocautery is placed too near the pulse generator of the artificial cardiac pacemaker?
96. How is the selection of drugs or anesthetic techniques altered by the presence of an artificial cardiac pacemaker in a patient?
97. Why should a magnet be kept in the operating room intraoperatively for a patient with an artificial cardiac pacemaker undergoing anesthesia?
98. What are some causes of temporary pacemaker malfunction? When is placement of a pulmonary artery catheter in a patient with an artificial cardiac pacemaker a risk?

ESSENTIAL HYPERTENSION

99. What is the definition of essential hypertension? What is the benefit of the long-term treatment of patients with essential hypertension?
100. What should be included in the preoperative evaluation of a patient with essential hypertension?
101. How should blood pressure medications be managed in the perioperative period in the patient with essential hypertension?

102. What other medical problems are frequently seen in patients with essential hypertension? Approximately what percent of patients with peripheral vascular disease can be assumed to have 50% or greater stenosis of one or more coronary arteries even in the absence of symptoms?
103. How is the curve for the autoregulation of cerebral blood flow altered in patients with essential hypertension?
104. What is the value of treating essential hypertension in patients before an elective procedure?
105. How do patients with essential hypertension frequently respond physiologically to the induction of anesthesia with intravenous medications? Why is this thought to occur?
106. How do patients with essential hypertension frequently respond physiologically to direct laryngoscopy? What are these patients at risk of during this time? How can this response be attenuated?
107. What is the goal for the anesthetic management of patients with essential hypertension?
108. How can the maintenance of anesthesia in patients with essential hypertension be achieved?
109. How might intraoperative hypotension be managed by the anesthesiologist in patients with essential hypertension?
110. What is the potential problem with regional anesthesia in patients with essential hypertension?
111. How frequently does hypertension occur in the early postoperative period in patients with essential hypertension? How can it be managed?

CONGESTIVE HEART FAILURE

112. What is the correlation between congestive heart failure and postoperative morbidity? What does this suggest for the patient scheduled for elective surgery in the presence of congestive heart failure?
113. What is the goal of the anesthetic management of patients with congestive heart failure who are undergoing urgent or emergent surgery? What medicines may be useful to achieve this?
114. How does positive-pressure ventilation of the lungs affect patients in congestive heart failure?
115. For major surgery in patients with congestive heart failure, what monitoring may be necessary?
116. For peripheral surgery in patients with congestive heart failure, can regional anesthesia be selected as an anesthetic option?

HYPERTROPHIC CARDIOMYOPATHY

117. What is another name for hypertrophic cardiomyopathy? What pathophysiology defines hypertrophic cardiomyopathy? What is the stroke volume in patients with hypertrophic cardiomyopathy?
118. What is the goal of the anesthetic management of patients with hypertrophic cardiomyopathy?
119. How can intraoperative hypotension be treated in patients with hypertrophic cardiomyopathy?
120. How can intraoperative hypertension be treated in patients with hypertrophic cardiomyopathy?
121. What is the problem with using β agonists for the treatment of hypotension or using nitrates for the treatment of hypertension in patients with hypertrophic cardiomyopathy?

COR PULMONALE

122. What is cor pulmonale?
123. What are some signs and symptoms associated with cor pulmonale?
124. What are some treatment methods for cor pulmonale?

125. What is the recommendation for the patient with cor pulmonale who is scheduled for an elective surgical procedure?
126. What is the goal of the anesthetic management of patients with cor pulmonale? How can this be achieved?
127. What is the advantage of monitoring pulmonary artery pressure during surgery in patients with cor pulmonale?

CARDIAC TAMPONADE

128. What is cardiac tamponade?
129. Name some manifestations of cardiac tamponade.
130. What is the treatment for cardiac tamponade? What are some temporizing measures for patients with cardiac tamponade awaiting definitive treatment?
131. What is the goal of the anesthetic management of cardiac tamponade?
132. What effect can the induction of anesthesia and positive-pressure ventilation of the lungs have on patients with cardiac tamponade?
133. What is the recommendation for anesthesia in patients with cardiac tamponade?
134. What pharmacologic agents may be useful in patients with cardiac tamponade?

ANEURYSMS OF THE AORTA

135. What is the most frequent cause of aortic aneurysms? Do most aortic aneurysms involve the thoracic or abdominal aorta?
136. What is a dissecting aneurysm?
137. When is elective resection of an abdominal aortic aneurysm recommended?
138. What are some medical problems frequently associated with aortic aneurysms?
139. What is the goal of the anesthetic management of patients undergoing resection of an abdominal aortic aneurysm? What monitoring is warranted in these procedures?
140. When are patients with coronary artery disease especially at risk of myocardial ischemia during surgery for resection of an aortic aneurysm?
141. How should intraoperative fluids be managed during surgery for resection of an aortic aneurysm?
142. Why does hypotension frequently accompany unclamping of the abdominal aorta during surgery for the resection of an aortic aneurysm? What are some methods for minimizing the hypotension?
143. What are some concerns regarding renal function in patients undergoing aortic aneurysm repair?
144. What are some concerns regarding spinal cord function in patients undergoing aortic aneurysm repair?

CARDIOPULMONARY BYPASS

145. How is blood drained from the venae cavae during cardiopulmonary bypass?
146. What are two different types of pumps that are used to return blood to the arterial system during cardiopulmonary bypass? Which results in less trauma to blood?
147. How is blood kept from entering the heart from the superior and inferior venae cavae during cardiopulmonary bypass for mitral valve or intracardiac surgery?
148. Under what conditions does the aorta need to be cross-clamped distal to the aortic valve and proximal to the inflow cannula during cardiopulmonary bypass?
149. How can venous drainage from the inferior and superior venae cavae during cardiopulmonary bypass be facilitated?
150. What is the required cardiac index delivered by the roller pump on the cardiopulmonary bypass machine dependent upon? What approximate cardiac index is usually sufficient?
151. What is the advantage of low flows during cardiopulmonary bypass?
152. What are two different types of oxygenators that are used to oxygenate blood that is returning to the arterial system during cardiopulmonary bypass?
153. What is the advantage of a bubble oxygenator? What is the disadvantage of a bubble oxygenator?

154. What is the advantage of a membrane oxygenator? What is the disadvantage of a membrane oxygenator?
155. How can the patient's body be heated or cooled by the cardiopulmonary bypass machine?
156. How is blood loss from the field recirculated to the patient during cardiopulmonary bypass?
157. What is a problem with the cardiotomy suction used during cardiopulmonary bypass?
158. Why might the left ventricle need a vent during cardiopulmonary bypass? How might this be achieved?
159. How are systemic emboli from cellular debris prevented from occurring during cardiopulmonary bypass?
160. What does priming of the cardiopulmonary bypass system refer to? What is the cardiopulmonary bypass system primed with?
161. What is the patient's hematocrit maintained at during cardiopulmonary bypass? Why is it important to hemodilute the patient's blood during cardiopulmonary bypass?
162. Why is it important to remove all air from the cardiopulmonary bypass system during cardiopulmonary bypass?
163. Why is heparin-induced anticoagulation of the patient's blood necessary during cardiopulmonary bypass? What dose of heparin is usually administered? How is the adequacy of anticoagulation confirmed?
164. What are some explanations for the low mean arterial pressure often seen after the institution of cardiopulmonary bypass? What blood pressure is typically considered acceptable?
165. Why does blood pressure slowly rise spontaneously after some time on cardiopulmonary bypass?
166. What are the dangers of hypertension while on cardiopulmonary bypass? How can hypertension under these circumstances be treated?
167. What are some methods by which the adequacy of tissue perfusion during cardiopulmonary bypass can be evaluated?
168. Why is diuresis induced during cardiopulmonary bypass?
169. What may be the cause of an increasing central venous pressure with or without facial edema while on cardiopulmonary bypass? How can this be confirmed?
170. What may be the cause of increasing abdominal distention while on cardiopulmonary bypass?
171. What are some complications of extracorporeal circulatory support or cardiopulmonary bypass?
172. How should ventilation of the lungs be managed during cardiopulmonary bypass?
173. What is the goal of myocardial preservation during cardiopulmonary bypass? What are some methods by which this can be achieved?
174. What is the oxygen consumption of a normally contracting heart at 30° C? What is the oxygen consumption of a fibrillating heart at 22° C? What is the oxygen consumption of an electromechanically quiet heart at 22° C?
175. How is the effectiveness of cold cardioplegia of the heart measured?
176. What are two potential negative effects of intramyocardial hyperkalemia due to cold cardioplegia after cardiopulmonary bypass? How can they be treated?
177. What are two potential sources for systemic hyperkalemia during cardiopulmonary bypass? How can the hyperkalemia be treated if it were to persist at the conclusion of cardiopulmonary bypass?
178. Why might supplemental intravenous anesthetics be administered during cardiopulmonary bypass?
179. Why might supplemental neuromuscular blocking drugs be administered during cardiopulmonary bypass?
180. Is supplemental anesthesia routinely required during rewarming after the conclusion of cardiopulmonary bypass?

181. What conditions in the patient must be present for cardiopulmonary bypass to be discontinued?
182. When are the aortic and vena cava cannulae removed after cardiopulmonary bypass?
183. What are some potential problems associated with persistent hypothermia after cardiopulmonary bypass?
184. What special precautions must be taken before discontinuing cardiopulmonary bypass in patients who have had the left side of the heart opened, as during valve replacement surgery? What is the potential risk?
185. For each of the following situations, please complete the diagnosis and appropriate therapy:

Blood Pressure	*Atrial Pressure*	*Cardiac Output*	*Diagnosis*	*Therapy*
Decreased	Increased	Decreased	—	—
Decreased	Decreased	Decreased	—	—
Decreased	Decreased	Increased	—	—
Increased	Increased	Decreased	—	—
Increased	Decreased	Increased	—	—

186. Why might a patient have posterior papillary muscle dysfunction after cardiopulmonary bypass? How would this be manifest on the pulmonary artery occlusion pressure tracing?
187. What is a mechanical addition to the pharmacologic support of cardiac output in patients with a poor cardiac output after cardiopulmonary bypass? How does it work? What physiologic alterations may interfere with its efficacy?
188. When is protamine administered after cardiopulmonary bypass? Why?
189. What are some possible side effects of protamine administration?
190. What does the perfusionist do with blood and fluid that remains in the cardiopulmonary bypass circuit after cardiopulmonary bypass?
191. Why might there be a gradient between central aortic and radial artery blood pressures in the early period after cardiopulmonary bypass? How long can this effect persist?

ANSWERS*

CORONARY ARTERY DISEASE

1. It is estimated that 40% of adult patients undergoing surgery have, or are at risk for, coronary artery disease. (384)
2. Components of a routine preoperative cardiac evaluation include the history and physical examination, evaluation of the patient's electrocardiogram, and reviewing or ordering more specialized procedures. Specialized methods of cardiac evaluation include a Holter monitor, exercise electrocardiogram, echocardiogram, radioisotope imaging, cardiac catheterization, and angiography. The ultimate purpose of a preoperative cardiac evaluation is to assess the patient's risk of an adverse perioperative cardiac event, to determine whether the patient is in optimal medical condition for surgery, and to reduce operative risk. (384)
3. Important aspects of the preoperative history taken from patients with coronary artery disease with respect to their cardiac status include their exercise tolerance, characteristics of their angina, and the presence of a previous myocardial

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

infarction. It is also important to learn what cardiac medicines the patient may be taking and what the potential interactions of these are with anesthetics that may be administered for surgery. (384)

4. Noncardiac diseases that are frequently present in patients with coronary artery disease include peripheral vascular disease, chronic obstructive pulmonary disease, renal dysfunction, chronic hypertension, and diabetes mellitus. (384)

5. A major coronary artery can be stenosed by as much as 50% to 70% in an asymptomatic patient. (384)

6. The best indicator for a patient's cardiac reserve is by evaluation of their exercise tolerance. A limited exercise tolerance in the absence of significant pulmonary disease gives evidence of a decrease in a patient's cardiac reserve. Alternatively, the cardiac reserve of a patient who is able to climb up two to three flights of stairs without stopping is probably adequate. (384)

7. Angina pectoris is considered "stable" when there has been no change in the patient's anginal symptoms for at least 60 days. Factors related to the angina that should be evaluated include the precipitating factors, frequency, and duration. (384)

8. Angina pectoris is considered "unstable" when there has been a change in the patient's anginal symptoms. Changes that should be evaluated include the degree of activity a patient can do before the onset of angina and the duration of each anginal episode. Another symptom of unstable angina is chest pain occurring at rest. The clinical implication of unstable angina is that the patient may be at risk of an impending myocardial infarction. (384)

9. Dyspnea after the onset of angina pectoris is likely an indication of acute left ventricular dysfunction due to myocardial ischemia and acute, transient cardiac failure. (384)

10. Angina pectoris due to spasm of the coronary arteries differs from classic angina pectoris in that the pain may occur at rest but may not occur during periods of exertion. Angina of this type is associated with ST segment changes on the electrocardiogram. This type of angina is referred to as Prinzmetal's or variant angina. (384)

11. Silent myocardial ischemia is myocardial ischemia that occurs in the absence of angina. This type of angina is more common in patients with diabetes mellitus and carries the same prognosis as myocardial ischemia associated with angina. (384)

12. The most common symptom of angina in men is dyspnea on exertion. Shortness of breath with climbing stairs is very common. Walking on a flat surface does not seem to be sufficient to elicit shortness of breath until the symptoms are severe. Waking from sleep with angina is also a symptom of severe angina. Women most commonly complain of nonspecific fatigue, making identification of angina more difficult. (384)

13. Approximately 70% of myocardial ischemic episodes are not associated with angina pectoris, and myocardial infarctions are not associated with angina pectoris approximately 15% of the time. (384)

14. Tachycardia is more likely than hypertension to result in myocardial ischemia in the patient with coronary artery disease secondary to an increased oxygen consumption with a decreased duration for coronary blood flow to the left ventricle. Tachycardia results in an increased myocardial oxygen requirement as oxygen consumption is per beat combined with a decreased myocardial perfusion time. Myocardial perfusion to the left ventricle, and thus myocardial oxygen supply, occurs during diastole. Hypertension, on the other hand, leads to an increased myocardial oxygen requirement, but it is also a simultaneous increase in myocardial perfusion. (384)

15. The basis for the common recommendation that elective surgery be delayed until 6 months after a prior myocardial infarction is based on numerous epidemiologic studies. These studies have shown that there is a 5% to 86% reinfarction rate in the perioperative period if previous myocardial infarction preceded the surgical procedure by less than 6 months. This rate of myocardial infarction is 1.5 to 10 times higher than if more than 6 months separated the previous myocardial infarction and the surgical procedure. (385)

16. The approximate incidence of perioperative myocardial infarction 6 months or more after a myocardial infarction is 5% to 6%, whereas the approximate incidence of perioperative myocardial infarction in patients who have not had a prior myocardial infarction is 0.13%. (385, Table 25-1)

17. Most perioperative myocardial infarctions occur in the first 48 to 72 hours postoperatively. (385)

18. Cardiac medications that patients with coronary artery disease are likely to be taking include β antagonists, nitrates, calcium channel blockers, antihypertensives, and diuretics. The recommendation is that patients continue taking their regular cardiac medicines throughout the perioperative period. (385)

19. Preoperative electrocardiograms may provide evidence of myocardial ischemia, prior myocardial infarction, cardiac hypertrophy, abnormal cardiac rhythm or conduction disturbances, and electrolyte abnormalities. (386)

20. Myocardial ischemia may appear as ST segment changes or T wave changes on an electrocardiogram. (386)

21. (386, Table 25-2)

Table 25-2

Electrocardiogram Lead	*Coronary Artery Responsible for Myocardial Ischemia*	*Area of Myocardium That May Be Involved*
II, III, aVF	Right coronary artery	Right atrium, atrioventricular node, right ventricle
V_3-V_5	Left anterior descending coronary artery	Anterolateral portion of left ventricle
I, aVL	Circumflex coronary artery	Lateral aspects of the left ventricle

22. Determinants of myocardial oxygen requirements and delivery are related to factors that affect myocardial oxygen supply or myocardial oxygen demand. Myocardial oxygen supply is decreased by tachycardia, hypotension, increased preload, hypocapnia, coronary artery spasm, anemia, and hypoxemia. Myocardial oxygen demand is increased by tachycardia, increased wall tension, and increased myocardial contractility. A goal of the anesthetic management of patients with coronary artery disease is maintenance of the balance between myocardial oxygen supply and demand to minimize the risk of myocardial ischemia. (389, Table 25-4)

23. In an attempt to decrease the risk of a perioperative myocardial infarction in patients at risk, the anesthesiologist should attempt to maintain stable patient hemodynamics. In general, the desired hemodynamics to minimize the risk of intraoperative ischemia include slower heart rates, lower filling pressures, and normal systolic blood pressures. A common recommendation for patients at risk of myocardial ischemia is that heart rate and blood pressure be maintained within 20% of awake values intraoperatively. Even so, approximately 50% of all new perioperative myocardial ischemic episodes are not preceded by or associated with changes in heart rate or blood pressure. Nevertheless, the anesthesiologist may choose to closely monitor the patient's more limited hemodynamic status using

invasive monitors to achieve these goals. He or she should also be prepared to intervene quickly with pharmacologic interventions should they become necessary. (389)

24. Risk stratification is the identification of risk factors in patients that lead to the determination of preoperative risk. Risk stratification does not actually decrease risk, it simply identifies it. Risk reduction requires changing the care provided to the patient either through medications such as the administration of perioperative blockade, or through an alteration in the anesthetic or surgical plan. (386-388, Table 25-2)

25. Patients with recent intracoronary stents have an increased risk of myocardial infarction and death if platelet inhibitors are withdrawn for surgery. Patients with bare metal stents likely require 3 or more months of antiplatelet therapy and those with drug eluting stents may require a year or more before risk is acceptable to discontinue platelet inhibitors for surgery. Many patients who have had percutaneous intervention should be operated on while on aspirin if surgical conditions allow. (388)

26. Two benefits of administering premedication preoperatively to patients with coronary artery disease are the decrease in the secretion of potentially harmful catecholamines and the potential to prevent the increase in myocardial oxygen requirements that may occur with tachycardia and hypertension related to anxiety. (390)

27. The induction of anesthesia in patients at risk for myocardial ischemia is typically achieved with great care. The patient's standard daily medications should be reviewed and administered if there are no specific contraindications. Patients on β-blockers should receive them. A preinduction intraarterial line may help recognize hemodynamic perturbations reducing risk. Infusions of phenylephrine are helpful to reduce hypotension on induction. Careful administration of intravenous induction agents, narcotics, and inhaled agents, combined with monitoring and careful vasoconstrictor use, are essential. It is important to avoid tachycardia with consummate increases in myocardial oxygen requirements. (390)

28. Direct laryngoscopy is associated with an increased risk of myocardial ischemia because it often produces intense sympathetic nervous system stimulation leading to tachycardia and hypertension. To minimize this risk, there must be adequate levels of anesthesia to suppress sympathetic nervous system stimulation. Volatile anesthetics, intravenous anesthetics other than ketamine, opioids, and lidocaine may all be used to blunt the response to direct laryngoscopy. β antagonists may be administered before induction to attenuate the increase in heart rate and blood pressure that can occur. (390)

29. The maintenance of anesthesia for the patient with coronary artery disease may be achieved through the administration of volatile anesthetics, propofol, dexmedetomidine, and opioids, with or without nitrous oxide. (391)

30. Coronary artery steal syndrome is a theoretical risk in which administration of a coronary artery vasodilator to a patient with coronary artery disease could result in diversion of blood flow from the ischemic areas, in which stenotic coronary arteries are maximally dilated, to areas in which the coronary arteries are patent and able to vasodilate. Isoflurane, of all the volatile anesthetics, is the most potent coronary vasodilator. It was once thought that isoflurane is the volatile anesthetic that is most likely to result in this syndrome. Clinically, however, the administration of isoflurane to patients with coronary artery disease has not been shown to increase the risk of myocardial ischemia through the coronary artery steal syndrome. (391)

31. The administration of a regional anesthetic to patients with coronary artery disease can result in hypotension, which may in turn lead to decreased blood flow through pressure-dependent stenosed coronary arteries. For this reason it is

important for the anesthesiologist to be prepared to treat decreases in blood pressure with induction of any anesthetic. An advantage of regional anesthesia for patients with coronary artery disease is that the anesthesiologist may continue to monitor the patient for symptoms of angina and treat them accordingly. (391)

32. Considerations in the selection of a neuromuscular blocking drug for patients with coronary artery disease should take into account the effects of the neuromuscular blocking drug on the cardiovascular system. For example, a neuromuscular blocking drug that may lower blood pressure through the release of histamine should be administered slowly to minimize those effects. Pancuronium causes mild increases in heart rate and blood pressure that may or may not be beneficial, depending on the status of the patient. (391)

33. Neuromuscular blockade may be reversed in patients with coronary artery disease in the usual manner with an anticholinesterase-anticholinergic drug combination. Care should be taken to avoid tachycardia and subsequent myocardial ischemia with reversal. Glycopyrrolate has less of a chronotropic effect on the heart, but either glycopyrrolate or atropine is acceptable for the reversal of neuromuscular blockade. Alternatively, avoiding reversal by appropriate timing and choice of nondepolarizing muscle relaxants can reduce the risk of tachycardia and other side effects of nondepolarizing muscle relaxant reversal. (392)

34. The intensity of intraoperative monitoring the anesthesiologist chooses to implement for a surgical procedure in a patient with coronary artery disease is influenced by the type of procedure the patient is undergoing, the severity of the patient's disease, the choice of anesthetic technique, and a risk-benefit analysis of each type of potential monitoring. (392)

35. While no clinical benefit has been shown of the use of a pulmonary artery catheter, it may be useful in patients with poor left ventricular function, valvular heart disease, a recent myocardial infarction, or pulmonary vascular disease, in situations of massive trauma, or in major vascular surgery. Information provided by a pulmonary artery catheter includes more accurate assessment of cardiac filling pressures than a central venous monitor in the presence of pulmonary vascular disease, left-sided heart dysfunction, or potential left-sided heart dysfunction due to myocardial ischemia. The pulmonary artery catheter can be used to measure cardiac output and calculate systemic vascular resistance. (392)

36. Information provided by an intraoperative transesophageal echocardiogram includes both functional and anatomic information including early detection of myocardial ischemia through the presence of new onset regional wall motion abnormalities, an assessment of the intravascular fluid volume status of the patient, an estimation of the cardiac output, an estimation of left ventricular afterload, and an evaluation of the cardiac valves. (392)

37. The detection of intraoperative myocardial ischemia should promptly lead to the treatment of any hemodynamic alterations in an attempt to increase myocardial oxygen supply while decreasing myocardial oxygen demand. Tachycardia may be treated with a β-adrenergic antagonist. These drugs decrease the demand of the myocardium for oxygen through its effects of decreases in heart rate and myocardial contractility. Administration of any medication should be judicious in patients with left ventricular dysfunction. Hypertension may be treated with a nitrate. Nitroglycerin may also be used in a situation in which there are ischemic changes on the electrocardiogram but blood pressure remains normal to high. Intravenous nitroglycerin administration may lead to reflex tachycardia. Hypotension may be treated with a sympathomimetic drug and intravascular fluids. (392)

38. Decreases in body temperature that may occur intraoperatively in patients with coronary artery disease can result in shivering on awakening. Shivering can significantly increase myocardial and systemic oxygen requirements and can

be especially detrimental to patients with coronary artery disease because it is often accompanied by tachycardia. (392)

39. It is important to control heart rate to avoid myocardial ischemia. Control of pain, stress, volume status, and administration of antiischemic agents is essential in the patient with coronary artery disease. Tachycardia from any cause (including pain, hypovolemia, atrial fibrillation, and stress) increases myocardial oxygen requirements and is detrimental to the patient with coronary artery disease. (392)

VALVULAR HEART DISEASE

40. Information that can be gained from Doppler echocardiography in patients with valvular heart disease includes the significance of cardiac murmurs, hemodynamic abnormalities, transvalvular pressure gradients, the orifice area of the cardiac valve, and the evaluation of prosthetic valve function. (393, Table 25-5)

41. Anesthetic drugs and neuromuscular blocking drugs should be selected for the patient with valvular heart disease based on the effects they may have on cardiac rhythm, heart rate, blood pressure, systemic vascular resistance, and pulmonary vascular resistance. The objective is to choose anesthetic drugs and neuromuscular blocking drugs that will not compromise cardiac output with their administration. (393)

42. Antibiotics used to be administered to patients with known valvular heart disease prophylactically to protect the patient from infective endocarditis. Administration of prophylactic antibiotics is now only recommended for patients with congenital heart disease, prosthetic heart valves, patients with a history of infective endocarditis, or heart transplant patients with a developing cardiac valvulopathy. Prophylaxis is recommended to minimize the risk of infection from a bacteremic event, such as surgical or dental procedures. Bacteremia does not seem to occur with orotracheal intubation, but it may occur with nasotracheal intubation independent of any surgical event. There are recommended prophylaxis regimens that vary depending on the site of surgery, mechanism of administration, and any history of allergies to antibiotics the patient may have. (393, Table 13-8)

43. Mitral stenosis is a mechanical obstruction to left ventricular diastolic filling secondary to a decrease in the orifice of the mitral valve. Measurement of the mitral valve area provides for the best indication of the severity of the disease. Mitral stenosis is classified as severe when the mitral valve area is less than 1 cm^2. Left atrial and pulmonary venous pressures are increased in patients with mitral stenosis. An increase in pulmonary vascular resistance is likely to be seen when the left atrial pressure is higher than 25 mm Hg on a chronic basis. (393)

44. The most common etiology for mitral stenosis is rheumatic heart disease. The mitral valve leaflets often fuse, scar, and fibrose during the healing process of acute rheumatic carditis. Mitral stenosis presents after a prolonged course of development, usually about 20 years after the initial episode of rheumatic fever. Often the disease presents with atrial fibrillation or when there is an increased demand for cardiac output, as may occur during pregnancy or exercise. Patients with mitral stenosis may have recurrent episodes of pulmonary edema, dyspnea, paroxysmal nocturnal dyspnea, chest pains, palpitations, and fatigue. (393)

45. Patients with mitral stenosis are at an increased risk of atrial fibrillation secondary to the distention of the left atrium. (393)

46. Patients with mitral stenosis are at an increased risk of thrombus formation in the left atrium because of the stasis of blood in that heart chamber. Thrombi in the left atrium may be ejected from the heart as systemic emboli. (393)

47. Considerations for the anesthetic management of patients with mitral stenosis include maintenance of a normal sinus rhythm and heart rate, maintenance of

a normal intravascular fluid volume, and the avoidance of increases in pulmonary vascular resistance. Patients with mitral stenosis have a greater reliance on atrial contraction for left ventricular filling. Alterations from sinus rhythm should be promptly treated chemically or with cardioversion. Tachycardia and bradycardia may both result in decreases in left ventricular filling. The intravascular fluid volume should be maintained at near-normal or maximally tolerated levels, while avoiding pulmonary edema. Increases in pulmonary vascular resistance and pulmonary hypertension may place the patient at an increased risk for pulmonary artery rupture with placement of a pulmonary artery catheter and repeated wedge pressure measurements. Care should be taken to avoid overtransfusion or the head-down position in these patients. Arterial hypoxemia or hypercarbia may exacerbate pulmonary hypertension and precipitate right ventricular failure and should be avoided. Central venous pressure monitoring may be useful to detect changes in the right ventricular pressure. (393)

48. The maintenance of anesthesia can be achieved in patients with mitral stenosis through the administration of volatile anesthetics, nitrous oxide, and opioids. Of greater importance is the management of the cardiovascular effects of these drugs to achieve the goal of the anesthetic management of patients with mitral stenosis and treatment of the unfavorable effects of these drugs, accordingly. For example, pancuronium may not be an appropriate choice for neuromuscular blockade in patients with mitral stenosis secondary to the increased speed of transmission of cardiac impulses through the atrioventricular node that result from this drug. This increased speed of transmission may be detrimental to patients prone to atrial fibrillation. Likewise, the administration of ketamine to these patients should be avoided. The increase in pulmonary vascular resistance that is associated with nitrous oxide is not usually sufficient enough to detract from its utility in patients with mitral stenosis. Drugs that are being administered for heart rate control should be continued throughout the perioperative period. (393-394)

49. Intraoperative monitoring of the right atrial pressure may be useful in assessing the adequacy of intravascular fluid replacement in patients with mitral stenosis. The monitoring of intraoperative fluid therapy in these patients is important because they are prone to intravascular fluid overload, leading to right heart failure and pulmonary edema. (394)

50. The mechanical support of ventilation may be required postoperatively in patients with mitral stenosis because they are susceptible to developing pulmonary edema and right-sided heart failure. This may be especially true in patients with mitral stenosis after major thoracic or abdominal surgery. (394)

51. Mitral regurgitation occurs as a result of an incompetent mitral valve. Physiologically, there is left atrial overload and a decreased left ventricular stroke volume in these patients. When mitral regurgitation develops over time, left ventricular dilation and left ventricular hypertrophy develop to maintain the left ventricular stroke volume. With progression of the disease, however, congestive heart failure can occur. Patients with chronic mitral regurgitation are frequently in atrial fibrillation. Acute mitral regurgitation results in acute increases in left atrial pressure and pulmonary artery pressures and can present as pulmonary congestion, pulmonary hypertension, and right-sided heart failure. Measurement of the regurgitant fraction provides for an estimate of the severity of the disease. For instance, a regurgitant fraction of 0.6 or greater is typically associated with congestive heart failure. A recording of pulmonary artery occlusion pressure tracings in a patient with mitral regurgitation would show prominent *v* waves that are characteristic of mitral regurgitation. (394, Figure 19-2)

52. The most common cause of mitral regurgitation is rheumatic heart disease. When mitral regurgitation is secondary to rheumatic heart disease it is often chronic, is accompanied by mitral stenosis, and progresses over years. The most

common cause of isolated mitral regurgitation is papillary muscle dysfunction, which is usually acute in onset with a corresponding acute onset of symptoms. Papillary muscle dysfunction usually occurs after a myocardial infarction or after rupture of the chordae tendineae secondary to infective endocarditis. (394)

53. Considerations for the anesthetic management of patients with mitral regurgitation include the avoidance of sudden decreases in heart rate, the avoidance of sudden increases in systemic vascular resistance, and minimizing drug-induced myocardial depression, because each of these will increase regurgitant flow. The size of the *v* wave on the pulmonary artery catheter tracing may be monitored as a reflection of mitral regurgitant flow. (394, Table 25-7)

54. The maintenance of anesthesia in patients with mitral regurgitation can be achieved through the administration of a volatile anesthetic, nitrous oxide, and an opioid. Of greater importance is the management of the cardiovascular effects of these drugs to achieve the goal of the anesthetic management of patients with mitral regurgitation and treatment of the unfavorable effects of these drugs accordingly. The goals include maintenance of normal to increased heart rate, normal to reduced systemic vascular resistance, and myocardial contractility. Nondepolarizing neuromuscular blocking drugs, including pancuronium, may be safely used in patients with mitral regurgitation. The increase in heart rate that can result from the administration of pancuronium can be beneficial to patients with mitral regurgitation. (395)

55. Aortic stenosis is the mechanical obstruction to the ejection of blood from the left ventricle secondary to a decrease in the orifice of the aortic valve. Increased left ventricular systolic pressure necessarily results from the chronic attempt of this chamber to maintain an adequate stroke volume through a narrowed aortic valve in aortic stenosis. The increased thickness of the left ventricular wall that is often seen in patients with aortic stenosis occurs in response to chronically increased intraventricular pressures. The severity of aortic stenosis is estimated by the degree of stenosis of the valve. A pressure gradient across the aortic valve that is in excess of 50 mm Hg is considered hemodynamically significant aortic stenosis. (395)

56. Two causes of aortic stenosis are rheumatic heart disease and the progressive calcification and stenosis of a congenitally abnormal valve. The congenital valve abnormality most often associated with aortic stenosis is a bicuspid valve. The natural course of aortic stenosis is one of an insidious, long progression of asymptomatic disease before the onset of symptoms. Symptoms may include angina, syncope, dyspnea on exertion, and congestive heart failure. (395)

57. Patients with aortic stenosis may have angina pectoris, which typically occurs with exertion despite the absence of coronary artery disease. Myocardial ischemia and angina occurs because of an increased demand for and decreased supply of myocardial oxygen. The increase in myocardial oxygen demand is due to left ventricular hypertrophy combined with increased left ventricular pressures and increased myocardial work. The decrease in myocardial oxygen delivery results from compression of subendocardial coronary blood vessels by increased left ventricular systolic pressures, as well as the gradient in pressure from the left ventricle to the coronary ostia caused by the stenotic valve. (395)

58. A systolic murmur heard best in the second right intercostal space characterizes the murmur of aortic stenosis heard on cardiac auscultation. It is important for the anesthesiologist to rule out aortic stenosis by auscultation preoperatively to best manage the patient. For instance, a precipitous drop in systemic vascular resistance, as may occur with a regional anesthetic or induction of general anesthesia, could be lethal to the patient with aortic stenosis. (395)

59. Consideration for the anesthetic management of a patient with aortic stenosis includes the maintenance of a stable blood pressure. Avoiding hypotension and

tachycardia are critical. The goal of the anesthetic management of patients with aortic stenosis is the maintenance of normal sinus rhythm, normal heart rates, and normal myocardial contractility, while avoiding sudden decreases in systemic vascular resistance, or hypovolemia. (395, Table 25-8)

60. Tachycardia in the patient with aortic stenosis increases oxygen consumption and decreases coronary filling time by shortening diastole. Tachycardia also decreases the amount of time for left ventricular filling, leading to a decrease in the stroke volume. Bradycardia can lead to an acute overdistention of the left ventricle in these patients. Sinus rhythm is desired because the contribution of the atrial contraction to left ventricular filling is greater in these patients. Decreases in systemic vascular resistance in patients with aortic stenosis can lead to decreases in coronary blood flow with myocardial ischemia, with rapid ventricular decompensation and death. (395)

61. The maintenance of anesthesia in patients with aortic stenosis can be achieved through the administration of narcotics, volatile agents, or intravenous anesthetics. Volatile anesthetics administered carefully to avoid excessive decreases in systemic vascular resistance and tachycardia are common. The most important point in patients with aortic stenosis is to carefully manage hemodynamics to avoid hypotension, tachycardia, myocardial ischemia, and ventricular dysfunction. Intraarterial pressure monitoring prior to the induction of anesthesia is mandatory, as is the availability of vasoconstrictors, both bolus and infusion, such as phenylephrine. (396)

62. Management of the intravascular fluid status of patients with aortic stenosis should be geared toward the maintenance of an adequate intravascular volume through the prompt, liberal correction of blood and fluid losses. (396)

63. The pulmonary artery occlusion pressure may not be reflective of the left ventricular end-diastolic volume in patients with chronic aortic stenosis secondary to the decrease in left ventricular compliance seen in these patients. (396)

64. External cardiac compressions administered during cardiopulmonary arrest are not effective in patients with aortic stenosis because of the greater pressures that are necessary to create forward flow through the stenosed aortic valve. (396)

65. Aortic regurgitation results from an incompetent aortic valve. Patients with aortic regurgitation have a decreased left ventricular stroke volume due to regurgitation of part of the ejected stroke volume from the aorta back into the left ventricle. This places an increased volume load on the left ventricle. Chronic aortic regurgitation results in eccentric hypertrophy of the left ventricle in an attempt to compensate for the regurgitation by increasing the stroke volume. Symptoms may include dyspnea, fatigue, and palpitations. (396)

66. Acute aortic regurgitation is most likely due to infective endocarditis, trauma, connective tissue disease, or a dissecting thoracic aortic aneurysm. Chronic aortic regurgitation is most likely due to prior rheumatic fever, but it may also be due to hypertension, syphilis, and other causes. (396)

67. Angina pectoris despite the absence of coronary artery disease in a patient with aortic regurgitation may occur as a result of increased myocardial oxygen requirements in the presence of a decreased supply. The increase in myocardial oxygen requirements is due to left ventricular hypertrophy. The decrease in myocardial oxygen supply is due to a decrease in aortic diastolic pressure, which decreases coronary blood flow. Coronary blood flow to the left ventricle occurs during diastole, so lower diastolic pressures compromise it. Angina resulting from aortic regurgitation is typically a late and dismal sign. (396)

68. The anesthetic management of aortic regurgitation resembles the anesthetic management for mitral regurgitation. Considerations for the anesthetic management of patients with aortic regurgitation include the avoidance of sudden

decreases in heart rate, the avoidance of sudden increases in systemic vascular resistance, and minimizing drug-induced myocardial depression. (396)

69. Mitral valve prolapse is a valvular disease in which the valve prolapses into the left atrium during contraction of the left ventricle. Valve prolapse is caused by an abnormality of the valve support structure. Mitral valve prolapse on cardiac auscultation is characterized by a systolic murmur with a clicking sound. It has been estimated that 5% to 15% of the adult population has mitral valve prolapse, also called click-murmur syndrome. Currently, this estimate is believed to be higher than the true prevalence. The diagnosis of mitral valve prolapse can be confirmed through echocardiography. (396)

70. Mitral valve prolapse is associated with atrial secundum defects, von Willebrand syndrome, and polycystic kidney disease, as well as with musculoskeletal abnormalities such as Marfan syndrome, pectus excavatum, and kyphoscoliosis. Females are more likely than males to have mitral valve prolapse. (396)

71. Patients with mitral valve prolapse typically are asymptomatic. Symptoms that can be associated with mitral valve prolapse include palpitations, dyspnea, atypical chest pain, dizziness, and syncope. (396)

72. Potential complications of mitral valve prolapse include mitral regurgitation, infective endocarditis, transient cerebral ischemic events, cardiac dysrhythmias, and sudden death. Sudden death is extremely rare, however. Cardiac dysrhythmias associated with atrioventricular bypass tracts and preexcitation syndromes are fairly common in these patients. Transient cerebral ischemic events may lead to the prescription of aspirin or anticoagulants for patients with mitral valve prolapse. (395-396)

73. The maintenance of anesthesia in patients with mitral valve prolapse should be geared toward the avoidance of cardiac emptying. Cardiac emptying results in increased prolapse of the mitral valve into the left atrium. Avoidance of sympathetic nervous system stimulation, decreases in systemic vascular resistance, and the performance of surgery with patients in the head-up or sitting position will all minimize cardiac emptying. The intravascular fluid volume of the patient should be maintained at normal or high normal for the same reason. Hypotension in patients with mitral valve prolapse can be treated with phenylephrine. Cardiac dysrhythmias that occur intraoperatively should be promptly treated. Ketamine is not recommended in patients with mitral valve prolapse because of its propensity to increase myocardial contractility and heart rate. (397)

74. The potential problem with regional anesthesia in patients with mitral valve prolapse is the decrease in systemic vascular resistance that can be detrimental to these patients. Appropriate monitoring can make regional anesthesia the preferred anesthetic approach for some surgical patients with valvular heart disease. (397)

DISTURBANCES OF CARDIAC CONDUCTION AND RHYTHM

75. Tools available to the clinician for the diagnosis of disturbances in cardiac conduction and rhythm include an electrocardiogram, Holter monitoring, or an electrophysiology (EP) study. A Holter monitor is an ambulatory electrocardiogram that can be worn for days to document the occurrence of cardiac dysrhythmias and to assess the efficacy of treatment interventions. (397)

76. The conduction system of the heart includes the sinoatrial node, atrioventricular node, the bundle of His, and Purkinje fibers of the right and left bundle branches. Types of conduction defects include sinus node block, atrioventricular conduction defects, and intraventricular conduction defects. Atrioventricular conduction defects are classified as first-, second-, or third-degree heart blocks. Intraventricular conduction defects include right bundle branch block, left bundle branch block, and left fascicular hemiblock. Heart block below the atrioventricular

node is usually progressive and permanent, whereas heart block above the atrioventricular node is usually transient and benign. (397, Table 25-10)

77. The placement of a prophylactic artificial cardiac pacemaker before surgery is not indicated in a patient with a bifascicular block. The theoretical concern in preoperative patients with a bifascicular block is that the single remaining intact fascicle will become compromised by perioperative events, such as changes in hemodynamics, oxygenation, or electrolytes. This would lead to acute third-degree atrioventricular heart block. Third-degree atrioventricular block is also referred to as complete heart block because all the electrical activity from the atria fails to be conducted to the ventricles. Ventricular contractions in patients with third-degree atrioventricular block occur at a rate of about 40 beats per minute, typically too slow to maintain an adequate cardiac output. Fortunately, there is no evidence that bifascicular blocks proceed to third-degree atrioventricular block with enough consistency to warrant the prophylactic placement of a pacemaker. (398)

78. Third-degree atrioventricular heart block is treated by the placement of an artificial cardiac pacemaker. There are various methods by which this can be accomplished. An endocardial pacemaker lead may be inserted intravenously, an epicardial or myocardial lead may be placed by the subcostal approach, or noninvasive transcutaneous cardiac pacing can be started. The pharmacologic treatment of third-degree heart block involves a continuous infusion of isoproterenol, which can act as a medical pacemaker until artificial electrical cardiac pacing is implemented. (398)

79. Sick sinus syndrome occurs as a result of degenerative changes in the sinoatrial node and is associated with an inappropriate sinus bradycardia. In sick sinus syndrome, rapid heart rates inhibit the normal pacemaker activity of the sinoatrial node and lead to periods of asystole. Sick sinus syndrome therefore usually presents as bradycardia with episodes of supraventricular tachycardia. Treatment is by administering medicines to control tachycardia. When these medicines result in bradycardia, medical management is said to have failed and artificial cardiac pacemakers become the next line of treatment. Patients with sick sinus syndrome may be at a high risk for pulmonary embolism and may therefore be started on anticoagulants. (398)

80. Ventricular premature beats occur as a result of ectopic pacemaker activity at a level below the atrioventricular node. The premature ventricular contraction then spreads through the ventricular conducting system. The premature ventricular contraction often blocks the sinoatrial node's subsequent depolarization, leading to a characteristic pause until the next normal sinus beat is generated. The hallmark features of a ventricular premature beat on an electrocardiogram are representative of the aberrant conduction associated with the ventricular contraction. They include a premature occurrence, the absence of a P wave preceding the QRS complex, a wide and bizarre appearing QRS complex, an inverted T wave, and a compensatory pause after the premature beat. (398)

81. Premature ventricular beats warrant treatment when they occur more frequently than six times a minute, are multifocal, occur in a train of three or more, or take place during the ascending limb of the T wave, that is, during the refractory period of the ventricle. Treatment is typically with lidocaine at a dose of 1 to 2 mg/kg. Recurrent premature ventricular beats can be treated with a lidocaine infusion. Additional therapy, if necessary, may include amiodarone, β antagonists, bretylium, procainamide, quinidine, verapamil, or overdrive pacing. A search for an underlying cause of the premature beats should be the primary goal. (398)

82. Causes of ventricular premature beats include myocardial ischemia, arterial hypoxemia, hypercarbia, hypertension, hypokalemia, and mechanical irritation of the ventricles. (398)

83. Ventricular tachycardia may be diagnosed with the appearance of three or more consecutive, wide QRS complexes on the electrocardiogram occurring at an effective heart rate higher than 120 beats per minute. The QRS complexes must be greater than 0.12 second. The P waves have no fixed relationship to the QRS complex because the beat originates in the ventricle. The onset of ventricular tachycardia can be life threatening. Ventricular tachycardia should be treated with intravenous amiodarone as a bolus followed by an infusion if the patient is hemodynamically stable. Hemodynamic instability, loss of consciousness, or myocardial ischemia should prompt immediate electrical cardioversion. (398)

84. Preexcitation syndromes are defined as an activation of a portion of the ventricles by cardiac impulses that have originated in the atria but were conducted to the ventricles by an accessory conduction pathway. Activation of the ventricles during this syndrome occurs sooner than it otherwise would have because of the accessory pathway, making the QRS complex appear sooner than it would have if sinus rhythm were maintained. (398)

85. WPW syndrome is the most commonly occurring preexcitation syndrome. The incidence of this syndrome is 0.3% in the general population. These patients may have sporadic supraventricular tachycardia or atrial fibrillation. In extreme cases, the rapid heart rate may be associated with syncope or congestive heart failure. On the electrocardiogram, WPW syndrome is characterized by a short P–R interval and a wide QRS complex. There is also a characteristic delta wave that appears on the electrocardiogram. The delta wave, together with the QRS complex, represents the composite of cardiac impulses conducted by both the normal and accessory pathways. (398)

86. The most common cardiac dysrhythmia associated with WPW syndrome is paroxysmal atrial tachycardia. WPW syndrome is most frequently treated by catheter ablation of the accessory pathway. Identification of the accessory pathway is accomplished by electrophysiologic mapping. (398)

87. The goal of the anesthetic management of a patient with WPW syndrome is the avoidance of any events, such as anxiety or drugs, that can result in sympathetic nervous system stimulation. Any cardiac antidysrhythmic drugs should be continued throughout the perioperative period. An adequate depth of anesthesia should be achieved before direct laryngoscopy to ensure that the patient does not respond to the noxious stimulus with sympathetic nervous system activity, placing the patient at an increased risk of tachyarrhythmias. Reduction in the stimulation of laryngoscopy can be achieved with adequate doses of an intravenous induction agent such as propofol, thiopental, benzodiazepines, opioids, β-blockers, or with a bolus of lidocaine just before direct laryngoscopy. Ketamine is not recommended as it stimulates the sympathetic nervous system. The duration of laryngoscopy should also be as short as possible. (398)

88. Methods for the treatment of paroxysmal atrial tachycardia or fibrillation that can occur in the perioperative period in patients with WPW syndrome include the administration of adenosine or procainamide. Adenosine acts by prolonging the refractory period of the atrioventricular node, whereas procainamide acts by increasing the refractory period of the accessory pathways. β-adrenergic antagonists can be used to control the heart rate. When the tachydysrhythmias become life threatening, emergent electrical cardioversion is indicated. Of note, drugs such as verapamil and digitalis may actually result in an increase in ventricular response during the dysrhythmia by accelerating the conduction in the accessory atrioventricular pathway. (399)

89. Prolonged QT interval syndrome can be congenital or acquired. Acquired prolonged QT interval syndrome can be due to quinidine, tricyclic antidepressants, subarachnoid hemorrhage, hypokalemia, hypocalcemia, or hypomagnesemia. It may also present in the postoperative period after right radical neck dissection.

The diagnosis of prolonged QT interval syndrome is made when the QT interval is chronically greater than 0.44 second. Adverse events that are associated with a prolonged QT interval include ventricular dysrhythmias, syncope, and sudden death. The pharmacologic treatment of a chronically prolonged QT interval can include β antagonists or a left stellate ganglion block. These treatments are empirical. (399)

90. A congenital cause of a prolonged QT interval is thought to be due to an imbalance of autonomic innervation to the heart caused by decreases in right cardiac sympathetic nerve activity. A left stellate ganglion block is thought to work by decreasing left cardiac sympathetic nerve activity, thereby balancing the autonomic innervation to the heart. (399)

91. The goal of the anesthetic management of a patient with a chronically prolonged QT interval includes the avoidance of any events or drugs that are likely to cause sympathetic nervous system stimulation. General anesthesia has triggered life-threatening ventricular dysrhythmia and cardiac arrest in patients with this syndrome. β-adrenergic blockade may be instituted preoperatively to minimize this risk. Although thiopental prolongs the QT interval in normal patients, it has been used for the induction of anesthesia in patients with the syndrome without any problems. Direct laryngoscopy should be performed with the patient deeply anesthetized. Should acute ventricular dysrhythmias occur, they can be treated with a β antagonist. Procainamide and quinidine are both known to prolong the QT interval in normal patients and should probably be avoided. Lidocaine, which also prolongs the QT interval in normal patients, has been used to successfully treat ventricular dysrhythmias in these patients. Electrical cardioversion may be necessary in the event of dysrhythmias that become life threatening. (399)

ARTIFICIAL CARDIAC PACEMAKERS

92. The preoperative evaluation of a patient with an artificial cardiac pacemaker should include an understanding of the underlying cardiac condition that required placement of the pacemaker and an assessment of the current function of the pacemaker, brand, model, make, and magnet mode. (399)

93. A pacemaker should be evaluated by the anesthesiologist preoperatively so that the anesthesiologist has a good understanding of the pacemaker and its programming. For instance, the anesthesiologist should be aware of what the default rhythm is (should the pacemaker not capture), the type of pacemaker, the chamber paced, the chamber sensed, how to detect deterioration in battery function, who can reprogram the pacemaker, and the current rate and sensitivity settings of the pacemaker and magnet mode. A discussion with the electrophysiology service or the pacemaker company representative can quickly resolve any issues. (399)

94. Intraoperative monitoring that is important in a patient with an artificial cardiac pacemaker includes the electrocardiogram, pulse oximeter, and possibly an intraarterial catheter. Intraarterial catheters or a pulse oximeter that are not affected by electrocautery may allow for diagnosis of interference of the pacemaker by electrocautery. In a patient with third-degree heart block and no escape rhythm, intraarterial catheters can be quite helpful. Inhibition of the pacemaker by electrocautery may lead to pacemaker inhibition and asystole in patients with third-degree heart block. The intraarterial catheter or pulse oximeter provides a measure of blood flow and cardiac output during that period allowing rapid diagnosis of the interference between the electrocautery and the pacemaker. (399)

95. If the ground plate for the electrocautery is placed too near the pulse generator of the artificial cardiac pacemaker, there could be electromagnetic interference that is interpreted as spontaneous cardiac activity by the pacemaker. This interference may result in asystole due to an inhibition of pulse generator activity by the pacemaker. The ground plate should be placed as far away as possible from the pulse generator but at least 15 cm away. Other potential sources of mechanical

interference include electroconvulsive shock therapy, succinylcholine-induced fasciculations, and myoclonic movements. (399)

96. The selection of drugs or anesthetic techniques for a patient should not be altered by the presence of an artificial cardiac pacemaker. However, patients with pacemakers or implantable cardiac defibrillators have an increased risk of coronary artery disease and ventricular dysfunction and should be monitored and anesthetized with added caution. (399)

97. A "pacemaker" magnet should be kept in the operating room intraoperatively for patients with artificial cardiac pacemakers to convert the pacemaker modes to an asynchronous mode, or fixed rate, should it become necessary. For instance, if the patient's pacemaker stops functioning intraoperatively, placement of an external converter magnet over the pulse generator may convert the pacemaker to an asynchronous mode. The function of the magnet should be reviewed by the anesthesiologist before surgery. (399)

98. The most common cause of temporary pacemaker malfunction is the disruption of contact between the pacemaker electrode wires and the endocardium. Some causes of this disruption include muscular exertion, blunt trauma, cardioversion, and positive-pressure ventilation. When this occurs, pacemaker spikes will continue to be seen on the electrocardiogram, although there is no myocardial activity or pulse. Placement of a pulmonary artery catheter in a patient with an artificial cardiac pacemaker may disrupt the placement of transvenous endocardial electrodes if they have been placed in the 2 weeks preceding the procedure. (400)

ESSENTIAL HYPERTENSION

99. Essential hypertension has been defined as a sustained elevated blood pressure on more than one reading without any known cause. Systolic blood pressure greater than 160 mm Hg or diastolic blood pressure greater than 90 mm Hg have been arbitrarily defined as the limits at which hypertension begins. The benefits of the long-term treatment of patients with essential hypertension include decreases in the incidence of cerebrovascular accidents, congestive heart failure, and renal disease. (400)

100. The preoperative evaluation of a patient with essential hypertension should include a determination of the adequacy of blood pressure control, a review of the pharmacology of the antihypertensive drugs, and an evaluation of effects of the hypertension on other organs. (400)

101. Antihypertensives include angiotensin-converting enzyme inhibitors, calcium channel blockers, β-adrenergic antagonists, diuretics, and vasodilators. It is generally recommended that blood pressure medications be administered on their routine schedule in the perioperative period in the patient with essential hypertension. This includes medicines on the morning of the surgical procedure. Withdrawal of medications in the perioperative period can lead to an increase in complications and should be avoided. (400)

102. Medical problems that are frequently seen in patients with essential hypertension include congestive heart failure, coronary artery disease, cerebral ischemia, renal dysfunction, and peripheral vascular disease. Approximately 50% of patients with peripheral vascular disease can be assumed to have 50% or greater stenosis of one or more coronary arteries, even in the absence of symptoms. (400)

103. The curve for the autoregulation of cerebral blood flow in patients with essential hypertension is shifted to the right, such that autoregulation occurs at a higher pressure than it would for a normotensive patient. This implies that the same degree of absolute hypotension in patients with a history of hypertension may be more harmful than the same blood pressure would be for a normotensive patient.

Thus maintenance of blood pressure in the perioperative period should be relative to what the preoperative resting blood pressure is specific to that patient. (400)

104. Treating essential hypertension in patients before an elective procedure has been shown to be beneficial in decreasing the risk of intraoperative hypotension and myocardial ischemia. There have been multiple studies conducted regarding this topic. Studies have also shown that there is not an increased incidence of cardiac complications in hypertensive patients in the perioperative period as long as the diastolic blood pressure was not higher than 110 mm Hg preoperatively. (400)

105. Patients with essential hypertension frequently respond to the induction of anesthesia with an exaggerated decrease in blood pressure. This hypotension is thought to occur as a result of an unmasking of a decreased intravascular fluid volume status. (400-401)

106. Patients with essential hypertension are especially likely to respond to direct laryngoscopy with exaggerated increases in blood pressure, placing them at risk of myocardial ischemia. This response can be attenuated with adequate levels of anesthesia. It must be done with caution in hypertensive patients, because an excessive depth of anesthesia may produce hypotension in these patients as well. Other methods may be used to attenuate the sympathetic nervous system response to direct laryngoscopy and the associated exaggerated hypertension. For instance, esmolol or lidocaine may be administered just before direct laryngoscopy. In addition, the duration of direct laryngoscopy should be minimized. (401)

107. The goal for the anesthetic management of patients with essential hypertension is to minimize the fluctuations in blood pressure characteristic of these patients with anesthetics and antihypertensive medications as appropriate. The patient should also be continually monitored for evidence of myocardial ischemia via a continuous electrocardiogram. (401, Table 25-11)

108. The maintenance of anesthesia in patients with essential hypertension can be achieved through the administration of a volatile anesthetic in conjunction with an opioid, intravenous agents, or nitrous oxide. An anesthetic dose sufficient to attenuate hypertensive responses to surgical stimulation should be administered. The maintenance of normotension intraoperatively may also require the administration of other medicines, such as β antagonists, vasoconstrictors, or nitrates. (401)

109. Intraoperative hypotension in patients with essential hypertension can be managed by the administration of intravenous fluids, by decreasing the concentration of volatile anesthetics, and by the administration of vasopressors as necessary. (401-402)

110. Regional anesthesia is frequently an excellent choice in appropriate surgical cases for patients with cardiovascular disease. The administration of regional anesthesia in patients with essential hypertension has the theoretical problem of causing excessive decreases in systemic blood pressure. Hypotension can occur secondary to vasodilation associated with the sympathetic nervous system blockade in combination with the decreased intravascular fluid volume status often seen in patients with chronic hypertension. The anesthesiologist must be prepared to support the blood pressure as necessary when a regional anesthetic is administered to these patients. (401)

111. Hypertension occurs frequently in the early postoperative period in patients with a diagnosis of essential hypertension. Hypertension secondary to inadequate pain control should be considered. If hypertension persists despite adequate analgesia, the administration of additional doses of antihypertensives is likely necessary. (402)

CONGESTIVE HEART FAILURE

112. Congestive heart failure is highly correlated with postoperative morbidity. In fact, preoperative congestive heart failure is the single greatest preoperative risk factor for predicting postoperative morbidity. This suggests that the preoperative patient with congestive heart failure scheduled for elective surgery should not have his or her surgery until treatment of the congestive heart failure can be instituted and the patient's medical status optimized. (402)

113. The goal of the anesthetic management of patients with congestive heart failure who are undergoing urgent or emergent surgery is the optimization of cardiac output. Optimal cardiac output in patients with congestive heart failure undergoing anesthesia may be best achieved with careful hemodynamic management. The patient's chronic medications should be given preoperatively if there are no specific contraindications. Volatile anesthetics may produce a dose-dependent depression of cardiac muscle function that is greater in patients with congestive heart failure than in patients without congestive heart failure. In addition, the maintenance of myocardial contractility may necessitate the continuous administration of β-adrenergic agonists and vasoactive agents in the perioperative period. Avoidance of the administration of β-adrenergic agonists, if possible, may reduce overall risk. (403)

114. Positive-pressure ventilation of the lungs of patients in congestive heart failure may be beneficial because of its effect of decreasing pulmonary vascular congestion and improvement in arterial oxygenation. (403)

115. Monitors in the patient with congestive heart failure undergoing major surgery include an intraarterial catheter. Although there is no evidence to support the use of pulmonary artery catheters to monitor central filling pressures and cardiac output, they can be used to monitor the effects of inotropic, vasoactive agents, and volume status. Transesophageal echocardiography may be more useful than pulmonary artery catheterization but is not required. Monitors chosen should be influenced by the patient's medical status, risk-benefit ratios, and the surgical procedure. (403)

116. Regional anesthesia for peripheral surgery in patients with congestive heart failure can be administered safely but is not proven to have reliably better outcomes than general anesthesia for these patients. Mild decreases in the systemic vascular resistance produced by an epidural or spinal anesthetic may provide for improvement in cardiac output in the patient with congestive heart failure. Greater decreases in the systemic vascular resistance should be avoided if possible. (403)

HYPERTROPHIC CARDIOMYOPATHY

117. Hypertrophic cardiomyopathy is a genetically transmitted disease also known as idiopathic hypertrophic subaortic stenosis. The pathology that defines hypertrophic cardiomyopathy is the obstruction to left ventricular outflow produced by asymmetric hypertrophy of the intraventricular septal muscle. As a result of the obstruction to ventricular outflow, left ventricular hypertrophy develops to the degree that the volume of the left chamber is decreased. As the disease advances, the increased muscle mass in the subaortic region can lead to complete obstruction of left ventricular outflow. The stroke volume in patients with hypertrophic cardiomyopathy remains normal despite the physiologic changes. The normal stroke volume is reflective of the hypercontractile state of the myocardium. (403)

118. The goal of the anesthetic management of patients with hypertrophic cardiomyopathy is geared toward decreasing the pressure gradient across the obstructed left ventricular outflow tract. There are several methods of decreasing the left ventricular outflow obstruction in patients with hypertrophic cardiomyopathy. These include decreasing myocardial contractility, as with the administration of β antagonists; increasing the dose of volatile agents; increasing preload with increased intravascular fluid volume; and increasing afterload with α-adrenergic stimulation as is produced by phenylephrine. (403)

119. Intraoperative hypotension in patients with hypertrophic cardiomyopathy can be treated with the administration of intravascular fluids as well as phenylephrine. (404)

120. Intraoperative hypertension in patients with hypertrophic cardiomyopathy can be treated with the administration of increased concentrations of volatile anesthetics. (404)

121. The administration of β agonists for the treatment of hypotension in patients with hypertrophic cardiomyopathy can result in an increase in myocardial contractility and a corresponding increase in left ventricular outflow obstruction. Likewise, the administration of nitrates such as nitroprusside or nitroglycerin to these patients can increase left ventricular outflow obstruction by decreasing systemic vascular resistance, making them an unlikely choice for the treatment of hypertension. (404)

COR PULMONALE

122. Cor pulmonale is right ventricular hypertrophy and cardiac dysfunction that occurs as a result of pulmonary hypertension. The most likely cause of cor pulmonale is chronic obstructive pulmonary disease with associated chronic arterial hypoxemia leading to chronic pulmonary vascular vasoconstriction. Vascular smooth muscle hypertrophy and permanently increased pulmonary vascular resistance results from sustained pulmonary vascular vasoconstriction. When systemic acidosis is also present, there is a synergistic effect between arterial hypoxemia and acidosis on the pulmonary vasculature. In general, when the cause of the increased pulmonary vasculature resistance is due to arterial hypoxemia from chronic obstructive pulmonary disease, the prognosis is somewhat favorable if the arterial hypoxemia can be reversed with the administration of oxygen. Other causes of increased pulmonary vascular resistance leading to cor pulmonale, such as primary pulmonary hypertension or pulmonary fibrosis, have less favorable outcomes. (404)

123. Symptoms of cor pulmonale are often masked by the symptoms associated with the existence of coexisting chronic obstructive pulmonary disease. As the right ventricle becomes increasingly impaired, patients may experience syncope with exertion. Patients may also have chronic dependent edema, an enlarged liver, ascites, and dilated neck veins. On the lateral chest radiograph, right ventricular hypertrophy may present as a decrease in the retrosternal space. There may also be a decrease in pulmonary vascular markings. Right ventricular hypertrophy on the electrocardiogram would show peaked P waves in leads II, III, and aVF. Often there will also be right-axis deviation. On right-sided heart catheterization, the mean pulmonary artery pressure will be elevated, whereas the pulmonary artery occlusion pressure is normal. Pulmonary hypertension is considered mild with mean pulmonary artery pressure between 20 and 35 mm Hg and moderate when the pressure is greater than 35 mm Hg. (404)

124. The treatment of cor pulmonale is directed toward decreasing right ventricular work by decreasing the pulmonary vascular resistance. This reduction in pulmonary vascular resistance may be achieved through the correction of the patient's pH and through the administration of oxygen to reverse arterial hypoxemia if possible. Diuretics may also be administered for patients with congestive heart failure. Nitroglycerin administration may result in lowering of the pulmonary artery pressure and a decrease in pulmonary vascular resistance. Pulmonary vasodilation with prostaglandins, endothelial receptor antagonists, inhaled nitric oxide, type 5 phosphodiesterase inhibitors, or soluble guanylate cyclase inhibitors has been tried with variable success. (404)

125. Just as in any other patient, the patient with cor pulmonale who is scheduled for an elective surgical procedure should be medically optimized before the procedure. Any pulmonary infections should be treated. Patients should have any

bronchospasm reversed, be well hydrated, and have their electrolytes evaluated and corrected if necessary. (404)

126. The goal of the anesthetic management of patients with cor pulmonale is the avoidance of events or drugs that could result in an increase in pulmonary vascular resistance, thereby worsening right ventricular failure. Events that may result in an increase in pulmonary vascular resistance include arterial hypoxemia, hypercapnia, acidosis, and decreases in body temperature. An abrupt or significant decrease in the systemic vascular resistance should be avoided. Nitrous oxide should be avoided because of its potential for increasing pulmonary vascular resistance. Although positive-pressure ventilation may increase pulmonary vascular resistance, its potential benefit for improving arterial oxygenation likely outweighs its risk. An intraarterial catheter allows for arterial blood gas analysis to assess the effects of any interventions on the patient's arterial oxygenation and pH and should be considered essential. (404)

127. The advantage of monitoring pulmonary artery and central venous pressure during surgery in patients with cor pulmonale is the ability of the anesthesiologist to assess the hemodynamic effects of the surgical procedure and optimize pharmacologic and hemodynamic management. (404)

CARDIAC TAMPONADE

128. Cardiac tamponade occurs as a result of increased intrapericardial pressure from the accumulation of fluid in the pericardial space. The increase in pericardial pressures causes a decrease in compliance of the right ventricle, reducing right ventricular filling, stroke volume, and cardiac output, thus causing hypotension. The decrease in stroke volume results in sympathetic nervous system activation in an attempt to maintain cardiac output. Cardiac output and systemic blood pressure in these patients become dependent on heart rate and on a central venous pressure that exceeds the right ventricular end-diastolic pressure. (404)

129. Manifestations of cardiac tamponade include hypotension, tachycardia, vasoconstriction, equalization of diastolic filling pressures, increased central venous pressure, and a fixed stroke volume. These patients also have pulsus paradoxus. Pulsus paradoxus is a decrease in the arterial blood pressure by greater than 10 mm Hg during inspiration. This change in pressure is the opposite of what would be expected in normal patients and reflects the decrease in ventricular stroke volume that occurs with inspiration. On the chest radiograph, there may be a change in the cardiac silhouette when 250 mL or greater of fluid has accumulated in the pericardial space. Decreased voltages through all leads may be seen in patients with cardiac tamponade. Cardiac tamponade is best diagnosed through echocardiography. (404)

130. The definitive treatment of cardiac tamponade is the drainage of the pericardial fluid. Drainage can be achieved either percutaneously or by a pericardiotomy in the operating room under general or local anesthesia. Temporizing measures until definitive treatment include the expansion of the intravascular fluid volume; the administration of agents that will increase myocardial contractility, such as epinephrine, norepinephrine, or dopamine; and the correction of metabolic acidosis, which may depress myocardial contractility. Definitive care requires drainage of the pericardial fluid and may be life saving. (404)

131. Prior to the induction of general anesthesia, the patient should be prepped and draped and the surgeons scrubbed and ready to make an incision. Immediate hemodynamic collapse may occur with induction of general anesthesia that can only be resolved with surgical relief of the pericardial tamponade. The goal of the anesthetic management of patients with cardiac tamponade is the avoidance of events or drugs that could result in a decrease in cardiac output. Myocardial contractility, arterial blood pressure, increased heart rate, and venous return must

all be maintained. Rapid surgical drainage of the tamponade is critical to avoid hemodynamic collapse and death. (405)

132. The induction of anesthesia and positive-pressure ventilation of the lungs of patients with cardiac tamponade can result in profound, irreversible hypotension. Hypotension that occurs in response to positive-pressure ventilation of the lungs of these patients results from anesthetic-induced peripheral vasodilation, direct myocardial depression, and decreases in venous return from positive intrathoracic pressure. The recommendation for patients with cardiac tamponade is that, if at all possible, percutaneous pericardiocentesis be performed under local anesthesia to relieve some of the tamponade before the induction of anesthesia. This drainage should be done in the operating room with the patient spontaneously breathing and continually monitored. If time permits, monitors may include an intraarterial catheter for continuous arterial blood pressure monitoring and a central venous catheter to monitor central venous pressures. The ability to immediately surgically drain the pericardium should be established prior to the induction of general anesthesia. (404-405)

133. The recommendation for anesthesia in patients with cardiac tamponade is that percutaneous pericardiocentesis be performed under local anesthesia before the induction of anesthesia. If that is not possible, an awake orotracheal intubation should be considered. The patient should have the urgency of the need to perform the procedure explained, and the airway should be anesthetized topically. After confirmed orotracheal intubation, the patient can then be gently sedated while still spontaneously ventilating the lungs. Small doses of ketamine may be administered to the patient to provide analgesia and sedation during pericardiocentesis. The induction of anesthesia and positive-pressure ventilation if required for further surgical exploration should not be instituted until immediate drainage of the pericardial space can be achieved. (404-405)

134. Sympathetic nervous system stimulants, such as epinephrine, norepinephrine, dopamine, dobutamine, or isoproterenol, administered as continuous infusions may be useful in patients with cardiac tamponade although they will not preclude or prevent hemodynamic collapse and cardiac arrest with loss of ventricular filling. The pericardium must be drained to allow venous filling and cardiac output. (405)

ANEURYSMS OF THE AORTA

135. Most aortic aneurysms involve the abdominal aorta. About 95% of abdominal aortic aneurysms are due to atherosclerosis, in contrast to about 50% of thoracic aortic aneurysms. Other causes of aortic aneurysms include trauma, mycotic infection, connective tissue disorders such as Marfan syndrome, and syphilis. Only about 0.5% of abdominal aortic aneurysms extend into the renal arteries. (405)

136. A dissecting aneurysm occurs when a tear in the intima of the aorta separates the layers of the wall of the aorta. Blood is then allowed to enter and penetrate between the intima on one side and the media and adventitia layers on the other, creating a false lumen. The dissection can then reenter the true lumen through another tear in the intima, or it may rupture through the adventitia. Acute dissection may present as excruciating chest pain and patients may appear to be in shock. Peripheral pulses may be difficult to palpate. The treatment for aortic dissection is either surgical excision, usually followed by placement of a graft, or endovascular graft placement. Short-term management until a definitive treatment can take place may include decreasing blood pressure to the lowest acceptable level and the relief of pain. (405)

137. The risk of rupture of an abdominal aortic aneurysm is best predicted by the diameter of the aneurysm, as well as its rate of expansion. Elective resection of an abdominal aortic aneurysm is recommended when the diameter of the aneurysm is estimated to be 5 cm or greater. This recommendation is made based on the dramatic increase in the likelihood of spontaneous rupture of the aneurysm when

the size of the aneurysm exceeds 5 cm. Abdominal aortic aneurysms with a diameter less than 5 cm are typically followed with serial measurements to evaluate their rate of expansion. If the aneurysm expands by more than 0.5 cm in a 6-month period, or if the patient becomes symptomatic, surgical repair is recommended. (405)

138. Medical problems frequently associated with aortic aneurysms include hypertension, diabetes mellitus, ischemic heart disease, and atherosclerosis. (405)

139. The goal of the anesthetic management of patients undergoing resection of an abdominal aortic aneurysm is aimed toward the maintenance of cardiovascular and hemodynamic parameters at or near normal. Aggressive intraoperative monitoring is necessary to achieve this goal. Patients should have their intraarterial blood pressure closely monitored throughout the case. Perioperative administration of β-adrenergic antagonists, statins, and aspirin may reduce cardiac risk. (405)

140. Patients with coronary artery disease are especially at risk of myocardial ischemia during surgery for resection of an aortic aneurysm during cross-clamping of the aorta. Cross-clamping of the aorta at the suprarenal or supraceliac level creates the greatest increase in systemic vascular resistance and central venous pressure, and a decrease in cardiac output. On the pulmonary artery catheter, cross-clamping of the aorta would result in an increase in the pulmonary artery occlusion pressure. In contrast, cross-clamping the aorta below the level of the renal arteries creates minimal hemodynamic changes. The hemodynamic response to aortic cross-clamping is influenced by the patient's cardiac status, intravascular fluid volume, and anesthetic drugs and technique. Management of the patient during aortic cross-clamping should be aimed toward decreasing the systolic blood pressure and cardiac filling pressures. Pharmacologic agents that could be administered might include inhaled anesthetic agents, nitroprusside, or nitroglycerin. (405)

141. Intraoperative fluid management during surgery for resection of an aortic aneurysm is best guided by the data obtained from hemodynamic monitors, either from arterial pulse pressure variation, stroke volume variation, central venous and pulmonary arterial pressures, or transesophageal echocardiography. Optimal fluid management can be administered with appropriate hemodynamic monitoring. (405)

142. Hypotension frequently accompanies unclamping of the abdominal aorta during the resection of an aortic aneurysm. The hypotension is believed to occur as a result of the sudden increase in venous capacitance that accompanies unclamping. Even when the aortic cross-clamp is infrarenal, unclamping can result in a decrease in the systolic blood pressure by about 40 mm Hg. Methods for minimizing the hypotension include adequate volume replacement before unclamping and the gradual removal of the aortic cross-clamp to allow time for the pooled venous blood to circulate. It is prudent to use only short-acting vasodilators, such as inhaled agents, nitroprusside, or nitroglycerin, to treat increases in the systemic vascular resistance during aortic cross-clamping so that their effects can be reversed with titration or by discontinuation before unclamping of the aorta. The systemic vascular resistance may be increased after unclamping with the administration of phenylephrine if necessary. (405)

143. Renal function may become impaired postoperatively to the extent that hemodialysis is required after aortic aneurysm repair, particularly if the aortic cross-clamp was suprarenal. Coexisting renal disease appears to place the patient at the greatest risk of postoperative renal dysfunction, but other risk factors include the duration of aortic cross-clamp time, thrombotic or embolic interruption of renal blood flow, hypovolemia, and hypotension. Hypothermia may protect the kidneys during periods of ischemia. In an effort to decrease the risk of postoperative renal dysfunction, the intravascular fluid volume should be

maintained and the urine output should be closely monitored during aortic aneurysm repair. Mannitol is frequently given just before aortic cross-clamping to facilitate diuresis and maintain glomerular function. A loop diuretic may be also be administered in selected cases if the urine output is unsatisfactory. Alternatively, a continuous dopamine infusion at low doses may be started to dilate renal blood vessels to maintain renal blood flow and urine output. Unfortunately, none of these therapies have been definitively demonstrated to have efficacy for the prevention of renal dysfunction. (405)

144. Spinal cord ischemia and paraplegia can occur after supraceliac aortic cross-clamping for thoracic aortic aneurysm repair. The mechanism for the ischemia is most likely due to an interruption of a portion of the blood supply to the spinal cord. The spinal cord blood supply is from two posterior arteries and one anterior spinal artery. The greatest contributor to the blood supply of the anterior spinal artery is the artery of Adamkiewicz, whose origin is between T9 and T12 in 75% of patients. The anterior spinal artery supplies the motor tracts in the spinal cord. Mechanisms employed to reduce the risk of spinal cord ischemia include cerebrospinal fluid drainage, intrathecal papaverine injection, naloxone administration, barbiturate administration, hypothermia, and partial bypass. Hypothermia is believed to be the most effective method of neuroprotection through its effects of decreasing oxygen requirements. Cerebrospinal fluid drainage is thought to improve spinal cord perfusion because the spinal cord perfusion pressure is the distal mean aortic pressure minus the cerebrospinal fluid pressure. Cerebrospinal fluid drainage to improve spinal cord perfusion during aortic aneurysm repair remains controversial. (405)

CARDIOPULMONARY BYPASS

145. Blood is drained from the venae cavae during cardiopulmonary bypass by siphon action caused by gravity. The blood then passes from the cardiotomy reservoir, through a pump, a heat exchanger, an oxygenator, and a filter before it is returned to the arterial system. (406, Figure 25-3)

146. The two different types of pumps that are used to return blood to the arterial system during cardiopulmonary bypass are the roller pump and the centrifugal pump. The roller pump works by compressing the tubing that contains the fluid between a roller and curved metal back plate, producing flow. In contrast, the centrifugal pump produces flow and less trauma to blood. The flow rate generated by the centrifugal pump is affected by the resistance of the tubing and the patient's systemic vascular resistance. (406-407)

147. Blood is kept from entering the heart from the superior and inferior venae cavae during cardiopulmonary bypass for open heart or intracardiac surgery by placing both a superior and inferior vena caval cannulae, as well as ligatures placed around the superior and inferior vena cava proximal to the cannulae, thereby occluding the cava and preventing flow into the heart. All returning blood from the patient's venous system enters the cardiopulmonary bypass machine via the two large cannulae, which are placed in the superior and inferior venae cavae. (406-407)

148. The aorta is cross-clamped distal to the aortic valve and proximal to the inflow cannula during cardiopulmonary bypass to allow cardioplegic arrest. An incompetent aortic valve, in an arrested heart, without this cross-clamp, would allow blood to flow retrograde from the aorta into the heart, stretching the myocardium, and causing permanent muscle injury and ventricular dysfunction. (407)

149. Venous drainage from the inferior and superior venae cavae during cardiopulmonary bypass, which is achieved by gravity, can be facilitated by raising the operating table to a higher level, creating a larger vertical distance between the operating room table and the cardiopulmonary bypass machine or by adding negative pressure or suction to the cardiotomy reservoir. (407)

150. The required cardiac index that is delivered to the patient by the roller pump on the cardiopulmonary bypass machine depends on the patient's body temperature and oxygen consumption. A cardiac index of 2 to 2.4 L/min per meter squared is usually sufficient in the normothermic or slightly hypothermic patient. Flows of about half these levels have also been used without adverse effects. (407)

151. The advantage of low flows during cardiopulmonary bypass is that less trauma is sustained to the blood. Less noncoronary collateral blood flow returns to the heart as well, which may lead to better myocardial protection because less warm blood is entering the heart and counteracting the cold myocardial preservation solutions. (407)

152. Two different types of oxygenators that are used to oxygenate blood that is returning to the arterial system during cardiopulmonary bypass are a bubble oxygenator and a membrane oxygenator, although bubble oxygenators are rarely used at the present time. (407)

153. Advantages of a bubble oxygenator over a membrane oxygenator include its relative simplicity and lower cost. Disadvantages of a bubble oxygenator include an increase in the amount of turbulence and foaming it produces, and denaturing of blood proteins by direct contact with gas, resulting in trauma to blood that increases with the duration of the bypass time. Bubble oxygenators are rarely used in the current era. (407)

154. An advantage of a membrane oxygenator includes the relatively less trauma produced to the blood than that produced by a bubble oxygenator by avoiding direct exposure of blood to gas. Disadvantages of a membrane oxygenator include its increased complexity and cost. (408)

155. In addition to the usual methods of heating a patient's body intraoperatively, the body can also be heated or cooled during cardiopulmonary bypass through the use of heat exchangers that are incorporated into the extracorporeal circuit. These heat exchangers are able to heat or cool blood as it circulates through the extracorporeal circuit via a countercurrent flow system. (408)

156. Blood loss from the field can be recirculated to the patient during cardiopulmonary bypass by having the blood that is suctioned return to a cardiotomy reservoir. In the cardiotomy reservoir the blood is filtered, defoamed, and returned to the oxygenator. The blood is then recirculated to the patient after oxygenation. (408)

157. A problem with the cardiotomy suction used during cardiopulmonary bypass is that it is a significant contributor to the hemolysis and particulate emboli that occurs during cardiopulmonary bypass. (408)

158. Venting of the left ventricle may be necessary to prevent harmful left ventricular distention during cardiac surgery in which the heart is not opened. Persistent left ventricular distention may lead to permanent damage to the myocardial contractile elements. There are at least three reasons why the left ventricle might need a vent during cardiopulmonary bypass. First, incompetence of the aortic valve can lead to the retrograde flow of blood from the aorta to the heart. Second, there may be a large degree of blood flow from the coronary sinus and bronchial circulation back to the heart. Third, surgical positioning may result in backward flow from the aorta into the heart, or from the heart into the pulmonary veins. Finally, venting of the ventricle or pulmonary artery can help reduce risks of elevated pulmonary artery pressures during cardiopulmonary bypass. Venting of the left ventricle is achieved through the placement of a catheter into the left ventricle, usually through a pulmonary vein or via the left atrium. (407)

159. Systemic emboli from cellular debris are prevented from occurring during cardiopulmonary bypass through the use of filters that are incorporated into

the extracorporeal circuit in the cardiotomy reservoir and downstream after the oxygenator. (408)

160. Priming of the cardiopulmonary bypass system refers to the filling of the tubing of the cardiopulmonary bypass system with fluid and sometimes blood. The fluid consists of an osmotically active substance, an osmotic diuretic, an antibiotic, and electrolyte supplements. Blood is added if the patient's hematocrit necessitates it. (408)

161. Hemodilution of the patient's blood to a hematocrit of 20 to 25 during cardiopulmonary bypass lessens the viscosity of the blood. This decrease is important to facilitate circulation through the small vessels during hypothermia. (408)

162. It is essential to remove all air from the cardiopulmonary bypass system during cardiopulmonary bypass to prevent the pumping of air into the arterial system of the patient. (408)

163. Heparin-induced anticoagulation of the patient is mandatory before the institution of cardiopulmonary bypass to prevent patient death through clotting of the blood both in the patient and in the cardiopulmonary bypass machine. The dose of heparin that is usually administered is 300 to 400 units/kg. The adequacy of anticoagulation must be confirmed before the placement of the venous and aortic cannulae used for cardiopulmonary bypass. The adequacy of anticoagulation is usually confirmed by evaluating the activated clotting time, which should remain longer than 450 seconds throughout the course of cardiopulmonary bypass. The activated clotting time should be evaluated periodically during the course of cardiopulmonary bypass and additional heparin administered as necessary. After the cannulae are removed from the patient and cardiopulmonary bypass terminated, the effects of heparin may be reversed with the administration of protamine. The activated clotting time should return to baseline, typically between 90 to 120 seconds, after the administration of protamine. (408)

164. The low mean arterial pressure often seen after the institution of cardiopulmonary bypass is believed to be due to the peripheral vasodilation caused by the decreased viscosity, decreased temperature, and low oxygen content of infused priming solution. What pressures during cardiopulmonary bypass are sufficient to allow for coronary and cerebral perfusion is a subject of great debate. Most institutions prefer the mean arterial pressures to be about 50 mm Hg and to administer phenylephrine if blood pressure support is needed. Other institutions allow the mean arterial blood pressure to decrease to 40 mm Hg without any adverse effect. The perfusion pressures for extracorporeal circulatory support are even lower in infants and children. (408)

165. Blood pressure slowly rises spontaneously after some time on cardiopulmonary bypass as a result of vasoconstriction. The vasoconstriction may be in response to stimulation of the sympathetic nervous system or the renin-angiotensin system. It may also be an indication of inadequate perfusion to some tissues. (408)

166. The potential dangers of hypertension while on cardiopulmonary bypass include aortic dissection, intracerebral hemorrhage, and an increase in coronary and bronchial artery circulation, leading to increased return of warm blood to the heart during a time of cold cardioplegia. Hypertension under these circumstances can be treated by decreasing the systemic vascular resistance with a nitrate or a volatile anesthetic. Vaporizers have been incorporated into the cardiopulmonary bypass circuit for the administration of a volatile anesthetic to patients while on cardiopulmonary bypass. (409)

167. The patient can be monitored for adequate tissue perfusion during cardiopulmonary bypass several ways. First, urine output can be monitored as

a guide to renal perfusion. A renal output of 1 mL/kg each hour is considered sufficient. Second, the patient's acid-base status can be monitored for any evidence of a progressive metabolic acidosis. Third, the patient's mixed venous oxygen tension can be monitored for evidence of excessive oxygen extraction. A mixed venous P_{O_2} lower than 40 mm Hg is generally regarded as evidence of inadequate tissue perfusion. Finally, the nasopharyngeal temperature can be compared with a core temperature such as the bladder, rectum, skeletal muscle, or skin temperature. Whereas bladder temperature represents core temperature, the nasopharyngeal temperature is an indicator of perfusion to the brain. The greater the discrepancy between these two, the greater the indication of poor cerebral perfusion. Cerebral oximetry using infrared light can monitor adequacy of cerebral perfusion and may reduce risk of central nervous system injury. (409)

168. Diuresis is induced during cardiopulmonary bypass due to the inclusion of mannitol in the priming solution, hypothermia which interferes with renal tubular absorption, and well-perfused renal glomeruli with blood low in oncotic pressure due to hemodilution. For this reason during cardiopulmonary bypass the minimally acceptable urine output is 1 mL/kg/hr. Adequate urine output is important for the excretion of potassium administered in the cardioplegia solution. When the urine output is less than desired, a mechanical obstruction to urine flow in the catheter should be considered before instituting methods to increase the urine output. (409)

169. Causes of an increasing central venous pressure with or without facial edema while on cardiopulmonary bypass include aortic cannula flow into the carotid artery, obstruction of the superior vena cava cannula, and obstruction of jugular venous drainage by either a cannula, head position, or neck compression. Inadequate venous return from the patient to the cardiopulmonary bypass machine is an indication that one of these may have occurred. (409)

170. Causes of increasing abdominal distention while on cardiopulmonary bypass include obstruction of the inferior vena cava cannula, intraabdominal hemorrhage or ascites, or gastrointestinal distention by gas or fluid. (409)

171. The most serious complications of cardiopulmonary bypass include aortic dissection, carotid artery dissection, air in the aortic inflow tubing, and clotting of the bypass circuit. (409)

172. Ventilation of the lungs of a patient is not necessary during cardiopulmonary bypass. The lungs can be ventilated with oxygen during partial cardiopulmonary bypass, or when there is partial pulmonary blood flow. Evidence of pulmonary blood flow is seen as pulsatile pulmonary artery flow on the pulmonary artery catheter tracing. (409)

173. The goal of myocardial preservation during cardiopulmonary bypass is the minimization of the effects of ischemia on the heart. Myocardial protection is achieved in a variety of ways, all of which are aimed toward reducing the myocardial oxygen requirement of the heart during that period. Myocardial cooling can be achieved by hypothermic cardiopulmonary bypass, by the direct placement of ice on the epicardium, through pericardial irrigation with iced fluid, and by the intracoronary infusion of a cold cardioplegia solution. Myocardial arrest is achieved by the infusion of cardioplegia solution containing potassium both through a cannula at the aortic root and by retrograde flow through the coronary sinuses. The potassium causes cessation of electrical and mechanical cardiac activity by blocking the initial phase of myocardial depolarization. The prevention of myocardial rewarming during cardiopulmonary bypass can be achieved by placing a vent in the left ventricle or by placing a cross-clamp in the aorta distal to the aortic valve. (409)

174. The oxygen consumption of a normally contracting heart at 30° C is 8 to 10 mL/100 g of heart muscle in a minute. The oxygen consumption of a fibrillating

heart at 22° C is 2 mL/100 g per minute, and the oxygen consumption of an electromechanically quiet heart at 22° C is approximately 0.3 mL/100 g per minute. (409)

175. The effectiveness of cold cardioplegia of the heart can be measured by placing a temperature probe in the left ventricle and directly measuring the temperature of the heart. The absence of any electrical activity on the heart is also a good indication that the heart muscle is effectively quiescent. (409)

176. Two potential negative effects of the intramyocardial hyperkalemia of the cold cardioplegia solutions after cardiopulmonary bypass are decreased myocardial contractility and an increased incidence of atrioventricular heart block while coming off cardiopulmonary bypass. These can both be treated with the administration of calcium and, if necessary, insulin with or without glucose. In addition, the atrioventricular block can be treated through the use of an artificial cardiac pacemaker. The pacemaker is usually only needed temporarily because the atrioventricular block typically only lasts for 1 to 2 hours after discontinuing cardiopulmonary bypass. (409)

177. Two potential sources for systemic hyperkalemia during cardiopulmonary bypass are the recirculation of cardioplegia solution that has drained into the blood and decreased renal function. Hyperkalemia that persists at the conclusion of cardiopulmonary bypass can be treated with the administration of insulin and glucose in addition to calcium, or by ultrafiltration on the extracorporeal bypass circuit, or by administration of diuretics such as furosemide. (410)

178. Although there is a decreased minimum alveolar concentration (MAC) under hypothermic conditions, the decrease in MAC may not be sufficient to offset the sudden dilution of anesthetics that occurs when the patient is placed on cardiopulmonary bypass. For this reason, supplemental intravenous anesthetics may be needed during cardiopulmonary bypass in some cases to ensure an adequate depth of anesthesia. (410)

179. There is a sudden dilution of the neuromuscular blocking drug level that occurs when the patient is placed on cardiopulmonary bypass. Supplemental neuromuscular blocking drug should be administered just prior to the initiation of extracorporeal circulatory support or cardiopulmonary bypass to ensure there is a neuromuscular blocking drug level sufficient to prevent patient movement during this important portion of the procedure. (410)

180. Although supplemental anesthesia is not routinely required during rewarming after the conclusion of cardiopulmonary bypass, it is important that the anesthesiologist be aware that the rewarming patient could be returning to consciousness in a paralyzed state. Low-dose inhaled agents reduce the risk of intraoperative awareness. There are a number of choices for post bypass anesthesia, including dexmedetomidine, propofol, opiates, benzodiazepines, volatile agents, or a combination of agents. Intravenous infusions allowing continued sedation into the intensive care unit are commonly chosen. (410)

181. Conditions in the patient that must be present for the discontinuation of cardiopulmonary bypass include hemodynamic stability; normothermia; the venting of all arterial air; an adequate cardiac rate, rhythm, and output; normal acid-base status and electrolyte levels; ventilation of the lungs; and an adequate intravascular status and hematocrit. (410, Table 25-15)

182. The aortic and vena cava cannulae are removed after an adequate blood pressure and cardiac output have been maintained by the heart for several minutes. For optimal safety, the ability to rapidly reestablish cardiopulmonary bypass should be maintained for some time after the discontinuation of cardiopulmonary bypass. (412)

183. Potential problems associated with persistent hypothermia after cardiopulmonary bypass include coagulopathy, hypertension, tachycardia and sympathetic nervous system stimulation, shivering, metabolic acidosis, and difficulty in defibrillating the heart and maintaining a normal cardiac rhythm. The effects of persistent hypothermia on the heart are particularly evident at temperatures less than 34° C. Rewarming a patient's body can be achieved more rapidly after systemic vasodilation through the administration of a vasodilator, such as nitroprusside, or a volatile anesthetic. (410)

184. A special precaution that must be taken before discontinuing cardiopulmonary bypass in patients who have had the heart opened, as during valve replacement surgery, is the venting of all air from the heart. This can be accomplished by surgical massage of the left atrium and ventricle. In addition, rotating the table from side-to-side simultaneous with the maintenance of positive-pressure ventilation of the lungs and placement of the patient's head at a lower level than the heart may assist in venting any air from the heart. Positive pressure of the lungs should be maintained during the removal of the left ventricle vent cannula. The avoidance of nitrous oxide administration after cardiopulmonary bypass might minimize the potential increase in the size of microemboli that may have occurred. The potential risk of air remaining in the heart at the conclusion of cardiopulmonary bypass is the embolization of air to the arterial circulation, especially the coronary and cerebral circulations. Air is most likely to embolize from the heart after cardiopulmonary bypass during manipulation of the heart and alterations in the anatomy, closure of the sternum, and movement of the patient. (410-412)

185. (411, Table 25-5)

Table 25-5

Blood Pressure	*Atrial Pressure*	*Cardiac Output*	*Diagnosis*	*Therapy*
Decreased	Increased	Decreased	Left ventricular dysfunction	Inotrope Vasodilator Mechanical assistance
Decreased	Decreased	Decreased	Hypovolemia	Intravascular fluid administration
Decreased	Decreased	Increased	Vasodilation, low blood viscosity	Erythrocyte administration
Increased	Increased	Decreased	Vasoconstriction, left ventricular dysfunction	Vasodilator Inotrope
Increased	Decreased	Increased	Hyperdynamic	Volatile anesthetic β antagonist

186. Posterior papillary muscle dysfunction after cardiopulmonary bypass can occur as a result of inadequate cooling of the posterior myocardium during cardiopulmonary bypass. The posterior myocardium is the portion of the heart muscle that is most vulnerable to inadvertent warming of the heart from the return of blood from the coronary and bronchial circulations, as well as any potential blood that flows retrograde via an incompetent aortic valve. Posterior papillary muscle function impairment would manifest as mitral regurgitation. In addition, prominent *v* waves would be evident on the pulmonary artery occlusion pressure tracing. (411)

187. In some situations the cardiac output of the patient on discontinuation of cardiopulmonary bypass is inadequate because of either poor myocardial function

or refractory myocardial ischemia. Under these circumstances the intraaortic balloon pump is a mechanical addition to the pharmacologic support of cardiac output. An intraaortic balloon pump is a balloon that is 25 cm long and mounted on a long plastic catheter. The pump is advanced from the left femoral artery to the aorta. The pump inflates and deflates timed to the electrocardiogram. Inflation of the balloon, which occurs during diastole, increases the diastolic blood pressure and increases the coronary perfusion pressure gradient. Deflation of the balloon occurs just before systole. This allows for a reduction of afterload and the pressure against which the heart has to pump. Overall the intraaortic balloon pump increases coronary blood flow by increasing diastolic pressure while decreasing the work of the myocardium and thus the myocardial oxygen requirement. The efficacy of the balloon pump is altered by rapid heart rates, cardiac dysrhythmias, and aortic insufficiency. (411-412)

188. Protamine administration after termination of extracorporeal circulatory support, cardiopulmonary bypass, should take place prior the removal of the aortic cannulae to allow rapid return to extracorporeal circulatory support in the case of severe protamine reaction. If a protamine reaction occurs and return to extracorporeal circulatory support is required, additional heparin in doses of 300 to 400 units/kg may be required depending on the dose of protamine administered. Protamine is administered to reverse the anticoagulant effects produced by heparin. (412)

189. Side effects associated with the administration of protamine include hypotension due to vasodilation, myocardial depression, pulmonary hypertension, histamine release, and, rarely, anaphylactic or anaphylactoid reactions. Anaphylactic and anaphylactoid reactions can be associated with bronchospasm and pulmonary edema. These potential effects of protamine call for the careful, slow titration of protamine administration. (412)

190. Blood and fluid that remain in the cardiopulmonary bypass circuit after cardiopulmonary bypass are washed, collected, and placed in plastic bags by the perfusionist. The blood and fluid can then be administered to the patient. (412)

191. A gradient between central aortic and radial artery blood pressures can exist in the early period after cardiopulmonary bypass. Although the exact mechanism for this is not known, it is believed to be due to vasoconstriction in the extremity. The discrepancy can be determined by the surgical placement of a needle in the aorta and transduction of the pressure. Although the duration of this effect is typically only about 60 minutes, a femoral artery catheter can be placed for the transduction of arterial pressure if the discrepancy is large. (412)

Chapter

23 CONGENITAL HEART DISEASE

Isobel A. Russell

FUNDAMENTAL PATHOPHYSIOLOGY IN CONGENITAL HEART DISEASE

1. When does shunting occur in congenital heart disease?
2. What is the usual limitation to the direction and amount of shunt flow?
3. When does a left-to-right shunt occur?
4. What is the physiologic effect of a left-to-right shunt on the pulmonary blood flow (Qp) relative to the systemic blood flow (Qs)?
5. What are the long-term effects of increased pulmonary blood flow that occurs in a left-to-right shunt?
6. Give an example of a congenital heart defect that results in a left-to-right shunt.
7. When does a right-to-left shunt occur? What is the physiologic effect of this?
8. Give an example of a congenital heart defect that results in a right-to-left shunt.
9. What are mixing lesions in congenital heart disease? How do mixing lesions affect the systemic arterial oxygen saturation?
10. What determines the Qp:Qs ratio in mixing lesions?
11. What is the ideal Qp:Qs ratio in mixing lesions? Why?
12. What are some factors that can increase systemic vascular resistance?
13. What are some factors that can decrease systemic vascular resistance?
14. What are five factors that increase pulmonary vascular resistance?
15. What are five factors that decrease pulmonary vascular resistance?
16. What is Eisenmenger syndrome?

PERIOPERATIVE MANAGEMENT

17. What are some ways an anesthesiologist can prepare for a patient requiring surgery for congenital heart disease?
18. What preexisting conditions might be important to the care of patients with congenital heart disease?
19. What information might be gained from preoperative echocardiograms or magnetic resonance imaging (MRI)?
20. What is a risk factor from a previous sternotomy?
21. What are the fasting recommendations for infants and children scheduled for congenital heart surgery?
22. What is the most important feature of the intravenous administration set up for the patient scheduled for congenital heart surgery?
23. What are some common side effects of the induction of anesthesia using inhaled agents, such as sevoflurane or halothane?
24. What are some side effects of an intravenous induction of anesthesia using opioids such as fentanyl?
25. What are some side effects of an intravenous induction of anesthesia using ketamine, a drug that preserves sympathetic nervous system tone?

26. What are some general principles for the induction of anesthesia that might apply to all patients with congenital heart disease?
27. What are the goals for the anesthetic management in patients with a left-to-right shunt?
28. What are the goals for the anesthetic management in patients with a right-to-left shunt?
29. What are some considerations for the ventilatory management in patients with congenital heart disease?
30. For lesions with excessive pulmonary blood flow such as ventricular septal defects or atrioventricular septal defects, how should the pulmonary vascular resistance be managed prior to cardiopulmonary bypass?
31. For critically ill patients such as those with truncus arteriosus, what is an important feature of ventilator management prior to cardiopulmonary bypass?
32. For the Norwood procedure for hypoplastic left heart syndrome, what is an important aspect of anesthetic management prior to cardiopulmonary bypass?
33. During the Glenn procedure, what is an important aspect of anesthetic management?
34. What are poor prognostic factors of a successful Fontan procedure?
35. What are some common congenital lesions that result in inadequate pulmonary blood flow? What would be an important aspect of ventilatory management of patients with these lesions?
36. Where is the appropriate placement of an arterial line during surgery for coarctation of the aorta?
37. During induction of anesthesia for patients with obstructive lesions such as aortic stenosis, what is the most important to avoid?
38. What are some common abnormalities seen in patients with Williams syndrome?
39. How should the size of the endotracheal tube be selected?
40. What are some monitors that might be required for children undergoing surgery for congenital heart disease?
41. What are some general requirements for the selection of blood products for infants requiring cardiac surgery?
42. What are some antifibrinolytic drugs used in congenital heart surgery?
43. How is anesthesia maintained prior to cardiopulmonary bypass?
44. What patients may be able to have early extubation of the trachea?
45. What is a useful way to monitor the cardiac output and circulatory system?
46. How is anticoagulation for cardiopulmonary bypass achieved?
47. What is the target activated clotting time (ACT) value?
48. How are flow rates adjusted during cardiopulmonary bypass for infants and children?
49. How does the perfusionist control oxygenation and ventilation during cardiopulmonary bypass?
50. How is blood temperature adjusted during cardiopulmonary bypass?
51. How is mechanical quiescence and myocardial protection provided during cardiopulmonary bypass?
52. What is the lowest acceptable level of anemia during cardiopulmonary bypass?
53. What measures are used to provide cerebral and myocardial protection during cardiopulmonary bypass?
54. Which surgical repairs require the use of deep hypothermic circulatory arrest?
55. What are some potential negative effects of persistent hypothermia after cardiopulmonary bypass?
56. How can relative bradycardia and atrioventricular node conduction failure during separation from cardiopulmonary bypass be treated?
57. How are patients with long-standing excessive pulmonary blood flow treated on separation from bypass?
58. What is the best approach to the management of a patient who has had a palliative procedure and is left with a mixing lesion? What is an effective monitoring tool in these patients?
59. What are some common vasoactive drugs used during separation from cardiopulmonary bypass?

60. What are some causes of difficulty in separation from cardiopulmonary bypass in congenital heart surgery?
61. What rescue measure can be used if a patient cannot be weaned from cardiopulmonary bypass?
62. What are important complications of protamine administration?
63. What are contributors to postoperative coagulopathy in congenital heart surgery?
64. What is the best method to replace blood components in infants?
65. What is a common side effect of the administration of citrated blood products?
66. What agents can be used for refractory bleeding after cardiopulmonary bypass?
67. What are common parameters to be actively managed after pediatric cardiac surgery in the intensive care unit?

ANSWERS*

FUNDAMENTAL PATHOPHYSIOLOGY IN CONGENITAL HEART DISEASE

1. Under normal physiologic conditions, pulmonary blood flow and systemic blood flow do not mix, and the entire cardiac output flows in one direction. Shunting occurs when a portion of the venous return is redirected back to the arterial outflow of the same circulation. The shunt occurs when there is an abnormal communication between the pulmonary blood flow and systemic blood flow. (418)
2. A shunt occurs when there is an abnormal communication, or defect, between the pulmonary and systemic circulations. The direction of the shunt flow is dictated by the relative pressures between the communicating structures. The amount of shunting is limited by the size of the defect. (418)
3. A left-to-right shunt occurs when part of the pulmonary venous return is redirected toward the pulmonary arterial system. This can occur through anomalies in the pulmonary veins, atrial septum, ventricular septum, or at the great vessels. (419)
4. The physiologic effect of a left-to-right shunt is that the total pulmonary blood flow (Qp) is greater than the systemic blood flow (Qs); that is Qp becomes greater than Qs. This can result in hypotension and pulmonary edema. (419)
5. Long-term effects of an increase in pulmonary blood flow, as occurs in a left-to-right shunt, are an increase in pulmonary vascular resistance and abnormal cardiac chamber dilation. In addition, prolonged hypotension can lead to circulatory shock and multiple organ failure. (419)
6. An example of a left-to-right shunt congenital heart lesion would be an atrial septal defect (ASD). (419)
7. A right-to-left shunt occurs when a portion of the systemic venous return is redirected to the systemic arterial outflow without first circulating through the lung. Physiologically this would result in desaturated blood returning to the systemic circulation, and potentially arterial hypoxemia. The degree of hypoxemia would be dictated by the magnitude of the shunt. (419)
8. An example of a right-to-left shunt congenital heart lesion would be tetralogy of Fallot. (419)
9. Mixing lesions in congenital heart disease describes a complete blending of the pulmonary and systemic circulations such that there is identical or nearly identical oxygen saturations in both circulatory systems. In mixing lesions the systemic arterial oxygen saturation decreases. (419)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

10. In mixing lesions, the Qp:Qs ratio is determined by the relative resistance of blood flow in the pulmonary and systemic circulatory systems. That is, in mixing lesions, the ratio of blood flow is determined by pulmonary vascular resistance and systemic vascular resistance. (420)

11. The ideal Qp:Qs ratio in mixing lesions is 1. Any preferential flow toward the systemic circulation would be at the expense of greater desaturation and therefore less oxygen delivery. Conversely, any preferential flow toward the pulmonary circulation would be at the expense of cardiac output, and therefore less oxygen delivery to the tissues. (420)

12. Factors that can increase systemic vascular resistance are light anesthesia, systemic nervous system activation, administration of α agonists, and physical manipulations such as flexing the hips of infants and small children. (420, Table 26-2)

13. Factors that can decrease systemic vascular resistance are deep anesthesia and the administration of vasodilating drugs, such as nitrates and inhaled anesthetics. (420, Table 26-2)

14. Five factors that increase pulmonary vascular resistance are alveolar hypoxemia, hypercapnia, acidosis, light anesthesia, and hypothermia. Other factors include high lung volumes and pressures, or low lung volumes with atelectasis. (Table 26-2)

15. Five factors that decrease pulmonary vascular resistance are hyperventilation with resultant hypocarbia, alkalosis, oxygenation, pulmonary vasodilators such as inhaled nitric oxide, warmth, and bronchodilators such as albuterol. (Table 26-2)

16. Eisenmenger syndrome is a condition that can develop when pulmonary blood flow is increased over a long period of time, and the direction of the shunt flow becomes irreversibly left-to-right. This syndrome occurs due to a remodeling of pulmonary vasculature, an increase in pulmonary vascular resistance, and ultimately pulmonary hypertension yielding a pulmonary systolic blood pressure that is higher than systemic systolic blood pressure. (420)

PERIOPERATIVE MANAGEMENT

17. An anesthesiologist should prepare by understanding the physiology of the congenital heart lesion and the subsequent effects of the planned surgery. Aspects of the patient's condition that can be improved prior to surgery should be identified. (421)

18. Preexisting conditions that might be important to the care of patients with congenital heart disease include a history of prematurity, trisomy 21, DiGeorge syndrome, and chronic illness such as renal dysfunction, pulmonary edema, and electrolyte abnormalities. In addition, the preoperative evaluation of morning admission patients scheduled for congenital heart surgery should include the usual preoperative evaluation of pediatric patients, such as evaluation for new upper respiratory tract infections. (421)

19. Important preoperative information that could be derived from the magnetic resonance imaging (MRI) and echocardiograms would be anatomic manifestations of disease, such as an existing ventricular septal defect and concomitant right ventricular hypertrophy. (421)

20. Risk factors from previous sternotomy include increased operative blood loss and cardiac trauma during dissection secondary to adhesions that may have formed adherent to the sternum and chest wall. (421)

21. Fasting recommendations for infants and children scheduled for congenital heart surgery should follow the standard American Society of Anesthesiologist guidelines. (421)

22. The most important feature of intravenous administration set up for patients scheduled for congenital heart surgery is to meticulously de-air the system. The inadvertent introduction of an air bubble into the patient's vascular system via the intravenous tubing can result in an air embolus entering the systemic circulation in a patient with a left-to-right shunt. Although the risk is greater in patients with right-to-left shunts, patients with left-to-right shunts may have reversal of their shunt during certain phases of the cardiac cycle, during cardiopulmonary interventions as during manual manipulation of the heart during surgery, or with coughing in the awake patient. (421)

23. Some common side effects of induction of anesthesia with inhaled agents, such as sevoflurane or halothane, include myocardial depression, decreased heart rate and myocardial contractility, and decreased systemic vascular resistance. A halothane induction may also have associated myocardial dysrhythmia and ventricular irritability. (422-424, Table 26-4)

24. Some side effects of an intravenous induction of anesthesia using opioids such as fentanyl would include bradycardia and loss of sympathetic tone. (425, Table 26-4)

25. Some side effects of an intravenous induction of anesthesia using ketamine might include increases in heart rate and myocardial depression. (425, Table 26-4)

26. Some general principles for the induction of anesthesia that might apply to all patients with congenital heart disease would include the avoidance of dehydration, maintaining the patient in sinus rhythm, avoiding myocardial depression, and avoiding air entrapment in the intravenous and pressure tubings. (423, Table 26-5)

27. The goals for the anesthetic management in patients with a left-to-right shunt are aimed toward the avoidance of hemodynamic changes, such as an increase in systemic vascular resistance that will increase the magnitude of the shunt. Decreases in the magnitude of the shunt can be achieved through decreases in the arterial pressure and increases in the pulmonary vascular resistance, as with positive-pressure ventilation.

28. The goals for the anesthetic management in patients with a right-to-left shunt are aimed toward the avoidance of worsening arterial hypoxemia by increasing the magnitude of the shunt. Decreases in systemic vascular resistance and increases in pulmonary vascular resistance should be avoided.

29. Ventilatory management of the patient with congenital heart disease depends on how the circulatory system will be affected by changes in the pulmonary vascular resistance relative to the systemic vascular resistance. The goal is to minimize the impact on blood flow across shunts, and the cardiac lesion must be understood to best manage the patient. Adjustments in the fractional inspired oxygen concentration, minute ventilation, peak inspiratory pressure, and the possible use of the positive end-expiratory pressure are all considerations. (425)

30. For lesions with excessive pulmonary blood flow, such as ventricular septal defects or atrioventricular septal defects, one should avoid decreases in the pulmonary vascular resistance prior to cardiopulmonary bypass. (Table 26-5)

31. For critically ill patients such as those with truncus arteriosus, an important feature of ventilator management prior to cardiopulmonary bypass is to closely manage the ratio of systemic to pulmonary vascular resistance. (Table 26-5)

32. During the Norwood procedure (stage I for hypoplastic left heart syndrome), an important aspect of anesthetic management prior to cardiopulmonary bypass is to maintain the infusion of prostaglandins, maintain nearly equal systemic and pulmonary blood flow, and protect against myocardial depression and air embolism. (Table 26-5)

33. During the Glenn procedure (stage II procedure for hypoplastic left heart syndrome), an important aspect of anesthetic management is to maintain a high hematocrit and recognize that positive-pressure ventilation might decrease pulmonary blood flow and cardiac output. (Table 26-5)

34. Poor prognostic factors of a successful Fontan procedure (stage III procedure for hypoplastic left heart syndrome) include high pulmonary vascular resistance, tricuspid regurgitation, and decreased ventricular function. (Table 26-5)

35. Common congenital lesions that result in inadequate pulmonary blood flow include transposition of the great arteries, tetralogy of Fallot, tricuspid or pulmonary atresia, and total anomalous venous return. An important aspect of the ventilatory management of patients with these lesions would be to decrease pulmonary vascular resistance. (Table 26-5)

36. The appropriate placement of an arterial line during surgery for coarctation of the aorta is in the right arm. (Table 26-5)

37. During induction of anesthesia for patients with obstructive lesions such as aortic stenosis, it is most important to avoid tachycardia. (Table 26-5)

38. Some common abnormalities seen in patients with William syndrome are supravalvar aortic stenosis, pulmonary arterial stenosis, and coronary artery abnormalities. (Table 26-5)

39. The endotracheal tube size should be selected according to the age and size of the patient. (Table 26-5)

40. Some monitors that might be required for children undergoing surgery for congenital heart disease would include arterial pressure monitoring and transesophageal echocardiography. Monitors are selected on a case-by-case basis and what is standard for the institutional practice. (425)

41. Some general requirements for the selection of blood products for infants requiring cardiac surgery are that the blood should be the freshest when possible, that is less than 5 days of storage. Older blood can become significantly hypokalemic and result in leftward shifting of the oxygen-hemoglobin dissociation curve. (425)

42. Examples of commonly used antifibrinolytic drugs used in congenital heart surgery are aminocaproic acid and tranexamic acid. (426)

43. Prior to cardiopulmonary bypass, maintenance of anesthesia is usually achieved with a combination of intravenous agents and volatile anesthetics to avoid myocardial depression. (426)

44. Early extubation of the trachea may be performed in patients with simple defects, good cardiac reserve, and those undergoing the Glenn or Fontan procedure. (426)

45. A useful way to monitor the cardiac output and circulatory system is to conduct early and repeated arterial blood gas measurements to allow for appropriate ventilator and acid-base management. (426)

46. Anticoagulation for cardiopulmonary bypass is achieved using unfractionated heparin (3 to 4 mg/kg). (426)

47. The target activated clotting time (ACT) value is over 400 but the level required varies in individual practices. (426)

48. Flow rates are adjusted during cardiopulmonary bypass to maintain an age appropriate mean arterial blood pressure. Parameters used to calculate the flow rate needed to maintain metabolic function are the patient's size and estimated blood volume. (426)

49. The perfusionist controls oxygenation and ventilation during cardiopulmonary bypass by adjusting the blend of air and oxygen (F_{IO_2}) and the flow rate (sweep) of the fresh gas. (426)

50. Blood temperature is adjusted during cardiopulmonary bypass by running cooled or warmed water through a coil in contact with the blood path. (426)

51. Mechanical quiescence and myocardial protection is provided during cardiopulmonary bypass through the administration of cold hyperkalemic crystalloid solution. (426)

52. The lowest acceptable level of anemia during cardiopulmonary bypass varies from institution to institution, but is commonly in the range of 20% to 30%. (427)

53. During cardiopulmonary bypass, cerebral and myocardial protection is achieved by mild to moderate systemic hypothermia. Active rewarming is usually initiated toward the end of cardiopulmonary bypass. (427)

54. Surgical repairs of the aorta and aortic arch require deep hypothermic circulatory arrest. (427)

55. Potential negative effects of persistent hypothermia after cardiopulmonary bypass include myocardial ischemia, cardiac dysrhythmias, elevated pulmonary vascular resistance, coagulopathies, and renal dysfunction. (427)

56. Relative bradycardia or atrioventricular node conduction failure that occurs during separation from cardiopulmonary bypass can be treated by temporary cardiac pacing. (427)

57. Patients with long standing excessive pulmonary blood flow may have underlying pulmonary hypertension, and may benefit from maneuvers that minimize pulmonary vascular resistance during separation from bypass. (427)

58. When a patient has had a palliative procedure and is left with a mixing lesion, the best approach to management is to balance the circulatory system so that the pulmonary vascular resistance and systemic vascular resistance yield a balanced circulation. An effective monitoring tool in these patients is the pulse oximeter. A balanced circulatory system in these patients will result in a systemic oxygen saturation of 80%. Excessive pulmonary blood flow exists when systemic oxygen saturation is greater than 85% to 90%, whereas when the systemic oxygen saturation is lower than 70% there may be inadequate pulmonary blood flow. (427)

59. Some common vasoactive drugs used during separation from cardiopulmonary bypass in congenital heart surgery are dopamine, epinephrine, norepinephrine, and milrinone. (427, Table 26-6)

60. Some causes of difficulty in separation from cardiopulmonary bypass in congenital heart surgery include inadequate pulmonary blood flow (arterial hypoxemia), inadequate systemic blood flow (hypotension and metabolic acidosis), valvular dysfunction, decreases in cardiac output, decreased systemic vascular resistance, cardiac rhythm disturbances, and hypovolemia. (428, Table 26-7)

61. A rescue measure that can be used if a patient cannot be weaned from cardiopulmonary bypass is extracorporeal life support. (428)

62. Important complications of protamine administration include anaphylactic, anaphylactoid, hypotensive, or severe pulmonary hypertensive reactions. (428)

63. Contributors to postoperative coagulopathy in congenital heart surgery include coagulation factor deficiencies, hypothermia, and hypocalcemia. (428)

64. The best method to replace blood components in infants is noting their small intravascular volume, and administering products carefully in aliquots. (428)

65. A common side effect of the administration of citrated blood products is hypocalcemia. (429)

66. Refractory bleeding after cardiopulmonary bypass can be treated with recombinant factor VIIa when conventional hemostatic therapy has failed to stop the bleeding. (429)

67. Common parameters that are actively managed after pediatric cardiac surgery in the intensive care unit involve the correction of various electrolyte, glucose, and ventilatory, circulatory, and hematologic parameters. (429)

Chapter

24 CHRONIC PULMONARY DISEASE

Luca M. Bigatello

OBSTRUCTIVE PULMONARY DISEASE

1. What are some examples of obstructive pulmonary disease?
2. What is obstructive pulmonary disease?
3. Why does arterial hypoxemia occur in patients with obstructive pulmonary disease?
4. Why does carbon dioxide retention occur in patients with obstructive pulmonary disease?
5. What are common physical, radiographic, and functional findings in patients with obstructive pulmonary disease?

ASTHMA

6. What characterizes asthma?
7. How is the diagnosis of asthma made?
8. What are some of the physical examination findings noted in patients with asthma during periods of normal pulmonary function? What are some of the physical examination findings noted in patients with bronchial asthma during periods of exacerbation of their asthma?
9. What are some findings found in the pulmonary function studies and flow-volume loops during asthma exacerbations?
10. What agents are commonly used for the chronic treatment of asthma?
11. How can an acute asthmatic attack be treated?
12. How should the patient with asthma be assessed preoperatively?
13. How should a patient with asthma be assessed before a thoracic or abdominal procedure?
14. Is regional anesthesia the preferred anesthetic choice in patients with bronchial asthma scheduled to undergo surgery on the extremities?
15. What is the goal of the anesthetic management of patients with asthma?
16. What agents may be used for the induction of general anesthesia in patients with asthma? What is an advantage and a disadvantage of ketamine for these patients?
17. Which neuromuscular blocking drugs are associated with histamine release? What is the concern regarding the use of these neuromuscular blocking drugs in patients with asthma?
18. What is the benefit of using a slow respiratory rate when mechanically ventilating the lungs of a patient with asthma?
19. What is a benefit of maintaining adequate hydration intraoperatively in patients with asthma and chronic obstructive pulmonary disease (COPD)?
20. What are the options for extubation of the trachea that will minimize the degree of airway hyperreactivity in response to manipulation of the endotracheal tube?
21. How can the reversal of neuromuscular blocking drugs with anticholinesterases cause bronchospasm?

22. Name five potential causes of intraoperative bronchospasm.
23. How should intraoperative bronchospasm be treated?

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

24. What characterizes pulmonary emphysema physiologically?
25. What characterizes chronic bronchitis physiologically?
26. How do emphysema and chronic bronchitis differ clinically?
27. Why is the work of breathing increased in patients with pulmonary emphysema?
28. For patients with COPD scheduled to undergo a surgical procedure, what should the preoperative evaluation include? When might preoperative pulmonary function tests be necessary?
29. What are some pulmonary function test and arterial blood gas measurement results that indicate that the patient is at an increased risk of postoperative respiratory failure? What are some treatment interventions that may be warranted by the preoperative evaluation of the patient's pulmonary function?
30. What are the main considerations for the anesthetic management of patients with COPD?
31. What are some potential disadvantages of using nitrous oxide as part of a general anesthetic in patients with COPD?
32. What are two methods by which anesthesiologists may minimize the drying of secretions in the airways of patients with COPD in the intraoperative period?
33. What ventilatory settings are appropriate for intraoperative mechanical ventilation of the lungs of patients with COPD?
34. What characterizes chronic bronchitis physiologically? What is the major predisposing factor to the development of chronic bronchitis?
35. What is the impact of COPD on the postoperative course?
36. What is the clinical significance of an exacerbation of COPD, and what is its implication on an upcoming surgical procedure?

PULMONARY HYPERTENSION

37. How is pulmonary hypertension defined? What is the most common form of pulmonary hypertension?
38. What are the physiologic effects of pulmonary hypertension?
39. How can pulmonary hypertension affect the performance of the left ventricle?
40. What are the main anesthetic considerations for patients with pulmonary hypertension?

OBSTRUCTIVE SLEEP APNEA

41. Is obstructive sleep apnea a rare or common disease?
42. What are the physiologic characteristics of sleep apnea that may affect anesthetic management and outcome?
43. What are the main anesthetic implications of obstructive sleep apnea?

ANESTHESIA FOR LUNG RESECTION

Preoperative Evaluation and Preparation

44. What are some preoperative considerations for the patient scheduled to undergo thoracic surgery?
45. What are some specific preoperative history and physical examination findings that are indicative of an increased risk of postoperative pulmonary complications after thoracic surgery?
46. What are some preoperative prophylactic measures that may be taken in an attempt to minimize postoperative pulmonary complications?
47. How does cigarette smoking affect the lungs physiologically?
48. What is the benefit of the preoperative cessation of cigarette smoking? After what duration of time after the cessation of smoking are these benefits noted to occur?
49. For which patients are preoperative pulmonary function tests indicated?

50. What values derived from pulmonary function tests are indicative of an increased risk of postoperative pulmonary morbidity after a pneumonectomy?
51. What are PPO — FEV_1 (predicted postoperative FEV_1) and PPO – DLCO (predicted postoperative DLCO)?

Management of Anesthesia

52. What are some benefits of the administration of volatile anesthetics for patients undergoing thoracic surgery?
53. What is a disadvantage of the administration of nitrous oxide for patients undergoing thoracic surgery?
54. What is a benefit of the administration of nondepolarizing neuromuscular blocking drugs for patients undergoing thoracic surgery?

ISOLATION OF THE LUNGS

55. What are some absolute indications for one-lung ventilation during surgery and anesthesia? What are some relative indications for one-lung ventilation during surgery and anesthesia?
56. What is the most frequently used double-lumen endotracheal tube used for the isolation of the right or left lung or for one-lung ventilation during thoracic surgery?
57. What is the potential problem with an endobronchial tube placed in the right bronchus for isolation of the right lung? How can this problem be avoided?
58. What size double-lumen endotracheal tube is usually appropriate for adult patients? What depth in centimeters typically places the endobronchial tube in approximately the correct position in most adult patients of average height?
59. What is the technique for placement of a left-sided double-lumen endotracheal tube? How is the proper placement of a double-lumen endotracheal tube best confirmed?
60. What is the single-lumen Univent tube? What is its potential advantage for ventilation?
61. What is a Arndt endobronchial blocker?
62. What is a Cohen tip deflecting endobronchial blocker?
63. How does a bronchial blocker compare to a double-lumen endotracheal tube?

GAS EXCHANGE DURING ONE LUNG VENTILATION

64. How does the lateral decubitus position during mechanical ventilation of the lungs affect the ventilation-to-perfusion ratio in the lungs?
65. What are four factors that influence the amount of perfusion that goes to the nondependent, unventilated lung during ventilation of a patient in the lateral decubitus position with a double-lumen endotracheal tube?
66. What are the interventions that can be made when arterial hypoxemia is noted in a patient during ventilation for thoracic surgery?

CONCLUSION OF SURGERY

67. Why is the placement of chest tubes after thoracic surgery necessary postoperatively?
68. When should extubation of the trachea after thoracic surgery occur?

POSTOPERATIVE PULMONARY COMPLICATIONS

69. What are the common postoperative pulmonary complications after thoracic surgery?
70. What is the importance of adequate analgesia after thoracic surgery?

MEDIASTINOSCOPY

71. What is the most frequent reason for the performance of a mediastinoscopy?
72. What are the complications associated with mediastinoscopy?

ANSWERS*

OBSTRUCTIVE PULMONARY DISEASE

1. Examples of obstructive pulmonary disease include asthma, emphysema, chronic bronchitis, and cystic fibrosis. Emphysema and chronic bronchitis are overlapping clinical manifestations of the same disease – COPD. Obstructive pulmonary disease is characterized by the progressive, persistent obstruction to air flow, particularly expiratory flow. Asthma is an acute form of obstructive disease, which is treatable and at least partially reversible even when established. If asthma persists over time, either because it is untreated or because it is particularly severe, it may develop irreversible air flow obstruction and become a chronic disease not significantly different from emphysema and chronic bronchitis. (431)
2. Obstructive pulmonary disease is chiefly characterized by expiratory flow limitation due to increased airway resistance coupled with the loss of elastic lung recoil. These factors lead to lung hyperinflation, increased work of breathing, and impaired gas exchange. Obstructive pulmonary disease is the most frequent cause of chronic pulmonary disease. (431)
3. Arterial hypoxemia occurs in patients with obstructive pulmonary disease because of ventilation-perfusion mismatch. Decreased ventilation (which preferentially leads to hypoxemia) occurs because of the progressive destruction of functional alveoli. (433)
4. Carbon dioxide retention occurs in patients with obstructive pulmonary disease because of ventilation-perfusion mismatch. Both decreased ventilation and decreased perfusion (dead space) lead to hypercarbia. Initially, this is compensated by hyperventilation. As patients become older and weaker, such compensation fails, leading to chronic carbon dioxide retention. (433)
5. Patients with obstructive pulmonary disease often appear dyspneic, with a hyperinflated, "barreled" chest. Upon careful examination, you will notice a prolonged expiratory phase often terminated by obvious expiratory muscle activity – an attempt to exhale the whole tidal volume. On chest auscultation, lung sounds are distant (because of the hyperinflation), sometimes with associated wheezing. On the chest radiogram the lungs appear very "tall" and the diaphragm flattened. The lung fields may appear hyperlucent, and the vasculature may be difficult to discern. Pulmonary function studies in patients with obstructive pulmonary disease will reveal a decreased volume of the gas that can be forcefully exhaled in 1 second (FEV_1). The vital capacity may also be decreased, but not to as great an extent as the FEV_1, resulting in a decreased FEV_1/FVC ratio. (431)

ASTHMA

6. Asthma is characterized by reversible expiratory flow obstruction, airway hyperreactivity, and chronic inflammation leading to airway edema, secretions, and progressive thickening. (431)
7. The diagnosis of asthma is made primarily on the clinical history of increasing coughing and wheezing spells with or without the identification of a supposed trigger. Common triggers include pollens, medications, cold air temperature, and exercise. Spirometry shows an obstructive defect (low FEV_1) that is partially reversible (12% to 15%) with inhaled bronchodilators. The sputum taken from patients with asthma often contains eosinophils, in contrast to the neutrophils most commonly found in the sputum of patients with bronchitis. (341, Figure 27-1)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

8. Patients with asthma during periods of normal pulmonary function are typically devoid of any signs of pulmonary disease, although scattered expiratory wheezing can still be heard. During periods of exacerbation, typical signs and symptoms include breathlessness, coughing fits, and chest tightness, associated with the objective finding of a prolonged expiratory phase and wheezing, sometimes audible without the aid of a stethoscope.

9. Pulmonary function studies during asthma exacerbations reveal a decrease in the FEV_1 and FEV_1/FVC. The FEV_1 may be used as a measure of the degree of obstruction and the effectiveness of interventions. A flow-volume loop during an asthma exacerbation reveals a downward scooping of the expiratory phase, with a normal shape of the inspiratory phase. A significant response to a bronchodilator may normalize the aspect of the loop that is characteristic of bronchial asthma and increase the FEV_1. An increase of 12% is judged clinically significant, and is used to separate asthma from COPD by functional criteria. (431-433, Figure 27-1; Table 27-1)

10. Chronic treatment of asthma includes antiinflammatory agents and bronchodilators. Inhaled corticosteroids (beclometasone and fluticasone) have potent antiinflammatory effects and are considered a mainstay of chronic asthma treatment. Long-acting β_2-adrenergic agonists (salmeterol and formoterol) and anticholinergics (tiotropium) are effective bronchodilators used to treat moderate to severe asthma. Their advantage in respect to the traditional counterparts (see later discussion) is their longer duration of action that allows single daily administration. With that, they are also not indicated in the treatment of an acute exacerbation. Other antiinflammatory agents effective in the chronic (and not in the acute) setting are the leukotriene antagonists and synthesis inhibitors (montelukast, zafirlukast, and zileuton). Methylxanthines (aminophylline, theophylline) are no longer recommended in the treatment of asthma. (431-432)

11. An acute asthmatic attack should be treated with the administration of oxygen, nebulized β_2-agonists and anticholinergics, and intravenous glucocorticoids. Subcutaneous epinephrine is also rapidly effective, but the side effects need to be balanced with its need in each patient. Occasionally standard therapy will not be sufficient, as evidenced by persistent respiratory distress, worsening hypercapnea, hypoxemia, and mental status changes. In these cases, non-invasive ventilation may be very effective, as it will support ventilation and avoid fatigue while the pharmacologic treatment takes its effect. Tracheal intubation has become a rare occurrence in the acute treatment of asthma, and is reserved for the most severe and persistent cases and *status asthmaticus*. In unusual and extreme circumstances, inhalational anesthetic agents have been successfully administered through an intubated airway. All halogenated agents (isoflurane, sevoflurane, and desflurane) have direct bronchodilator properties, independent of catecholaminergic and cholinergic receptors, thus working as an addition to the ongoing therapy. (432-433)

12. The preoperative assessment of patients with asthma should include a detailed history, including any recent exacerbation, the occurrence of emergency room visits and/or hospitalizations, and mechanical ventilation for asthma. Physical examination may reveal tachypnea, dyspnea, and, on auscultation, expiratory wheezing. Patients with a benign history and physical examination do not require any special intervention other than continuing their current medications. If on inhaled bronchodilators on an "as needed" basis, they should be instructed to use the bronchodilator on the morning of surgery and to bring it to the operating room. Patients who are symptomatic or who have suffered a recent exacerbation may benefit from postponement of elective surgery until their medical status can be optimized. (432, 434)

13. Open abdominal and thoracic surgery is associated with the highest incidence of respiratory complications because of a combination of the effects of postoperative pain, as well as respiratory muscle dysfunction. Hence, additional preoperative

testing may be warranted if the clinical suspicion of severe or untreated respiratory disease arises. This assessment should be carried out by a pulmonologist familiar with the perioperative challenges of obstructive pulmonary disease, and may include the performance of pulmonary function studies. Of particular utility to the anesthesiologist is to know whether the possible expiratory flow limitation (i.e., a low FEV_1) is reversible with bronchodilators. (432, 434)

14. Regional anesthesia may be preferred over general anesthesia in patients with asthma scheduled for surgery on the extremities. It avoids manipulation of the airway and the risk of bronchospasm. However, modern medications and anesthetic techniques are safe in patients with less than severe, symptomatic asthma. Ventilation through a laryngeal mask airway is less stimulating than through an endotracheal tube; many anesthetic drugs are also bronchodilators, such as halogenated inhalational agents and propofol. (432)

15. The goal of the anesthetic management of patients with asthma is to avoid precipitating bronchoconstriction. While regional or neuraxial anesthesia may be preferable, a well-conducted general anesthetic also has advantages, including the ability to deliver bronchodilators (volatile anesthetic agents) and to provide pulmonary toilet by deep tracheal suction and/or bronchoscopy. A sufficient depth of anesthesia before intubation of the trachea minimizes the risk of acute bronchospasm at the time of the induction of anesthesia. This can be accomplished both with intravenous agents and volatile anesthetics. The latter can be used as the sole induction agent (rarely used in adults because of the length of time needed for establishing adequate intubating conditions) or by mixing them during an intravenous induction. (432)

16. Currently available induction agents such as propofol and ketamine have bronchodilating effects. Propofol is a more manageable agent devoid of potential psychogenic side effects. On the other hand, ketamine has a substantial analgesic effect that may turn out to be helpful in particular circumstances where opiate agents may not be desired. (432)

17. Neuromuscular blocking drugs associated with histamine release include succinylcholine, atracurium, and mivacurium. Histamine release may precipitate/aggravate bronchospasm, although this is a rare occurrence. Regardless, the availability of nonhistamine releasing neuromuscular blocking drugs such as vecuronium, rocuronium, and cisatracurium allows the anesthesiologist to safely choose the preferred agent based on individual priorities. (432)

18. A slow respiratory rate during mechanical ventilation of the lungs of a patient with asthma allows time for maximal exhalation of gases from obstructed airways. (432)

19. Adequate intraoperative hydration of patients with asthma may facilitate the removal of secretions from the airways by making the secretions less viscous. (432, 434)

20. Extubation of the trachea in the asthmatic patient may be challenging. The presence of an endotracheal tube in the airway of a sufficiently awake patient may trigger irritation and bronchospasm. Two different approaches may be used. The first is to extubate the trachea while the patient is still deeply anesthetized. This requires that (1) no contraindication to having an unprotected airway, such as gastroesophageal reflux, upper gastrointestinal surgery, etc., and (2) spontaneous breathing with no or only partial ventilatory support, to avoid inflation of the stomach with positive pressure ventilation. Care should be paid to suction the airway above the tracheal tube cuff before deflating it. Alternatively, the patient can be allowed to be fully awake before the endotracheal tube is removed. This approach, however, may trigger bronchospasm, which can be minimized by administering additional inhaled bronchodilator prior to awakening.

21. The reversal of neuromuscular blocking drugs with an anticholinesterase such as neostigmine has the potential to cause bronchospasm from cholinergic

stimulation. However, the anticholinesterase is administered in association with an anticholinergic agent that selectively blocks the muscarinic effects of acetylcholine (bronchospasm, hyperperistalsis, tachycardia), leaving the nicotinic effects (neuromuscular junction) intact. Atropine and glycopyrrolate are prototype agents in this group. (432)

22. Potential causes of intraoperative bronchospasm include acute bronchial asthma, inadequate depth of anesthesia, endobronchial intubation, aspiration of gastric contents, pneumothorax, and foreign body in the airways. (432)

23. Intraoperative bronchospasm is rarely due to an acute asthma exacerbation, except for patients who were already symptomatic preoperatively. Once mechanical causes are ruled out and treated (e.g., pneumothorax, foreign body in the airways), intraoperative treatment of bronchospasm does not differ significantly to its treatment outside the operating room, except for the additional measure of deepening the level of anesthesia when possible. The first-line drugs are the inhaled bronchodilators (β_2-agonists and anticholinergics), preferably administered with a spacer that allows collection of the drug and subsequent delivery during inspiration. Corticosteroids can also be used, although their onset of action is not immediate. If central venous access is available, a low dose of epinephrine (less than 1 μg/min) can be very effective and mostly devoid of side effects. Alternatively, epinephrine can be administered subcutaneously. (432-433)

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

24. Pulmonary emphysema is characterized by the loss of elastic recoil of the lungs due to the progressive destruction of lung parenchyma. The loss of elastic recoil leads to collapse of relatively small airways during exhalation, and in turn an increase in airway resistance. This results in hyperinflation of the alveoli, and the destruction of interalveolar septa with the creation of bullae, and an increase work of breathing. All these phenomena accelerate the progression of the disease toward severe COPD. Gas exchange in patients with COPD is characterized by ventilation to perfusion mismatch leading to hypoxemia, which in turns leads to polycythemia, pulmonary hypertension, and in severe cases supplemental oxygen requirements. (433)

25. Chronic bronchitis is characterized by an increased airway resistance due to excessive mucous secretion in the tracheobronchial tree. Long-standing increased airways resistance results in increased work of breathing, dynamic hyperinflation and auto-PEEP, and the predisposition to pulmonary infections such as acute tracheobronchitis and pneumonia. All these phenomena accelerate the progression of the disease toward severe COPD. (433)

26. Emphysema and chronic bronchitis constitute two somewhat different ways to arrive at the same pathologic endpoint: COPD. Emphysema occurs more on the basis of progressive destruction of the lung parenchyma, particularly elastic fibers, and loss of expiratory recoil of the lung. Chronic bronchitis occurs more on the basis of chronic respiratory infection. Hence, the distinction between emphysema and chronic bronchitis is more academic than clinical and it has faded away in the recent literature, which considers them variants of the same disease: COPD, with similar etiologic factors (cigarette smoking), evolution, and complications. (433)

27. The loss of elastic recoil may prevent the lungs to reach functional residual capacity (FRC) at end expiration as they normally would. Ending expiration at a lung volume above FRC exerts a pressure in the alveoli higher than atmospheric (which by convention we call 0 mm Hg). This pressure is often called “intrinsic positive expiratory pressure” (intrinsic PEEP) or “auto-PEEP” and just like PEEP it is related to an increased FRC. Unlike externally applied PEEP, however, intrinsic PEEP needs to be fully overcome before gas flow in the airways becomes negative and inspiration starts. This occurs at every breath and it may be taxing depending upon the magnitude of auto-PEEP and the conditions of the patient. (433)

28. The preoperative evaluation of patients with pulmonary emphysema should include an assessment of the patient's current symptoms of dyspnea, cough, and sputum production. Exercise tolerance should also be assessed. Based on the clinical history, physical examination findings, and the surgical procedure, preoperative pulmonary function tests and arterial blood gas measurements may be indicated. These studies may help to determine the extent of disease, whether there are any reversible components of the disease such as bronchospasm or infection, and the risk of postoperative respiratory failure. (432-444)

29. The major concern for patients with pulmonary emphysema scheduled to undergo surgical procedures is the risk of postoperative respiratory failure and the need for prolonged intubation of the trachea. Pulmonary function test results that indicate that the patient is at an increased risk for postoperative respiratory failure include an FEV_1 less than 2 L and or less than 50% of predicted, or the presence of arterial hypoxemia or hypercarbia. A $Paco_2$ measurement of 50 mm Hg or higher is an indication that the patient is at an increased risk of postoperative respiratory failure. Arterial hypoxemia warrants treatment with supplemental oxygen in an attempt to improve peripheral oxygen availability, as well as decrease pulmonary vascular resistance and possibly the pressure load of the right ventricle. (434)

30. Intraoperative management of patients with COPD implies similar consideration as those for asthma patients, except that airway irritability is generally less severe. Nonetheless, it is advisable to minimize airway stimulation, to use regional anesthesia if the procedure allows it, to consider extubating the trachea during deep anesthesia, and to always deliver generous bronchodilation. The latter can be accomplished by administering inhaled β_2-agonists, anticholinergic agents, and halogenated inhalational agents. When possible, management of the airway by mask or LMA is preferable to endotracheal intubation. When intubated, the airways can be thoroughly suctioned with the aid of a bronchoscope to facilitate secretion clearance in the immediate postoperative period. (433)

31. Disadvantages of using nitrous oxide as part of a general anesthetic in patients with pulmonary emphysema include the potential for nitrous oxide to diffuse into bullae and cause its expansion or even rupture, leading to a tension pneumothorax. In addition, using nitrous oxide obviously limits the inspired fraction of oxygen that can be administered concurrently. (434)

32. Two methods by which anesthesiologists may minimize the drying of secretions in the airways of patients with pulmonary emphysema in the intraoperative period is through the humidification of inspired gases and the maintenance of adequate hydration. (432, 433)

33. Mechanical ventilation of the lungs of patients with COPD may be complicated by the presence of significant expiratory flow limitation, which is present in different degrees at baseline and may be aggravated by intraoperative bronchospasm. Expiratory flow limitation tends to impede the elimination of CO_2, and ultimately causes hypercapnia and acute respiratory acidosis. Allowing a long expiratory phase facilitates expiratory emptying of the lungs and CO_2 clearance. However, this strategy may be limited by the necessity to deliver a minute ventilation sufficient to maintain adequate CO_2 clearance. Increasing tidal volume over respiratory rate may accomplish the goal to a degree, but this also is limited by the potential for alveolar overdistention and barotrauma. Hence, there is no specific formula for success, and various combinations of the above may be tried and may work differently in each individual patient. It is important also to remember the reason for the expiratory flow limitation (high expiratory resistance, bronchospasm) and treat it with generous administration of bronchodilators. (432, 433)

34. Chronic bronchitis is a state of chronic inflammation of the airways with excessive secretions of mucus that causes a progressive increase in airway resistance to air flow. Predisposition to frequent bronchial infection aggravates the clinical

picture by adding a purulent component to the tracheobronchial secretions and the general debilitating effects of recurrent infections. The major predisposing factor to the development of chronic bronchitis, as with pulmonary emphysema, is cigarette smoking. (433)

35. COPD affects multiple aspects of lung physiology, principally gas exchange and respiratory mechanics. Hence, they have a much narrower margin of reserve and are at high risk to develop postoperative respiratory complications including pneumonia, and the need for prolonged mechanical ventilation. Interventions that may limit respiratory complications include: (1) preoperative optimization of symptoms like bronchospasm and excessive secretions; (2) careful intraoperative management including either a regional anesthetic or a general anesthetic with generous administration of bronchodilators, retrieval of secretions by deep tracheal suctioning or bronchoscopy, and sufficient hydration; (3) effective postoperative pain control, possibly including regional techniques such as epidural analgesia or continuous peripheral blocks through an indwelling catheter; and (4) a careful evaluation and control of comorbidities such as ischemic heart disease, arrhythmia, and gastroesophageal reflux, which may coexist and contribute to the development of acute respiratory failure. (433)

36. Acute exacerbations of COPD are characterized by acute worsening of dyspnea, sputum production, and sputum purulence. They generally imply a new or renewed respiratory infection, and, in the general outlook of the disease, further decline of respiratory function. When occurring in proximity to a scheduled operation, they constitute an increased risk factor for postoperative respiratory complications. If at all possible, surgery should be postponed and the patient treated with established protocols for COPD exacerbation, including antibiotics, bronchodilators, and often a corticosteroid taper. (433-434)

PULMONARY HYPERTENSION

37. Pulmonary hypertension is defined as a mean pulmonary artery pressure greater than 30 mm Hg. Pulmonary hypertension is most commonly secondary to cardiac (congestive heart failure, mitral valve disease) and pulmonary (COPD) disease. Primary pulmonary hypertension is rarer and also more severe. (434)

38. Pulmonary hypertension physiologically leads to an increased pressure in the pulmonary vascular bed constituting an increased pressure load to the right ventricle, which initially compensates with dilation and hypertrophy that allow for the preservation of myocardial stroke volume. As the load to the right ventricle persists or increases, the right ventricle eventually fails and stroke volume and cardiac output fall, leading to chronic right-side congestive heart failure or *cor pulmonale*. Clinical signs of right ventricular failure include peripheral edema, hepatomegaly, jugular vein distention, and eventually hypoxemia and dyspnea. (434, 435)

39. Pulmonary hypertension may affect the performance of the left ventricle via the development of right ventricular pressure and then volume overload. As the right ventricle responds to the increased pressure afterload, it first hypertrophies and then dilates. As this occurs, the right ventricle assumes a spherical shape and pushes the interventricular septum into the left ventricular cavity. As a result, the volume of the left ventricle decreases, and diastolic filling is compromised, which in turn results in a smaller stroke volume and lower cardiac output. (434)

40. Patients with significant pulmonary hypertension are at risk of developing acute right-side congestive heart failure during anesthesia. Attention must be paid to minimize stimuli that may further increase pulmonary artery pressure, such as hypoxemia, hypercarbia, acidemia, and high catecholamine discharge, as it may occur from acute stress due to light anesthesia. It is important to preserve the preload to the right ventricle by careful maintenance of circulating volume during large open procedures or significant blood loss. On the other hand, excessive

volume overload will eventually result in failure of the right ventricle similarly to what happens with the left ventricle. It is then easy to see how such delicate equilibrium may need to be monitored closely (with, for example, a pulmonary artery catheter or a transesophageal echography). Treatment of acute on chronic RV failure is often disappointing, as few selective pulmonary vasodilators are available and are not always effective. These include phosphodiesterase inhibitors (milrinone), inhaled prostacyclin (Flolan), and inhaled nitric oxide. (434, 435)

OBSTRUCTIVE SLEEP APNEA

41. Obstructive sleep apnea is very common, particularly in the male gender, since it may affect as many as 25% of men in the United States. Obesity is by far the most significant risk factor, but obstructive sleep apnea can also occur independently of airway anatomy (central sleep apnea). (435)

42. Obstructive sleep apnea is generally associated with obesity; hence, all the cardiorespiratory and metabolic consequences of obesity are often present in patients with obstructive sleep apnea. When untreated, obstructive sleep apnea causes frequent periods of severe hypoxemia, with the consequent development of pulmonary hypertension over time. Most relevant for anesthesia, physiologic abnormalities of obstructive sleep apnea include a high Mallampati score, low lung volumes, a decreased functional residual capacity, chronic hypoxemia and hypercarbia, atherosclerotic and hypertensive cardiovascular disease, congestive heart failure, gastroesophageal reflux, and metabolic disease, in particular type 2 diabetes mellitus. (435)

43. There are several anesthetic considerations for the patient with obstructive sleep apnea. These patients may have a more challenging airway due to the large amount of redundant tissue that may make ventilation and intubation of the trachea difficult. For this reason it may be preferable to induce general anesthesia in a rapid sequence, avoiding attempts at ventilation all together, after a prolonged preoxygenation, possibly in a slight reversed Trendelenburg position, and prepared with alternative tracheal intubation techniques. Intraoperatively, attention has to be paid to avoid major alveolar collapse by administering positive end-expiratory pressure and occasional large breaths. Extubation should be carried out with the patient wide awake and ready to collaborate with deep breathing. Pharmacologic management of the patient with obstructive sleep apnea should be aimed toward the maintenance of a patent airway. Preoperative benzodiazepines may relax the airway tissues such that pharyngeal space becomes reduced and hypoventilation ensues. Medications that depress the central nervous system may augment this effect and lead to hypopnea, arterial hypoxemia, and hypercapnia both prior to the induction of anesthesia and upon awakening. Opioids can decrease the respiratory drive and further contribute to these complications. If the patient used CPAP at home, it should be available in the postoperative period and used if necessary. (435-436)

ANESTHESIA FOR LUNG RESECTION

Preoperative Evaluation and Preparation

44. Preoperative considerations for the patient scheduled to undergo thoracic surgery include the medical management of the pulmonary disease, the evaluation of coexisting disease and its management, the evaluation of pulmonary function with pulmonary function tests, the selection of intraoperative anesthetics and monitors, the effect of ventilation and/or the lateral decubitus position that may be required intraoperatively, the plan for postoperative pain control, and the potential need for continued mechanical ventilation of the lungs in the postoperative period. Perhaps the main purpose of the preoperative evaluation of patients scheduled to undergo thoracic surgery is to institute perioperative therapy in an effort to minimize postoperative complications. (436)

45. Preoperative history and physical examination findings that are indicative of an increased risk of postoperative pulmonary complications after thoracic surgery include dyspnea, cough, sputum production, wheezing, a history of cigarette smoking, obesity, and advanced age. Another risk factor for postoperative pulmonary complications after thoracic surgery is an inexperienced surgeon. (432, 436)

46. Preoperative prophylactic measures that may be taken in an attempt to minimize postoperative complications include the discontinuation of smoking cigarettes, treatment of any pulmonary infections, treatment of any reversible component of increased airway resistance, mobilization of any secretions, and teaching the patient deep breathing exercises and coughing exercises. These prophylactic measures should be instituted at least 48 to 72 hours before surgery. (436)

47. Cigarette smoking increases the irritability of the small airways, causes mucus hypersecretion, and decreases mucociliary transport. Carbon monoxide may also have negative inotropic effects. The net effect of this for patients scheduled to undergo thoracic surgery is an increase in the incidence of complications in the postoperative period. (433, 436)

48. There are many benefits of the preoperative cessation of cigarette smoking. Twelve to twenty-four hours after the cessation of cigarette smoking, there are significant decreases in the carboxyhemoglobin level and a decrease in nicotine-induced tachycardia. The oxyhemoglobin dissociation curve shifts to the right, making more oxygen available at the tissues. One to two weeks after the cessation of cigarette smoking, there begins to be a decrease in the amount of mucus secretions in the airways; 8 to 12 weeks after the cessation of cigarette smoking, there is marked improvement in mucociliary transport, small airway reactivity, and secretions in the small airways. This is evidenced by the decrease in postoperative respiratory complications in patients who have quit smoking cigarettes for at least 8 weeks before surgery. (436)

49. Preoperative pulmonary function tests predict which patients may be at an increased risk for postoperative pulmonary complications after thoracic surgery. Patients with a history of chronic pulmonary disease or with severe, limiting pulmonary symptoms in the presence of abnormal findings on the physical examination or chest radiograph are candidates for preoperative pulmonary function studies. (436)

50. The following values from a pulmonary function test are indicative of increased risk of postoperative pulmonary morbidity after a pneumonectomy: FEV_1 less than 2 L or FEV_1 predicted less than 80%. Similarly DLCO less than 80% predicted is also associated with increased morbidity. A decrease in oxygen consumption, less than 10 mL/kg/min as measured by exercise testing, predicts a postoperative mortality rate of 25% to 50% and should prompt discussion of alternatives to surgical resection. (436-37, Figure 27-2)

51. The lung has 42 segments (22 segments on the right and 20 segments on the left). Depending on the number of segments of the lung that will be resected, an estimate of the postoperative FEV_1 can be obtained. Predicted postoperative FEV_1 (PPO FEV_1) = Preoperative FEV_1 − (1 − % functional lung tissue removed/100). A PPO FEV_1 of less than 40% is associated with poor outcomes. Similar to FEV_1, the DLCO estimate, based on the number of lung segments to be resected, is the predicted postoperative DLCO (PPO DLCO). A PPO DLCO of less than 40% carries an increased risk of postoperative complications. (436, Figures 27-2 and 27-3)

Management of Anesthesia

52. The benefits of the administration of volatile anesthetics for patients undergoing thoracic surgery include the effect of decreasing airway reflexes, the lack of influence on regional hypoxic pulmonary vasoconstriction, a high inspired

concentration of oxygen that may be delivered concurrently, and the ability to be eliminated postoperatively. (436)

53. Disadvantages of the administration of nitrous oxide for patients undergoing thoracic surgery include:
    - The limited concentration of oxygen that may be administered
    - A small decrease in the hypoxic pulmonary vasoconstriction response of the lung
    - The exacerbation of preexisting pulmonary hypertension

    Its potential to expand in closed airspace, such as during closure of a thoracotomy, or expansion of emphysematous bullae leading to pneumothorax. (434-436)
54. The benefits of the administration of nondepolarizing neuromuscular blocking drugs for patients undergoing thoracic surgery include improved conditions for endotracheal intubation, improved surgical exposure through rib separation. and the facilitation of controlled ventilation of the lungs. (436)

ISOLATION OF THE LUNGS

55. Absolute indications for one-lung ventilation during surgery and anesthesia include the need to isolate the lungs from each other to avoid contamination from one lung to the other of infected material or blood, the presence of a bronchopleural fistula, surgical opening of a major airway, a giant unilateral lung cyst or bullae, tracheobronchial tree disruption, life-threatening hypoxemia due to unilateral lung disease, and unilateral lung lavage of pulmonary alveolar proteinosis. Relative indications for one-lung ventilation during surgery and anesthesia include improving operating conditions during a lobectomy, pneumonectomy, resection of a thoracic aneurysm, or operations on the esophagus.
56. The Robertshaw endobronchial tube is the most frequently used double-lumen endotracheal tube for the isolation of the right or left lung for one-lung ventilation during thoracic surgery. The left-sided tube has a longer bronchial tube than the right-sided tube. Several manufacturers produce clear disposable polyvinyl chloride tubes. (438, Figure 27-5)
57. An endobronchial tube placed in the right bronchus for isolation of the right lung could potentially obstruct the lumen of the right upper lobe bronchus. This occurs secondary to the short distance between the carina and the takeoff to the right upper lobe bronchus. The right-sided double lumen tubes are designed to incorporate a separate opening in the bronchial lumen to allow ventilation of the right upper lobe. Proper positioning of a right-sided DLT must include fiberoptic guidance. (439, Figure 27-9)
58. For most adult women, a size 37 French double-lumen tube is appropriate, and for most men a 39 French tube is the appropriate size. Endobronchial tube placement is in the correct position at an average depth of insertion referenced to the corner of the mouth of 29 cm for patients 170 cm tall. For each 10-cm increase or decrease in the patient's height, the average depth of endobronchial tube placement correspondingly changes by 1 cm. (438)
59. The technique for placement of a left-sided double-lumen endotracheal tube begins with holding the tube with the distal curve facing anteriorly. Once the bronchial cuff is inserted past the vocal cords, the stylet is removed, the tube is rotated 90 degrees to the left, and the tube advanced until moderate resistance is encountered. The proper placement of a double-lumen endotracheal tube is best confirmed with fiberoptic visualization through the tracheal portion of the double-lumen tube. The desired position of the tube corresponds to visualization of the superior portion of the bronchial cuff, when inflated, just past the bifurcation of the carina. The bronchial side can be confirmed by its orientation to the tracheal rings, which are complete anteriorly. Confirmation of endobronchial tube placement by auscultation alone leads to error in up to 48% of placements. (439, Figure 27-7)

60. The Univent tube has two compartments: a main lumen for conventional air passage and a small lumen embedded in the anterior wall of the endotracheal tube that permits passage of the movable bronchial blocker. The bronchial blocker is a relatively stiff catheter that has an internal channel measuring 2 mm through which oxygen may be insufflated. After tracheal intubation with the bronchial blocker retracted, initial positioning is accomplished by rotating the tube to the right or left position, so that the BB is advanced into the corresponding mainstem bronchus. Fiberoptic visualization should be used to confirm appropriate mainstem intubation and to guide the depth of insertion. The advantage of the Univent tube is that it then converts to a single-lumen endotracheal tube with the withdrawal of the bronchial blocker when isolation of the lungs is no longer needed. An example in which this may be advantageous is when postoperative ventilation of the lungs is anticipated and changing a double-lumen tube to a single-lumen tube at the conclusion of the surgical procedure could be dangerous or difficult. (441-442, Figures 27-10 and 27-11)

61. The Arndt endobronchial blocker is a wire-guided catheter. The bronchial blocker is coupled to the bronchoscope through the guide loop after they are passed through a multiairway adapter. The bronchoscope is advanced to the desired mainstem bronchus. Since the bronchial blocker is coupled to the bronchoscope, it is in turn positioned in the desired bronchus. (442, Figure 27-12)

62. The Cohen tip deflecting endobronchial blocker is introduced into a single-lumen endotracheal tube. The flexible tip of the bronchial blocker is directed into the desired bronchus by using the control wheel on the proximal end of the blocker. (442, Figure 27-13)

63. Bronchial blockers provide equivalent surgical exposure (lung collapse) when compared with a left-sided double-lumen tube, during left-sided open or video assisted thoracoscopic surgery. But bronchial blockers require a longer time to position and need more frequent intraoperative manipulation. (442)

GAS EXCHANGE DURING ONE-LUNG VENTILATION

64. A patient in the lateral decubitus position undergoing mechanical ventilation of the lungs has an increase in pulmonary ventilation-to-perfusion mismatch. The effects on pulmonary blood flow are primarily due to gravity, lung volume, and regional vascular resistance. The dependent lung receives proportionally more blood flow than the nondependent lung. The dependent lung is ventilated relatively less secondary to the loss of lung volume from compression by the mediastinum, abdominal contents, and positioning support structures. These factors together create an increase in pulmonary ventilation-to-perfusion mismatching. The ventilation-to-perfusion ratio can be improved with the application of PEEP to the dependent lung. (442-444)

65. Four factors that influence the amount of perfusion that goes to the nondependent, unventilated lung during ventilation of a patient in the lateral decubitus position with a double-lumen endotracheal tube include gravity, hypoxic pulmonary vasoconstriction, direct surgical compression of blood flow, and presence of pulmonary artery hypertension. (444)

66. Arterial hypoxemia when noted during ventilation for thoracic surgery calls for confirming proper placement of a double-lumen endotracheal tube using a fiberoptic bronchoscope. Next, the administration of a low level (5 to 10 cm H_2O) of PEEP to the nondependent lung helps. Sometimes this may interfere with the surgical dissection. A slow inflation of 2 L/min of oxygen into the nonventilated lung for 2 seconds and repeated every 10 seconds for 5 minutes until the saturation rises has been shown to improve oxygenation during ventilation. Sustained lung inflation of 30 to 40 cm H_2O to the dependent lung along with application of PEEP helps in recruitment of collapsed lung. Although this may

improve arterial oxygenation, it may also cause an increase in the pulmonary vascular resistance in the ventilated, dependent lung and in turn worsen the hypoxia. (445, Table 27-2)

CONCLUSION OF SURGERY

67. Chest tubes are placed after thoracic surgery to ensure continued expansion of the lung by evacuating fluid and air that may leak from alveoli that have been incised. Kinking of a chest tube after thoracic surgery places the patient at risk for a tension pneumothorax. (446)

68. Extubation of the trachea after thoracic surgery should take place at the conclusion of the surgery to minimize the complications associated with mechanical ventilation (barotrauma, ventilator-associated pneumonia). (446)

POSTOPERATIVE PULMONARY COMPLICATIONS

69. The most common postoperative pulmonary complication after thoracic surgery is atelectasis. Other common postoperative pulmonary complications include hypoventilation and arterial hypoxemia. These problems may be related to intraoperative problems (aspiration, trauma) or problems during the postoperative period due to the inability to mobilize secretions and effectively expand the operative lung. Early mobilization after surgery reestablishes physiologic lung volumes and gas exchange, and seems to be the most effective way to prevent postoperative pulmonary complications. (446)

70. Adequate analgesia after thoracic surgery is important. Thoracic epidural analgesia (TEA) provides effective postoperative pain relief, improved pulmonary function, and prompt mobility. TEA is associated with a lower mortality rate and fewer respiratory complications. (446)

MEDIASTINOSCOPY

71. The most frequent reason for the performance of a mediastinoscopy is to determine the diagnosis and/or resectability of lung cancer. (446)

72. The most common complications that can occur after the performance of a mediastinoscopy include hemorrhage and a pneumothorax. Other potential complications include a recurrent laryngeal nerve injury, infection, air embolism, and phrenic nerve injury. (446)

Chapter

25 RENAL, LIVER, AND BILIARY TRACT DISEASE

Anup Pamnani, Vinod Malhotra

RENAL DISEASE

1. What are some essential physiologic functions of the kidneys?
2. Name some factors that place patients at an increased risk of acute renal failure in the perioperative period.
3. What percent of the cardiac output normally goes to the kidneys? What fraction of this goes to the renal cortex?
4. Over what range of mean arterial blood pressures do renal blood flow and the glomerular filtration rate (GFR) remain constant? How is this accomplished by the kidneys? Why is it important?
5. Even during normal kidney autoregulatory function, what two factors can alter renal blood flow?
6. What is renin? What is the secretion of renin usually in response to? What effect does renin have on renal blood flow?
7. What is the physiologic effect of the secretion of renin?
8. What triggers the release of prostaglandins that are produced by the renal medulla? What is the effect of prostaglandins released by the renal medulla?
9. What is the renal effect of arginine vasopressin released by the hypothalamus?
10. What is glomerular filtration? What is glomerular filtration dependent on?
11. What is the normal hydrostatic pressure of the glomerular capillaries? What is the normal plasma oncotic pressure in the afferent and efferent arterioles?
12. What is the average normal rate of glomerular filtration?
13. About what percent of the fluid shift from glomerular filtration is reabsorbed from renal tubules and ultimately returned to the circulation?
14. How is the GFR influenced by the renal blood flow?
15. What are the three mechanisms upon which the renal clearance of drugs depends?
16. Name some tests used for the evaluation of renal function. How sensitive are tests of renal function?
17. What degree of renal disease can exist before renal function tests begin to indicate possible decreases in renal function?
18. What is the normal level of blood urea nitrogen (BUN)?
19. What factors may influence the BUN level?
20. Why does the BUN concentration increase in dehydrated states? What is the serum creatinine level under these circumstances?
21. What do BUN concentrations higher than 50 mg/dL almost always indicate?
22. What is the source of serum creatinine? How is the serum creatinine level related to the GFR?
23. Why might a normal creatinine level be seen in elderly patients despite a decreased GFR?
24. Why might normal serum creatinine levels not accurately reflect the GFR in patients with chronic renal failure?

25. What is the creatinine clearance a measurement of?
26. Why is the creatinine clearance a more reliable measurement of the GFR than serum creatinine levels? What is a disadvantage of creatinine clearance measurements?
27. What are some nonrenal causes of proteinuria?
28. What are the differences in site of action of thiazide, spironolactone, and loop and osmotic diuretics?
29. What are the differences in pharmacologic action between dopamine and fenoldopam?
30. What are the systemic changes that frequently accompany end-stage renal disease (ESRD)?
31. What are some anesthetic considerations for the anesthetic management of patients with ESRD?
32. Should succinylcholine be avoided in patients with ESRD?
33. What are some causes of prerenal oliguria?
34. What is the treatment for prerenal causes of oliguria?
35. What are some causes of oliguria due to intrinsic renal disease?
36. For oliguria that is secondary to renal causes such as acute tubular necrosis, is the urine typically concentrated or dilute? Does the urine typically contain excessive or minimal stores of sodium?
37. What are some causes of postrenal oliguria?

LIVER AND BILIARY TRACT DISEASE

38. What are some physiologic functions of the liver?
39. What is the blood supply to the liver? What percent of the cardiac output goes to the liver?
40. What are some determinants of hepatic blood flow?
41. What is hepatic autoregulation? How is hepatic autoregulation affected by surgery and anesthesia?
42. What is the hepatic arterial buffer response? How is this hepatic response affected by anesthesia?
43. What results from sympathetic nervous stimulation of the liver?
44. How does positive pressure ventilation of the lungs affect hepatic blood flow?
45. How does congestive heart failure affect hepatic blood flow?
46. How do changes in cardiac output or myocardial contractility affect hepatic blood flow?
47. How do changes in arterial blood pressure affect hepatic blood flow?
48. How does the liver store glucose?
49. How does the liver maintain glucose homeostasis in times of starvation?
50. Why might patients with cirrhosis be more likely to develop hypoglycemia in the perioperative period?
51. What role does the liver play in blood coagulation? What is the clinical implication of this for the patient with liver disease?
52. How significant must liver dysfunction be before abnormal blood coagulation is noted? How can this be evaluated preoperatively?
53. What is the role of vitamin K in coagulation?
54. How does the liver facilitate the renal excretion of lipid soluble drugs?
55. How does chronic drug therapy affect the metabolism of anesthetic drugs by the liver?
56. How does chronic liver disease impact drug metabolism?
57. Why may hepatic drug metabolism be accelerated after the administration of certain medications?
58. What role does the liver play in the excretion of bilirubin? What is the clinical implication of this for the patient with liver disease?
59. What proteins are synthesized in the hepatocytes?
60. What is the role of the urea cycle in the hepatocytes?

61. What pathophysiologic changes are associated with end-stage liver disease (ESLD)?
62. What are the hemodynamic changes associated with ESLD?
63. What are some consequences of the portal hypertension seen in ESLD?
64. What are some of the symptoms of portal hypertension?
65. What are some complications that can occur as a result of the portal hypertension seen in ELSD?
66. What are some pulmonary complications that can be seen in ESLD?
67. What are some reasons why a patient with hepatic cirrhosis may have arterial hypoxemia? Does the administration of supplemental oxygen increase the oxygen saturation in these patients?
68. What are some causes of hepatic encephalopathy seen in patients with ESLD?
69. What is the therapy for hepatic encephalopathy? Is it effective?
70. What role does the liver play in drug binding to serum proteins? What is the clinical implication of this for the patient with liver disease?
71. Why is ascites thought to accumulate in patients with hepatic cirrhosis?
72. What are some complications associated with ascites?
73. What is the treatment for ascites?
74. How might renal function be affected in patients with hepatic cirrhosis?
75. What categories of hepatorenal syndrome have been described? Are there any therapies?
76. In the absence of surgical stimulation, how do regional and inhaled anesthetics affect hepatic blood flow?
77. Is there any evidence to suggest one inhaled anesthetic preserves hepatic autoregulation more than others?
78. What is halothane hepatitis? Are pediatric patients or adult patients more likely to develop halothane hepatitis?
79. What is the cause of halothane hepatitis?
80. How is the diagnosis of halothane hepatitis made?
81. Can volatile anesthetics, other than halothane, cause hepatotoxicity?
82. What are some commonly ordered liver function tests? What is the utility of liver function tests in the perioperative period?
83. What are some preoperative findings in patients with liver disease that are associated with increased postoperative morbidity?
84. What monitoring may be useful intraoperatively for patients with hepatic cirrhosis undergoing surgical procedures?
85. Why is the intraoperative maintenance of the arterial blood pressure particularly important in patients with hepatic cirrhosis?
86. When liver function tests become abnormal postoperatively, what is the most likely mechanism for the postoperative liver dysfunction? In what patients and types of surgeries are liver function tests most likely to become elevated postoperatively?
87. What are the most likely causes of postoperative liver dysfunction?
88. What laboratory values indicate an intrahepatic cause of liver dysfunction?
89. What are some causes of postoperative jaundice?
90. What is delirium tremens? How does it usually present?
91. What is the treatment of delirium tremens?
92. What is the mortality associated with delirium tremens? What is the usual cause of death in these patients?
93. What approximate percent of females and males aged 55 to 65 years are believed to have gallstones?
94. What is the potential problem with the use of opioids intraoperatively during a cholecystectomy or common bile duct exploration?
95. How can intraoperative spasm of the sphincter of Oddi be treated?
96. What are some anesthetic considerations for patients undergoing laparoscopic procedures?

ANSWERS*

RENAL DISEASE

1. Essential physiologic functions of the kidneys include the excretion of metabolic wastes; the retention of nutrients; the regulation of water, tonicity, and electrolyte and hydrogen ion concentrations in the blood; and the production of hormones that contribute to water regulation and bone metabolism. (448)
2. Factors that place patients at an increased risk of acute renal failure in the perioperative period include advanced age, emergent surgery, liver disease, high-risk surgery, body mass index, peripheral vascular occlusive disease, and COPD. (449, Table 28-1)
3. Although the kidneys typically constitute only 0.5% of body weight, about 20% of the cardiac output normally goes to the kidneys. Of the 20%, more than two-thirds goes to the renal cortex and the remaining blood flow supplies the renal medulla. (448)
4. Renal blood flow and the GFR remain constant when mean arterial blood pressures range between 80 and 180 mm Hg. This autoregulatory function of the kidneys is accomplished by the afferent arteriolar vascular bed. The afferent arterioles are able to adjust their tone in response to changes in blood pressure, such that during times of higher mean arterial blood pressure the afferent arterioles vasoconstrict, whereas the opposite occurs during times of lower mean arterial blood pressure. This is important for two reasons. The ability of the kidneys to maintain constant renal blood flow despite fluctuations in blood pressure ensures continued renal tubular function in the face of changes, especially decreases, in blood pressure. In addition, autoregulatory responses of the afferent arterioles protect the glomerular capillaries from large increases in blood pressure during times of hypertension, as may occur with direct laryngoscopy. When mean arterial blood pressures are less than 80 mm Hg or greater than 180 mm Hg renal blood flow is blood pressure dependent. (448)
5. Even during normal kidney autoregulatory function, renal blood flow can be altered by sympathetic nervous system activity and by circulating renin. (448)
6. Renin is a proteolytic enzyme secreted by the juxtaglomerular apparatus of the kidney. There are at least three things that stimulate the release of renin from the endothelial cells of the afferent arteriole: (1) Sympathetic nervous stimulation; (2) decreased renal perfusion; and (3) decreased delivery of sodium to distal convoluted renal tubules. Renin increases efferent renal arterial arteriolar tone at low levels and causes afferent arteriolar constriction at higher levels. (449)
7. Renin is the rate-limiting enzyme in the production of angiotensin II. After its secretion from the juxtaglomerular apparatus of the kidneys, renin acts on angiotensinogen. Angiotensinogen is a large glycoprotein released by the liver to the circulation. After being cleaved by renin, angiotensin I is formed from angiotensinogen. Angiotensin I is in turn cleaved by angiotensin converting enzyme in the lungs to form angiotensin II. Angiotensin II stimulates the release of aldosterone from the adrenal cortex and is a potent vasoconstrictor. It also inhibits renin secretion as part of a negative feedback loop. (449)
8. Prostaglandins are released from the renal medulla in response to angiotensin II, hypotension and sympathetic nervous system stimulation. Prostaglandins attenuate the actions of the sympathetic nervous system, arginine vasopressin,

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

norepinephrine, and the renin-angiotensin system on the kidney by maintaining cortical blood flow. Drugs that inhibit prostaglandins, such as nonsteroidal antiinflammatory agents and aspirin, may impair this protective effect of prostaglandins. (449)

9. Arginine vasopressin (previously known as antidiuretic hormone) release by the hypothalamus results in the renal tubular conservation of water, an increased urine osmolality, and a decrease in plasma osmolality. It is typically secreted in response to small increases in serum osmolality. (450)

10. Glomerular filtration is the filtration of water and low molecular weight substances from the blood in the renal afferent arterioles into Bowman's space through the glomerulus. Glomerular filtration is dependent on two things: the permeability of the filtration barrier (the glomerular membrane) and the net difference between the hydrostatic forces pushing fluid into Bowman's space and the osmotic forces keeping fluid in the plasma. (449-450)

11. The normal hydrostatic pressure of the glomerular capillaries is about 50 mm Hg. The normal plasma oncotic pressure in the afferent and efferent arterioles is 25 mm Hg and 35 mm Hg, respectively. The increase in oncotic pressure between the afferent and efferent arterioles reflects the effects of filtration. (449)

12. The average normal rate of glomerular filtration is 125 mL/min. (449)

13. About 90% of the fluids that have been filtered by the glomerulus into Bowman's capsule are reabsorbed from renal tubules and ultimately returned to the circulation. (449)

14. The GFR is decreased during times of decreased renal blood flow or decreased mean arterial blood pressure. (449)

15. The renal clearance of drugs or their metabolites depends on three things: glomerular filtration (GFR and protein binding), active secretion by the renal tubules, and passive reabsorption (favors nonionized compounds) by the tubules. (450)

16. Tests that are commonly used for the preoperative evaluation of renal function include a serum creatinine level, a BUN level, creatinine clearance, and urine protein levels. Tests that are commonly used for the preoperative evaluation of renal tubular function include the urine specific gravity, urine osmolarity, and urine sodium excretion. Most tests of renal function are not very sensitive. (450-451)

17. A significant degree of renal disease can exist before it is reflected in renal function tests. It is estimated that more than a 50% decrease in renal function may exist before these tests become abnormal. (450-451)

18. The normal BUN level in serum varies among individuals, typically ranging between 10 and 20 mg/dL. Urea is freely filtered by the glomerulus of the kidney, but its reabsorption from the tubules varies greatly. Although the BUN varies with changes in GFR, it is influenced by multiple other factors that decrease its utility as a measure of the GFR and of renal function. (450-452)

19. Factors that may influence the BUN level include dietary protein intake, gastrointestinal bleeding, decreased urinary flow, hepatic function, and increased catabolism as during trauma, sepsis, or febrile illness. (451)

20. The BUN concentration increases in dehydrated states as a result of the corresponding decrease in urinary flow through renal tubules. During low urinary flow rates, a greater fraction of the urea is reabsorbed by the kidney. During low urinary flow rates the serum creatinine level remains normal, such that the ratio of serum BUN to creatinine is increased during times of low urinary flow associated with hypovolemia. (451)

21. Blood urea nitrogen concentrations higher than 50 mg/dL are almost always a reflection of decreased GFR. (451)

22. Serum creatinine is a product of skeletal muscle protein catabolism. Serum creatinine levels are dependent on a patient's total body water, creatinine generation rate, and creatinine excretion rate. The generation of creatinine is relatively constant within an individual, making its release into the circulation relatively constant as well. Serum creatinine levels are believed to be reliable indicators of the GFR, because its rate of clearance from the circulation is directly dependent on the GFR. (451)

23. Elderly patients may have a normal creatinine level despite a decreased GFR secondary to the decrease in muscle mass that commonly accompanies aging. For this reason, even mild increases in the serum creatinine level of elderly patients may be an indication of significant renal dysfunction. (451)

24. Normal serum creatinine levels may not accurately reflect the GFR in patients with chronic renal failure for two reasons. First, patients with chronic renal failure may have decreased skeletal muscle mass, resulting in a decrease in creatinine production. Second, the excretion of creatinine occurs via nonrenal means in these patients. (451)

25. The creatinine clearance is a measurement of the excretion of creatinine into the urine after being filtered by the glomerulus. (451-452)

26. The creatinine clearance is a more reliable measurement of GFR than serum creatinine levels because the clearance does not depend on corrections for age or the presence of a steady state. A disadvantage of creatinine clearance measurements is the requirement of accurate, timed urine collections. (451-452)

27. Intermittent proteinuria occurs in healthy individuals after standing for long periods of time and after strenuous exercise. Proteinuria may also occur during febrile states and congestive heart failure. (452)

28. Thiazide diuretics cause diuresis by inhibition of reabsorption of sodium and chloride ions from the early distal renal tubules. Spironolactone, an aldosterone antagonist, blocks the renal tubular effects of aldosterone. Spironolactone is a potassium-sparing diuretic. Loop diuretics inhibit the reabsorption of sodium and chloride, and augment the secretion of potassium primarily in the loop of Henle. Osmotic diuretics, such as mannitol, produce diureses by being filtered at the glomeruli but not reabsorbed by the renal tubules. The excess osmolarity of the renal tubular fluid leads to excretion of water. (452)

29. Dopamine dilates renal arterioles by its agonist action at the DA-1 receptor and causes adrenergic stimulation leading to an increase in renal blood flow and GFR. Dopamine therapy when used to augment urine output has not been shown to alter the course of renal failure. Dopamine also potentially leads to tachydysrhythmias, pulmonary shunting, and tissue ischemia. Fenoldopam is a dopamine analog which also possesses DA-1 agonist activity, but lacks the adrenergic activity of dopamine. (453)

30. There are several systemic changes that accompany end-stage renal disease (ESRD). Cardiovascular disease is the predominant cause of death in patients with ESRD. Systemic hypertension is very common and can be severe and refractory to therapy. Acute MI, cardiac arrest/dysfunction and cardiomyopathy account for more than 50% of deaths in patients maintained on dialysis. Diabetes mellitus frequently presents concomitantly with ESRD. Electrolyte abnormalities also occur commonly as patients develop difficulty excreting their dietary fluid and electrolyte loads. A normochromic normocytic anemia is frequently present because of decreased erythropoiesis. Uremia-induced platelet dysfunction can lead to clinical coagulopathy. (453)

31. There are several considerations for the anesthetic management of patients with ESRD. These patients may benefit from extensive monitoring, such as direct arterial blood pressure monitoring and perhaps central venous pressure monitoring depending on the surgical case, comorbidities, and other factors. Hypotension can commonly occur in patients with ESRD, particularly after hemodialysis. Patients with arteriovenous fistulas should have the presence of the thrill monitored during positioning and intraoperatively. Patients with gastroparesis should be considered at increased risk for the aspiration of gastric contents. Electrolytes, especially potassium, should be evaluated preoperatively and intraoperatively if necessary. Finally, drugs or their metabolites that are renally excreted should be administered judiciously or avoided if possible. (453-454)

32. Succinylcholine is not contraindicated in patients with ESRD. The increase in serum potassium after a large dose of succinylcholine is approximately 0.6 mEq/L for patients both with and without ESRD. This increase can be tolerated without imposing a significant cardiac risk, even in the presence of an initial serum potassium concentration higher than 5 mEq/L. (454)

33. Prerenal oliguria is indicative of a decrease in renal blood flow, the most common causes of which include a decrease in the intravascular fluid volume and a decrease in the cardiac output. Another cause may be surgical compression of the renal arteries leading to obstructed blood flow to the kidneys, either directly through clamping or inadvertently through retraction or manual traction. Whatever the cause, the duration of oliguria should be minimized to decrease the risk of acute renal failure. (454, Table 28–6)

34. The treatment of prerenal causes of oliguria is dependent on whether the cause is secondary to a decrease in intravascular fluid volume or in cardiac output. A crystalloid fluid bolus would result in a brisk diuresis if in fact the cause was hypovolemia. A lack of response to the fluid bolus would indicate that perhaps the cause of the oliguria is a decrease in cardiac output or is a result of the secretion of antidiuretic hormone in response to surgical stress. A small dose of furosemide, 0.1 mg/kg intravenously, will lead to diuresis if the cause of the oliguria is antidiuretic hormone secretion. If there is no response to the intravenous administration of furosemide, a determination should be made as to whether the patient remains hypovolemic or there is a decrease in cardiac output. If the patient is at risk for a decrease in cardiac output, it may be worthwhile to monitor cardiac filling pressures to guide intravascular fluid replacement. If the cardiac filling pressures is high, a cause for the decrease in cardiac output should be sought. (454-455)

35. Acute tubular necrosis, glomerulonephritis, and acute interstitial nephritis are intrinsic renal causes of oliguria. (454, 455, Table 28-6)

36. Oliguria due to acute tubular necrosis is characterized by urine that is typically dilute and contains excessive sodium. (454, 455, Table 28-6)

37. Causes of postrenal oliguria include ureteral obstruction, bladder outlet obstruction, and obstruction or kinking of the Foley catheter. Postrenal causes of oliguria are frequently reversible. (455)

LIVER AND BILIARY TRACT DISEASE

38. Physiologic functions of the liver include protein synthesis, drug metabolism, fat metabolism, hormone metabolism, bilirubin formation and excretion, and glucose homeostasis. (455)

39. The liver receives its blood supply via the portal vein (70%) and hepatic artery (30%). Approximately 25% of the cardiac output goes to the liver. While the portal vein supplies 70% of hepatic blood supply, it only contributes 50% of the liver's oxygen supply. The remaining 50% of the liver's oxygen supply comes from the hepatic artery. (455)

40. Total hepatic blood flow is directly proportional to the perfusion pressure across the liver and is inversely proportional to splanchnic vascular resistance. There are many determinants of hepatic blood flow. Determinants intrinsic to the liver include hepatic autoregulation, metabolic control, and the hepatic arterial buffer response. Determinants extrinsic to the liver include sympathetic nervous system activity, surgical stimulation, and humoral factors. (455)

41. Hepatic autoregulation refers to the ability of the hepatic artery to alter its resistance in response to changes in arterial pressure to maintain hepatic artery blood flow. For example, hepatic artery resistance may decrease to maintain perfusion to the liver when portal vein flow is reduced. Of note, there does not appear to be autoregulation of the portal venous system. Instead portal venous blood flow parallels cardiac output. Surgery and anesthesia impair hepatic autoregulation and typically result in reduced hepatic perfusion. (455)

42. The hepatic arterial buffer response refers to the capacity of the liver to increase or decrease hepatic artery blood flow in response to decreases or increases in portal venous flow. For example, when portal venous flow decreases, the resistance of the hepatic artery decreases and hepatic artery blood flow increases. This reciprocal relationship allows for the hepatic oxygen supply and total hepatic blood flow to be maintained despite alterations in portal venous flow. This compensatory mechanism does not completely compensate for changes in portal venous flow, however. In addition, the hepatic arterial buffer response can be disrupted by several factors, including neural, humoral, and metabolic changes. This hepatic response is also disrupted by hepatic cirrhosis and volatile anesthetics. (455)

43. Innervation of the liver is by both the parasympathetic nervous system and the sympathetic nervous system. Generalized sympathetic nervous system stimulation, as can occur with arterial hypoxemia or hypercarbia, pain or surgical stress, results in an increase in the splanchnic vascular resistance. The increase in splanchnic vascular resistance yields a decrease in liver blood flow and blood volume. (455)

44. Positive pressure ventilation of the lungs decreases hepatic blood flow through its increase in hepatic venous pressure. Hepatic blood flow is decreased further by the application of positive end-expiratory pressure through the same mechanism. (455)

45. Congestive heart failure, particularly right-sided heart failure, decreases hepatic blood flow through its increase in hepatic venous pressure. (455)

46. Decreases in cardiac output or myocardial contractility result in decreases in hepatic blood flow. (455)

47. Decreases in arterial blood pressure result in decreases in hepatic blood flow. (455)

48. The liver stores glucose as glycogen in the hepatocytes. (456)

49. Glucose homeostasis is maintained during times of starvation by the breakdown of the glycogen to glucose in the hepatocytes. Glucose is then released into the circulation. The glycogen stores of the liver correspond to 24 to 48 hours of glucose supply during times of starvation. Prolonged starvation that results in the depletion of the glycogen stores requires that the liver convert lactate, glycerol, and amino acids to glucose. This is termed *gluconeogenesis*. (456)

50. Patients with cirrhosis may be more likely to develop hypoglycemia in the perioperative period as gluconeogenesis may be impaired. (456)

51. A normal liver synthesizes most of the proteins responsible for the coagulation of blood. A diseased liver may therefore manifest as coagulopathy in the patient. (456)

52. Bleeding can be prevented with only 20% to 30% of normal levels of clotting factors, so that abnormal blood coagulation manifests only after significant liver

disease. The coagulation status of a patient can be evaluated preoperatively by checking the patient's prothrombin time, partial thromboplastin time, and bleeding time. Indeed, the prothrombin time is frequently used as an evaluation of the synthetic function of the liver. (456)

53. Vitamin K plays an important role in the catalysis of some of the procoagulant proteins to produce factors II, VII, IX, and X. (456)

54. The liver facilitates the renal excretion of lipid soluble drugs by converting the drugs to more water soluble forms via mechanisms such as conjugation. (456)

55. Chronic drug therapy can inhibit anesthetic drug metabolism by inhibiting hepatic enzymes. Conversely, they can also enhance drug metabolism by inducing hepatic enzymes (particularly cytochrome P isoforms). (456)

56. Chronic liver disease may interfere with the metabolism of drugs because of the decreased number of enzyme-containing hepatocytes or the decreased hepatic blood flow that typically accompanies cirrhosis of the liver. (456)

57. Accelerated drug metabolism may be noted after the administration of certain drugs such as phenytoin. It is believed that exposure of the microsomal enzymes to these drugs causes an up-regulation, or induction, of their own synthesis. (456)

58. The conjugation of bilirubin with glucuronic acid takes place in the liver through the action of glucuronyl transferase. The conjugation of bilirubin allows it to become water soluble for renal excretion. Impairment of this function of the liver, as with liver disease, can lead to increased serum levels of unconjugated bilirubin. The liver is also responsible for the excretion of conjugated bilirubin into bile. This explains the elevated serum levels of conjugated bilirubin in the presence of liver disease. (456)

59. All proteins are synthesized in hepatocytes except for gamma globulins and factor VIII. (456)

60. The urea cycle is used by hepatocytes to convert the end products of amino acid degradation, such as ammonia and other nitrogenous waste products, to urea which is readily excreted by the kidneys. (456)

61. End-stage liver disease (ESLD) is associated with portopulmonary hypertension, hepatopulmonary syndrome (shunting due to impairment of hypoxic pulmonary vasoconstriction), atelectasis, pleural effusions, hepatic encephalopathy, impaired drug binding, coagulopathy, ascites, and renal dysfunction (due to various factors including the hepatorenal syndrome). (457)

62. Severe liver disease that has advanced to cirrhosis is associated with a hyperdynamic circulation. Patients typically have normal to low systemic blood pressure, increased cardiac output and decreased systemic vascular resistance due to vasodilation and shunting. (457)

63. Portal hypertension, as seen in ESLD, is the high resistance of blood flow through the liver. This results in an accumulation of blood in the vascular beds that normally drain to the liver, and these vessels become dilated and hypertrophy. Vessels draining the esophagus, stomach, spleen, and intestines are affected, resulting in varices. (457)

64. Some of the symptoms of portal hypertension include anorexia, nausea, ascites, esophageal varices, spider nevi, and hepatic encephalopathy. (457)

65. Complications that can occur as a result of the portal hypertension seen in ELSD include increased susceptibility to infection, renal failure, mental status changes, and massive hemorrhage through the rupture of the engorged dilated submucosal veins. Gastroesophageal varices are at the greatest risk of rupture. (457)

66. Pulmonary complications that can be seen in ESLD include pulmonary arteriovenous communications that are not ventilated, the impairment of hypoxic pulmonary vasoconstriction, atelectasis, and restrictive pulmonary disease due to ascites and pleural effusions. In less than 5% of patients with ESLD portopulmonary hypertension develops, whose cause is not well established. (457)

67. Patients with hepatic cirrhosis may have arterial hypoxemia for several reasons. Often, patients with hepatic cirrhosis have right-to-left pulmonary shunting in response to the portal vein hypertension. Patients with ascites and hepatomegaly may also have impairment of diaphragmatic excursion due to the weight of the abdominal contents, particularly in the supine position. In patients with significant ascites, pleural effusions may impair lung expansion. In the early stages of ESLD, supplemental oxygen may improve arterial hypoxemia, but as the disease progresses oxygen therapy may not be effective. (457)

68. The cause of hepatic encephalopathy seen in patients with ESLD is multifactorial. Hepatic encephalopathy is in part due to increased serum concentrations of chemicals normally cleared by the liver, especially ammonia. Other factors include disruption of the blood–brain barrier, increased central nervous system inhibitory neurotransmission, and altered cerebral energy metabolism. (457)

69. Therapy for hepatic encephalopathy revolves around reducing the production and absorption of ammonia. Neomycin is used to reduce ammonia production by urease-producing bacteria and lactulose is administered to reduce ammonia absorption. Some symptoms of hepatic encephalopathy are reversible with flumazenil therapy. These therapies are not completely effective because multiple other etiologic factors are associated with hepatic encephalopathy. It is also important to rule out other causes of altered mental status in the patient with ESLD. Other causes may include intracranial bleeding, hypoglycemia, or a postictal state. (457)

70. The liver synthesizes albumin, which binds drugs in the plasma. The binding of drugs to albumin decreases the free, or pharmacologically active, portion of the drug. When the liver is diseased the synthesis of albumin becomes impaired, decreasing the albumin available in the plasma for binding. As a result there is an increased concentration of free, unbound drug in the plasma. Patients with liver disease may manifest a more pronounced drug effect than patients with normal liver function after an intravenous injection of a specific drug dose. Increased drug effect secondary to a decrease in protein binding is more likely to be seen when the serum albumin concentration is less than 2.5 g/dL. (456-457)

71. Ascites affects 50% of patients with hepatic cirrhosis. Ascites is thought to accumulate secondary to a decrease in plasma oncotic pressure, a corresponding increase in the hydrostatic pressure in the hepatic sinusoids, and an increase in sodium retention by the kidneys due to increased circulating levels of antidiuretic hormone. (457)

72. Complications associated with ascites include marked abdominal distention that can lead to atelectasis and restrictive pulmonary disease, spontaneous bacterial peritonitis, and circulatory instability due to compression of the inferior vena cava and right atrium. (457)

73. The treatment for ascites is initially fluid restriction, reduced sodium intake, and diuretic therapy. In severe cases abdominal paracentesis temporarily effectively reduces abdominal distention and restores hemodynamic stability. (457)

74. Patients with hepatic cirrhosis tend to have a decrease in arterial blood volume, and consequently a decrease in renal blood flow and the GFR. Because of this patients with hepatic cirrhosis are at risk of developing hepatorenal syndrome, a serious

complication that is often fatal. The syndrome is characterized by intravascular fluid depletion, intrarenal vasoconstriction, worsening hyponatremia, hypotension, and oliguria. (457-458)

75. Two types of hepatorenal syndrome have been described. Type 1 hepatorenal syndrome presents as rapidly progressing prerenal failure. It is associated with a poor prognosis in the absence of therapeutic intervention. Type 2 hepatorenal syndrome presents with a milder degree of renal dysfunction. Treatment with octreotide, glucagon, and midodrine have shown promise at reversing type 1 hepatorenal syndrome. (457-458)

76. In the absence of surgical stimulation, regional and inhaled anesthetics decrease hepatic blood flow by 20% to 30%. Changes in hepatic blood flow in response to regional and inhaled anesthetics are believed to result from decreases in cardiac output, mean arterial pressure, or both. Volatile anesthetics may also decrease hepatic blood flow by impairing intrinsic hepatic mechanisms to maintain hepatic blood flow to varying degrees. (458)

77. There is some evidence to suggest that isoflurane inhibits hepatic autoregulation less than other inhaled anesthetics. (458)

78. There are two different forms of hepatotoxicity that can result from the administration of halothane. Halothane hepatitis typically refers to the more severe hepatotoxicity that can result in hepatic necrosis and death. Halothane hepatitis is extremely rare. Adult patients are more likely to develop halothane hepatitis than pediatric patients. Patients most likely to be affected are middle-aged, obese women who have had repeated administration of halothane anesthesia. (458)

79. Although the exact cause of halothane hepatitis is unclear, it is believed to be due to an immunologic response to a toxic metabolite of halothane. (458)

80. The diagnosis of halothane hepatitis is made after other causes of hepatitis have been excluded. Its rare incidence and the disappearance of halothane in modern clinical practice make the likelihood of halothane hepatitis extremely unlikely. (458)

81. The administration of all volatile anesthetics can result in a mild, self-limited form of hepatotoxicity. It can be seen in up to 20% of patients, but is associated with minimal sequelae. (458)

82. Commonly ordered liver function tests include serum bilirubin, aminotransferase enzymes, alkaline phosphatase, albumin, and the prothrombin time. Liver tests are very nonspecific, and significant liver dysfunction must occur before it is reflected in the majority of tests. Despite this, liver function tests have some utility in the perioperative period. Liver function tests may be useful preoperatively in detecting the presence of liver disease. Perioperatively, liver dysfunction may be classified as prehepatic, intrahepatic, or posthepatic through the evaluation of the results of the various liver function tests. (458-459, Table 28-7)

83. Preoperative findings in patients with liver disease that are associated with increased postoperative morbidity include marked ascites, markedly elevated prothrombin time and serum bilirubin level, markedly decreased serum albumin level, and encephalopathy. (459, Table 28–8)

84. Intraoperative monitoring for patients with hepatic cirrhosis should be guided by the surgical procedure. In general, monitoring of the arterial blood pressure with an intra-arterial catheter may be useful. This allows for monitoring of the arterial blood gases, pH, coagulation status, and glucose as well as the blood pressure. In addition, the urine output should be closely monitored due to the risk of postoperative renal dysfunction that can occur in patients with severe liver

disease. Central venous pressure or pulmonary artery catheter monitoring might be useful in the fluid management of patients with cardiomyopathy and congestive heart failure. The intravascular fluid balance of patients with liver disease and especially ascites can be difficult to manage. Finally, the use of an intraoperative transesophageal echocardiogram may be useful to monitor myocardial function and intravascular fluid status, but in patients with esophageal varices there exists a risk of bleeding with its insertion. (458-459)

85. The intraoperative maintenance of the arterial blood pressure is particularly important in patients with hepatic cirrhosis because these patients are dependent on hepatic arterial blood flow to provide oxygen to the hepatocytes. In the presence of portal hypertension, hepatic arterial blood flow is typically reduced from normal levels. The addition of anesthetics and the surgical procedure can exacerbate this reduction in hepatic blood flow and may contribute to postoperative liver dysfunction. (459)

86. Liver function tests are most likely to become abnormal secondary to an inadequate supply of oxygen to the hepatocytes intraoperatively. This is the most likely mechanism for mild, self-limited postoperative liver dysfunction. Abnormal postoperative liver function tests are most likely to occur in patients with preexisting liver disease whose hepatic oxygenation was marginal preoperatively or after surgery in which the operative site was in close proximity to the liver. (458)

87. The most likely causes of postoperative liver dysfunction include drugs, arterial hypoxemia, sepsis, congestive heart failure, cirrhosis, and a history of preexisting hepatic viruses. (457-58)

88. Elevated aminotransferase enzymes, decreased albumin, and a prolonged prothrombin time are all indicative of an intrahepatic cause of liver dysfunction. These alterations are reflective of direct hepatocellular damage. (460, Table 28-9)

89. Operations on the liver or biliary tract, multiple blood transfusions, resorption of surgical hematoma, antibiotics and other perioperative drugs and metabolic and infectious causes can all lead to postoperative jaundice. Rarely, inhaled anesthetic agents may be implicated. (459-460, Table 28-9)

90. Delirium tremens is a severe withdrawal syndrome in patients with a history of chronic alcohol abuse. The onset of delirium tremens is typically 48 to 72 hours after cessation of the ingestion of alcohol. Delirium tremens presents clinically as tremulousness, hallucinations, agitation, confusion, disorientation, and increased activity of the sympathetic nervous system. Increased activity of the sympathetic nervous system in these patients is manifest as diaphoresis, fever, tachycardia, and hypertension. In severe cases the syndrome may progress to seizures and death. (460)

91. The treatment of delirium tremens is primarily with the administration of central nervous system depressants, usually a benzodiazepine. If necessary, a β-adrenergic antagonist may be administered to offset sympathetic nervous system hyperactivity. The trachea may be intubated if indicated for airway protection. Other treatment is supportive as necessary, including hydration and the correction of electrolyte disorders. (460)

92. The mortality associated with delirium tremens can be as high as 10%. The usual cause of death in these patients is cardiac dysrhythmias or seizures. (460)

93. Approximately 20% of women and 10% of men aged 55 to 65 years are believed to have gallstones. Elevated serum bilirubin and/or alkaline phosphatase levels in these patients imply the presence of a stone in the common bile duct causing obstruction to the flow of bile. (460)

94. Opioids such as morphine, meperidine, and fentanyl may produce spasm in the sphincter of Oddi. This increases the pressure in the common bile duct in a dose-dependent manner and may be painful to an awake patient. The administration of these medicines intraoperatively could hinder the passage of contrast medium for exploration of the common bile duct. In clinical practice, however, the administration of opioids to these patients rarely results in difficulty with intraoperative cholangiograms. (460)

95. Intraoperative spasm of the sphincter of Oddi can be treated with naloxone, glucagons, or nitroglycerin. (461)

96. Anesthetic considerations for patients undergoing laparoscopic procedures are multiple. Included are the insufflation of the abdomen with carbon dioxide and the possible impairment of ventilation of the lungs in the presence of increased ventilatory requirements, the probable placement of the patient in the Trendelenburg position, the risk of puncture of bowel or vessels, and the potential for nitrous oxide to expand bowel gas. (460-461)

Chapter

26 NUTRITIONAL AND GASTROINTESTINAL DISEASE

Steve Hyman, William R. Furman

OBESITY

1. What is a desired body mass index (BMI)? What BMI defines morbid obesity? What BMI defines "super obese"? What BMI defines "super-super obese"?
2. What organ systems can be affected by obesity?
3. What is the metabolic syndrome and what is its significance?
4. How is the diagnosis of metabolic syndrome made?
5. What are the contributory factors to morbid obesity?
6. What are four main considerations when anesthetizing a morbidly obese patient?
7. What were some of the complications with the older weight loss operations such as jejunoileal bypass?
8. What are three significant and beneficial effects of modern gastric bypass?

MALNUTRITION

9. What is the definition of malnutrition? Why might malnutrition be present in surgical patients?
10. Is enteral or intravenous nutrition preferable for most patients who require supplemental feedings? Why?
11. What is refeeding syndrome? What is the pathophysiology of refeeding syndrome? What are the signs of refeeding syndrome?
12. What are four perioperative considerations for the malnourished patient? What are the considerations for the critically ill enterally fed patient?

INFLAMMATORY BOWEL DISEASE

13. What is the presumed pathophysiology of inflammatory bowel disease (IBD)? What are some of the factors that are associated with IBD?
14. What are the major differences between ulcerative colitis and Crohn's disease?
15. What is the preferred anesthetic technique for a patient with IBD?
16. How do drugs used in the treatment of IBD interact with anesthetic drugs?

GASTROESOPHAGEAL REFLUX DISEASE

17. What is the definition of gastroesophageal reflux disease (GERD)?
18. What is the pathophysiology of GERD?
19. What are the signs and symptoms of GERD?
20. What is the risk of pulmonary aspiration on induction of anesthesia?
21. Does the rapid sequence induction (RSI) with cricoid pressure (Sellick maneuver) prevent pulmonary aspiration? Why or why not?
22. What is the mechanism of development of subcutaneous emphysema, pneumomediastinum, or pneumoperitoneum after a Nissen fundoplication?

DIABETES MELLITUS

23. What is the definition of diabetes? What types of complications are associated with long-term poorly controlled diabetes?
24. What is autonomic neuropathy? What perioperative risks are associated with autonomic neuropathy?
25. Why are the historical classifications of insulin-dependent and noninsulin-dependent diabetes inferior to type 1 and type 2 diabetes?
26. What is the major treatment goal in both types of diabetes?
27. What are the four categories of oral hypoglycemic agents?
28. What is hemoglobin A1C (glycosylated hemoglobin)? What is its significance in the management of diabetes?
29. What is the recommended management of preoperative diabetes medicines?
30. What blood glucose levels should be maintained perioperatively? What are some potential complications of severe perioperative hyperglycemia?
31. At what level of preoperative glucose should an operation be postponed?

HYPERTHYROIDISM (THYROTOXICOSIS) AND THYROID STORM

32. What is the definition of hyperthyroidism?
33. What are some common causes of hyperthyroidism?
34. What is Graves's disease?
35. What are the signs and symptoms of hyperthyroidism?
36. What is the difference between hyperthyroidism and thyroid storm?
37. What are the signs and symptoms of thyroid storm?
38. What conditions may cause a thyrotoxic patient to develop thyroid storm?
39. What medications are used in the management of thyroid storm?
40. What is the Wolfe-Chaikoff effect?
41. What are the anesthetic considerations for a patient with hyperthyroidism?
42. How should perioperative thyroid storm be managed?

HYPOTHYROIDISM

43. What is the definition of hypothyroidism?
44. What are the causes of hypothyroidism?
45. What are the signs and symptoms of hypothyroidism?
46. What is the difference between primary and secondary hypothyroidism?
47. What are the airway considerations (both preoperative and postoperative) in a patient undergoing thyroid surgery?
48. Is it necessary to delay surgery in hypothyroid patients and achieve a euthyroid state before operating?
49. What is intraoperative laryngeal nerve monitoring and what is its impact on the anesthetic plan?

PHEOCHROMOCYTOMA AND PARAGANGLIOMA

50. What is the embryologic cell of origin of the pheochromocytoma and what is the difference between it and a paraganglioma?
51. What hormones are produced by these tumors and what are their common signs and symptoms?
52. How common are pheochromocytomas and paragangliomas tumors?
53. How should perioperative hypertension and tachycardia associated with pheochromocytoma and paraganglioma be managed?

MULTIPLE ENDOCRINE NEOPLASIA AND NEUROENDOCRINE TUMORS

54. What is the MEN-1 (multiple endocrine neoplasia-1) syndrome? What is its inheritance pattern?
55. What is the MEN-2 (multiple endocrine neoplasia-2) syndrome? What is its inheritance pattern?
56. What specific tumors are commonly found in patients with MEN-1?
57. What are the subtypes of MEN-2?
58. What are the anesthetic implications of MEN-1 and MEN-2?
59. What are carcinoid and neuroendocrine tumors and what hormones do they produce?

60. Why are midgut carcinoid tumors often asymptomatic? When do they become symptomatic?
61. What is carcinoid syndrome? What is the usual treatment for a carcinoid crisis?
62. What are the perioperative implications of carcinoid and neuroendocrine tumors?

ADRENAL INSUFFICIENCY AND STEROID REPLACEMENT

63. What are the principal hormones of the adrenal cortex?
64. What is the mechanism by which stress stimulates the release of cortisol?
65. What is the function of cortisol in the body?
66. What is Addison's syndrome? What are the symptoms?
67. What is the difference between primary and secondary (or tertiary) adrenocortical insufficiency?
68. What are the frequent causes of primary adrenocortical insufficiency?
69. What are the frequent causes of secondary or tertiary adrenocortical insufficiency?
70. What is addisonian crisis (acute adrenal failure)? What are its symptoms and causes?
71. What are the common causes of pituitary apoplexy? What are the signs, symptoms, and treatment of pituitary apoplexy?
72. What is the effect of etomidate on adrenal function?
73. What is the general approach to perioperative steroid replacement in the patient who has steroid-induced adrenal insufficiency?
74. What is critical illness-related corticosteroid insufficiency (CIRCI)?

CUSHING'S SYNDROME

75. What is Cushing's syndrome? What are the signs and symptoms of Cushing's syndrome and how is it diagnosed?
76. What is the difference between primary and secondary (or tertiary) Cushing's syndrome?
77. What is the difference between Cushing's syndrome and Cushing's disease?
78. What are the common causes of secondary Cushing's syndrome?
79. What are the anesthetic considerations in a patient with Cushing's syndrome?

ANSWERS*

OBESITY

1. A desirable BMI is generally considered to be 18 to 25. Morbid obesity is a BMI of 40 or more. Super obese is a BMI of 50 or more and super-super obese is a BMI of 60 or more. (463)

2. Morbid obesity can affect virtually any organ system of the body. Commonly affected systems are cardiovascular (hypertension, stroke, right heart failure), endocrine (reproductive hormonal imbalances, impaired fertility, diabetes), and gastrointestinal (hiatal hernias and gastroesophageal reflux from increased intraabdominal pressure). Involvement of the pulmonary system can include low residual volumes, rapid desaturation, restrictive lung disease, and obstructive sleep apnea. Skeletal problems may include back pain and osteoarthritis, particularly of the knees. Some malignancies (colon and breast) are associated with obesity as are some psychological disorders such as depression. (463)

3. Metabolic syndrome is a term that applies to the combined complications of obesity. There are six components of the metabolic syndrome: abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, insulin resistance (glucose intolerance), a proinflammatory state, and a prothrombotic state. Diagnosis and

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

treatment is important because it alone predicts approximately 25% of all new-onset cardiovascular disease. (463-464)

4. Diagnosis of metabolic syndrome is made by the presence of three out of five of the following: abdominal obesity, elevated triglycerides, low HDL, elevated blood pressure, elevated fasting glucose. (463)

5. The causes of obesity are multifactorial. They include genetic, environmental, metabolic, and psychosocial factors. While caloric consumption is important, the urge to eat (or overeat) can be modulated by hormones. Fasting releases several orexigenic (appetite-stimulating) hormones and can cause inflammation. (464)

6. Four major considerations in the anesthetic management of the morbidly obese patient include the risk of aspiration of gastric contents, securing the airway, the logistics of caring for a large patient, and emergence technique.

   In the 1970s, it was suggested that fasted obese patients might have larger than normal gastric volumes with a lower than normal pH. This assertion was not supported with strong scientific evidence. More recent studies appear to show that nondiabetic obese patients actually may have less volume at a higher pH than do lean nondiabetic patients.

   The most basic tasks may be difficult in the obese patient. Peripheral intravenous line placement may be difficult and central venous catheterization may be required. Blood pressure monitoring may be difficult because of the conical shape of the upper arm. Most blood pressure cuffs are designed for a more cylindrical profile and may not remain in position or function optimally on a cone-shaped arm. Practical options include a cuff on the forearm or calf, or an intraarterial catheter.

   Positioning is difficult because obese patients may be wider than the horizontal surface of the operating table. Also, the table must be able to support the patient's weight and move into required positions for surgical access. Extreme positions of tilt demand that the patient be well secured and that potential pressure points be addressed.

   Obesity is reported to increase the risk of a difficult laryngeal intubation. One recent study found the intubation difficulty score to be higher in obese patients, but time to intubation and Spo_2 levels to be the same as in lean patients. However, there is evidence that difficult intubation correlates better with male gender and a higher Mallampati airway evaluation score, as in the general population.

   During intubation, diminished functional residual capacity may lead to rapid desaturation. A reverse Trendelenburg position (head up) can reduce atelectasis in dependent lung areas and can help move chest, and breast tissue caudally, allowing easier access to the mouth for intubation.

   No induction or maintenance drug has a distinct advantage in the obese patient. Emergence can be slow because of a reduced rate of elimination of volatile anesthetic agents from adipose tissues. (464)

7. Unlike current operations that restrict the gastrointestinal tract, the jejunoileal bypass developed in 1954, was a malabsorptive operation developed for the treatment of hyperlipidemia, atherosclerosis, and obesity. It was abandoned by the 1980s because it causes unacceptable complications, including uveitis, kidney dysfunction, intestinal bacterial overgrowth, and liver damage. (464)

8. Gastric bypass patients generally have improvements in quality of life and comorbidities. There is improvement in hypertension, diabetes, and/or obstructive sleep apnea. Several orexigenic (appetite stimulating) hormones are diminished by bariatric surgery. Ghrelin secretion by the gastric fundus and proximal small intestine is increased after nonsurgical weight loss but is unchanged or decreased after bariatric surgical procedures. Other intestinal hormones that regulate appetite and glucose metabolism also are affected favorably by surgery. These include glucagon-like peptide-1, glucose-dependent insulinotropic peptide, and peptide YY. (464)

MALNUTRITION

9. Malnutrition may be present when there is weight loss of 10% to 20% over a short time, when weight is less than 90% of ideal body weight, or when BMI is less than 18.5. Healthy patients may quickly become malnourished after an accident or acute illness and critically ill patients develop malnutrition if they are not fed. Malnutrition can occur quickly when caloric requirements exceed intake due to decreased intake, impaired absorption, or an increased metabolic rate. (464-465)

10. Enteral nutrition is the preferred method of feeding because it is believed to maintain the absorptive gastrointestinal villi and reduce transmucosal bacterial transfer into the blood stream. It results in improved patient outcomes, less infection, less ventilator days, and less intensive care unit days. Long-term feeding usually requires a gastrostomy or jejunostomy. Postpyloric (jejunal) placement is frequently preferred as a means to limit regurgitation and the risk of aspiration, although the risk of aspiration with gastric feeding tubes is low. In patients who have pancreatitis, jejunal placement is favored in order to avoid stimulation of pancreatic enzyme secretion. In contrast, intravenous feeding (total parental nutrition or TPN) is preferred for patients who do not have a functioning gastrointestinal tract. TPN is considered acceptable for short-term feedings. Risks of long-term TPN include central venous catheter sepsis, thrombosis, hyperglycemia, iatrogenic hypoglycemia, and fatty liver. (465)

11. Refeeding syndrome is caused by rapid, acute nutritional replacement of a malnourished patient. It is characterized by increased ATP production, a significant fall in plasma phosphate, respiratory failure, and cardiac failure. Metabolic rate is increased with a significant rise in carbon dioxide (CO_2) production and respiratory acidosis. The syndrome may be prevented by slowly increasing the nutritional intake toward caloric goals. (465)

12. Perioperative considerations for the malnourished patient include muscle weakness, immunocompromise, preoperative fasting, and perioperative glucose monitoring. Muscle weakness may lead to respiratory failure and immunocompromise may predispose patients to infection. Preoperative fasting is often an issue in enterally fed critically ill patients, particularly burn and trauma patients. One must weigh the risk of aspiration on induction against the benefit of keeping nutrition at maintenance levels. In the absence of definitive studies, expert opinion generally supports efforts to continue nutrition as much as possible. However, preliminary data supports the safety of a short fast (45 minutes) when the feeding tube is located beyond the ligament of Treitz. Perioperative glucose monitoring is necessary in patients receiving TPN, because insulin is typically included. Blood glucose should be monitored for procedures more than 2 hours in duration. (465)

INFLAMMATORY BOWEL DISEASE

13. IBD is believed to result from an aberrant response by the bowel mucosal immune system to normal luminal flora. The precise trigger for the activation of the immune system in IBD is unclear and likely multifactorial. Patients typically present with complaints of abdominal pain, fever, and diarrhea. There may be a genetic basis since there is an increased risk in close family members. Caucasians are more susceptible to IBD and Jewish people are at greater risk for Crohn's disease. Environmental factors may include smoking, appendectomy, antibiotics, oral contraceptives, and NSAIDs. (465)

14. There are two categories of inflammatory bowel disease: ulcerative colitis and Crohn's disease. Ulcerative colitis is restricted to the large intestine and manifests itself as inflammation and loss of colonic mucosa. Crohn's disease can affect any part of the digestive tract and may cause transmural inflammation leading to abscesses or granulomatous disease. Although they are distinct entities, distinction between the two may be difficult to make when Crohn's manifests itself by only affecting the colon. (465)

15. Specific anesthetic agents are neither preferred nor contraindicated for patients with IBD. Patients taking steroids should continue prior to surgery and may require supplementation because of iatrogenic adrenal insufficiency. (465)

16. Certain medications prescribed to treat IBD may have anesthetic implications. Interactions between anesthetic and antineoplastic agents are not fully documented in the literature. Cyclosporine is reported to increase the minimum alveolar concentration of volatile agents and to be additive with barbiturates or fentanyl in an animal model. Phosphodiesterase effects of azathioprine may partially antagonize nondepolarizing neuromuscular blockade, although this is controversial. Cyclosporine, infliximab, and aminoglycosides potentiate the nondepolarizing neuromuscular blocking agents. (465-466)

GASTROESOPHAGEAL REFLUX DISEASE

17. GERD is the retrograde movement of gastric contents through the lower esophageal sphincter (LES) into the esophagus. If gastric contents also move past the upper esophageal sphincter into the pharynx, pulmonary aspiration of gastric acid and particulate matter may result. Pulmonary aspiration of gastric contents is a serious, potentially life-threatening complication. (466)

18. Reflux occurs when the lower esophageal sphincter is incompetent or when LES pressure is less than intraabdominal (or intragastric) pressure. This may result from esophageal dysmotility or from a hiatal hernia, where the LES may be displaced cephalad into the thoracic cavity. The LES loses the diaphragmatic contribution to its function and the diaphragm can also obstruct the esophagus. Associated conditions include pregnancy, obesity, obstructive sleep apnea, gastric hypersecretion, gastric outlet obstruction, gastric neuropathy, and increased intraabdominal pressure. (466)

19. GERD is an extremely common syndrome in which 20% of people have heartburn (the most reliable symptom) at least once per week. Four to ten percent have heartburn daily. Other problems include noncardiac chest pain, dysphagia, pharyngitis, cough, asthma, hoarseness, laryngitis, sinusitis, and dental erosions. (466)

20. The risk of pulmonary aspiration on induction of anesthesia is not well-established. Significant GERD occurs in at least 30% to 50% of pregnant women; however, the incidence of aspiration is low. The mechanism is primarily a progesterone-mediated relaxation of LES tone, with possible contributions from elevated intraabdominal pressure, delayed gastric emptying, and decreased bowel transit. (466)

21. The customary approach to induction is RSI with cricoid pressure (CP, also called Sellick's maneuver) to obstruct the potential flow of gastric contents into the pharynx and trachea. However, the putative benefits of the RSI and CP remain controversial.

    Cricoid pressure can be ineffective if not properly applied. Some undesired side effects of CP include increased risk of regurgitation and failed intubation. Based on studies of the radiographic anatomy, improperly performed CP may not align the cricoid and esophagus properly with the solid cervical spine underneath. If the cricoid and esophagus are displaced laterally, they may overlie muscle and the upper esophagus may not be occluded. The significance of this failure of alignment is by no means a settled issue. The exact opposite view, that lateral displacement does not impair barrier function, has also been articulated. Complications are more likely in the elderly, children, pregnant women, patients with cervical injury, patients with difficult airways, and patients where there is difficulty palpating the cricoid cartilage. (466, Table 29-1)

22. Nissen fundoplication surgery may be associated with subcutaneous air in the neck and chest, but is benign and self-limited because carbon dioxide (CO_2) gas is rapidly resorbed by the body. Likewise, pneumoperitoneum and

pneumomediastinum are common, occurring in up to 86% of patients due to dissection of the phrenoesophageal ligament. Pneumothorax, in contrast, is not a normal consequence of laparoscopic surgery. (466-467)

DIABETES MELLITUS

23. Diabetes mellitus is elevated blood glucose levels due to a relative lack of endogenous insulin. It is the most common endocrine disease and affects 15 to 20 million Americans (7% to 8% of the American population). It is associated with complications in most organ systems resulting largely from microangiopathy and macroangiopathy. Risk of complications of diabetes increases with increasing hemoglobin A1C levels. Large and small vessel coronary artery disease is common and was originally advanced as an indication for perioperative β-blockade in the original papers on the subject. Diabetic renal failure in young and middle-aged adults is the leading cause of renal failure requiring hemodialysis. Retinopathy occurs in 80% to 90% of those who require insulin for at least 20 years. Autonomic neuropathy occurs in 20% to 40% of patients with long-standing diabetes, particularly those with peripheral sensory neuropathy, renal failure, or systemic hypertension. Cardiac autonomic neuropathy may mask angina pectoris and obscure the presence of coronary artery disease. Gastroparesis, which may cause delayed gastric emptying, is a sign of autonomic neuropathy affecting the vagus nerves. (467)

24. Autonomic neuropathy is a dysfunction of the autonomic nervous system, which occurs as a result of damage to small nerve fibers. This results in loss of vagally controlled heart rate, a decrease in peripheral sympathetic nervous system tone resulting in orthostatic hypotension, decreases in peripheral blood flow, and diminished sweating. These patients are at an increased risk of delayed gastric emptying, perioperative hemodynamic instability, cardiac arrhythmias, silent myocardial infarction, impaired respiration, and cardiopulmonary arrest. In addition, these patients have a blunted response to atropine, making the early treatment of bradycardia essential. (467)

25. The historical classification of diabetes was made in terms of the presence or absence of insulin requirement. This was unsatisfactory because nearly all diabetics develop a need for insulin at some point. The current classification is Type 1 (T1DM) and Type 2 (T2DM) diabetes. T1DM is typically characterized by the absence of any insulin production from the pancreas. T2DM involves a relative lack of insulin plus resistance to endogenous insulin. (467)

26. Blood glucose control is the major treatment goal in both types of diabetes. T1DM always requires insulin to prevent hyperglycemia and ketoacidosis. It is commonly heralded at an early age by a dramatic episode of ketoacidosis. Type 2 diabetics may require insulin, but often only require oral hypoglycemic agents, weight loss, or dietary management. The onset of T2DM usually is more insidious and constitutes the majority of diabetics. They are often overweight, so dietary control and weight loss is important, but the cornerstone of management of both types is pharmacologic. (467)

27. There are four categories of oral hypoglycemic agents based on their function. Some increase pancreatic insulin production (glyburide and repaglinide). Some reduce glucose load by decreasing hepatic production (metformin). Some reduce intestinal absorption of glucose (acarbose) and others increase glucose uptake by fat and muscle (rosiglitazone). (467)

28. Glycosylated hemoglobin (hemoglobin A1C), or glycohemoglobin, is formed during hyperglycemia. Glucose can permanently combine with hemoglobin in erythrocytes and form hemoglobin A1C. Since the erythrocyte life span is 120 days, hemoglobin A1C levels give an indication of how well the diabetes is being controlled over time. Normal hemoglobin A1C levels are less than 6%. (467)

29. A well-controlled diabetic may not require special treatment before and during surgery. It is common in those on insulin treatment to reduce the morning dose by 30% to 50% to prevent hypoglycemia due to fasting. Sulfonylurea drugs may be continued until the evening before surgery, but these drugs may also produce hypoglycemia in the absence of morning caloric intake and are generally recommended to be held the morning of surgery.

Biguanides (phenformin) are associated with lactic acidosis and were replaced by metformin. On the basis of case reports, the common recommendation in the 1990s was to withhold metformin for 48 hours to avoid fatal lactic acidosis. This recommendation has not been studied scientifically and was called into question on the basis of a recent meta-analysis. (467-468)

30. The optimal level of glucose control in the perioperative and critical care setting remains controversial. Attempts to maintain glucose levels below 108 mg/dL in critically ill patients may result in excess cardiovascular mortality compared with those patients in whom the level was controlled in the 140 to 180 mg/dL range. There are several formulas for sliding scale insulin administration, maintenance infusions of 5% dextrose, and periodic blood glucose monitoring for the perioperative management of insulin-dependent diabetics. Some potential complications of severe perioperative hyperglycemia include ketoacidosis, dehydration, hyperosmolar nonketotic coma, secondary effects on neurologic outcome after cerebral ischemia, and the risk of surgical wound infection. (468)

31. There is no established standard to apply to the question of how high a preoperative glucose level is too high for surgery. (468)

HYPERTHYROIDISM (THYROTOXICOSIS) AND THYROID STORM

32. Hyperthyroidism is the condition caused by elevated circulating levels of the unbound thyroid hormones triiodothyronine (T_3), and tetraiodothyronine (thyroxine, or T_4). (468)

33. Some common causes of hyperthyroidism include Graves' disease, struma ovarii (thyroid tissue in an ovarian teratoma), a human chorionic gonadotropin hormone (hCG)-secreting hydatidiform mole, pregnancy (hCG has weak thyroid stimulating activity), and administration of iodinated contrast dye to a susceptible patient. Amiodarone can lead to both hypothyroidism and hyperthyroidism. (468)

34. Graves' disease is the most common cause of hyperthyroidism. It is an autoimmune condition where thyrotropin receptor antibodies continuously mimic the effect of thyroid-stimulating hormone (TSH). (468)

35. Mild to moderate hyperthyroidism is manifested by cardiac, neurologic, constitutional, and gastrointestinal signs and symptoms. Thyroid hormone increases cardiac sensitivity to catecholamines, causing hypertension, tachyarrhythmias, high-output congestive heart failure, and angina, even in the absence of coronary plaques. Patients may exhibit tremor, hyperreflexia, irritability, and periodic paralysis (hypokalemia and proximal muscle weakness). Constitutional signs may include fever and heat intolerance. Gastrointestinal symptoms may include nausea, vomiting, diarrhea, hepatic dysfunction, and jaundice. Hyperthyroidism is confirmed by demonstrating elevated thyroid hormone levels in blood. (468)

36. The difference between hyperthyroidism (thyrotoxicosis) and thyroid storm is a matter of degree. Thyroid storm is the most severe form of the disorder. It is a life-threatening, emergent clinical syndrome with a mortality rate of approximately 30% despite treatment. (468)

37. Worsening signs and symptoms of thyrotoxicosis characterize thyroid storm. There may be severe cardiac dysfunction, hyperglycemia, hypercalcemia, hyperbilirubinemia, hyperthermia, hypovolemia, altered mental status, seizures, or coma. (468)

38. Thyroid storm may be triggered in a thyrotoxic patient by any of several stresses, including infection, stroke, or trauma, especially to the thyroid gland. It may also occur with surgery, diabetic ketoacidosis, or incorrect antithyroid drug discontinuation. The administration of certain drugs including pseudoephedrine, aspirin, excess iodine intake, contrast dye, or amiodarone may also trigger thyroid storm. (468)

39. The initial medical treatment of thyroid storm is to reduce thyroid hormone synthesis. Thionamides, such as propylthiouracil (PTU) and methimazole (MMI), inhibit thyroid peroxidase (TPO), which catalyzes the incorporation of iodide into thyroglobulin to produce T_3 and T_4. At least an hour after giving the thionamide, large doses of stable iodide are given. β-blocking drugs are used to reduce adrenergic symptoms. Although propranolol is the traditional choice, other β-blockers (atenolol, metoprolol, or esmolol) have been used. Propranolol additionally inhibits peripheral conversion of T_4 to the more potent hormone T_3. Corticosteroids should also be administered since these patients usually have relative adrenal insufficiency. Finally, plasmapheresis may be a useful adjunct to reduce circulating thyroid hormone levels by removing T_3 and T_4 from the blood stream. (468)

40. The Wolfe-Chaikoff effect is a paradoxical effect whereby large doses of iodide suppress gene transcription of thyroid peroxidase rather than incorporate additional iodide into thyroglobulin. The large doses of iodine thus reduce the gland's capacity to produce and release hormone. This benefit is temporary, lasting about a week. (468)

41. There is limited evidence-based literature for operative anesthetic management of patients with hyperthyroidism, and no comparative data. It is usually recommended to favor agents that do not cause increased heart rate or sympathetic activation; however, this advice has never been subjected to testing. It is generally advisable to undertake only that which cannot be delayed until thyroid hormone secretion has been controlled by medical management or by radioiodine ablation. (468)

42. Although thyroid storm associated with surgery can occur intraoperatively, it is most likely to present 6 to 18 hours after the surgical procedure. Perioperative thyroid storm treatment is aimed toward decreasing the amount of circulating thyroid hormone and toward decreasing the increase in sympathetic nervous system stimulation. An esmolol infusion can be started and titrated to the desired hemodynamic and cardiovascular effects. Dexamethasone may be administered to block the release of thyroid hormone as well as from the thyroid gland and the peripheral conversion of T_4 to T_3. Propylthiouracil may be administered to block the uptake of iodine from the thyroid gland, after which iodine may be administered to inhibit the release of thyroid hormone from the thyroid gland. Treatment should also be supportive, with the monitoring and treatment of abnormalities in the patient's intravascular fluid status, electrolytes, glucose, and body temperature. Thyroid storm may be difficult to distinguish from other hypermetabolic states, including malignant hyperthermia, pheochromocytoma, neuroleptic malignant syndrome, and sepsis. Dantrolene can be beneficial and should be considered if there is suspicion of malignant hyperthermia. (469)

HYPOTHYROIDISM

43. Hypothyroidism is the condition caused by decreased circulating levels of the unbound thyroid hormones triiodothyronine (T_3) and tetraiodothyronine (thyroxine, or T_4). (469)

44. Hypothyroidism is either congenital (cretinism) or acquired. Acquired hypothyroidism may be due to an absence of dietary iodine (so-called "endemic goiter") or inflammation. Hashimoto's thyroiditis is a chronic autoimmune disease characterized by progressive destruction of the thyroid gland. Hypothyroidism may also be iatrogenic (from the medical or surgical treatment of hyperthyroidism). At least half of patients who receive radioactive iodine treatment for hyperthyroidism

are hypothyroid 10 years later. Hypothyroidism may also occur after hypothalamic or pituitary disease or surgery. (469)

45. The onset of hypothyroidism is usually insidious and the symptoms often nonspecific. There may be easy fatigability, lethargy, cold intolerance, periorbital edema, weakness, weight gain, dry skin, or brittle hair. There may be myxedema in severe cases with reduced cardiac output, attenuated deep tendon reflexes, and nonpitting pretibial edema. Untreated, there may be electrolyte disturbances, hypoventilation, hypothermia, or coma. (469)

46. Primary hypothyroidism is present if there are low T_3 and T_4 levels but an elevated TSH. In secondary hypothyroidism, all three thyroid-related hormones are reduced. Subclinical primary hypothyroidism is present in about 5% of the American population. It has a prevalence of more than 13% in otherwise healthy elderly patients, especially women.

47. Patients undergoing thyroid surgery may have physical or functional obstruction of the airway. An enlarged thyroid gland may deviate or compress the trachea, causing difficulty breathing when sleeping supine or during the induction of general anesthesia. Postoperative obstruction may occur if the patient develops a neck hematoma or tracheomalacia. Tracheomalacia can occur from chronic compression of the tracheal rings by a goiter. Deep extubation is sometimes used to minimize coughing, minimize straining, and reduce the theoretical likelihood of elevations of venous and arterial pressures in the neck. Functional obstruction may occur due to surgical trauma to the recurrent laryngeal nerves. Unilateral laryngeal nerve injury produces voice impairment, but is not a threat to airway function. Bilateral recurrent laryngeal nerve injury compromises the function of the posterior cricoarytenoid muscles, the muscles responsible for separating the cords during breathing. This can lead to life-threatening inspiratory airway obstruction, which may only be relieved by intubation or tracheostomy. Paralyzed vocal cords do not abduct during the respiratory cycle and may appear apposed in the midline when seen during direct laryngoscopy. Accidental removal of the parathyroid glands can occur in patients undergoing a total thyroidectomy. Clinically this can manifest as laryngospasm or inspiratory stridor secondary to the sensitivity of the laryngeal muscles to hypocalcemia. Signs of hypocalcemia after this complication do not usually manifest until 24 to 72 hours after the procedure. (469)

48. Asymptomatic mild to moderate hypothyroidism does not place a patient at an increased risk of perioperative morbidity. There is no unusual sensitivity to inhaled anesthetics, sedatives, or narcotics. Symptomatic or severe hypothyroidism should necessitate surgical delay for thyroid hormone replacement until resolution of neurologic and cardiovascular abnormalities. (469)

49. Some surgeons request the use of a laryngeal nerve monitoring (NIMS endotracheal tube) as a safety measure during thyroid surgery. These are specialized endotracheal tubes with electrodes positioned in the immediate vicinity of the vocal cords. They send an EMG signal to a receiver whenever the vocal cords contract, so if the surgeon stimulates a laryngeal nerve an audible signal provides a warning. With the NIMS tube, no muscle relaxant should be used. (469)

PHEOCHROMOCYTOMA AND PARAGANGLIOMA

50. A pheochromocytoma is a catecholamine-secreting adrenal medullary tumor. The cell of embryologic origin is the neural crest cell. Paraganglioma is the name given to these tumors when they occur outside the adrenal gland. (469-470)

51. These tumors typically produce the adrenal medullary hormones dopamine, norepinephrine, and/or epinephrine. The most common symptoms are headache, palpitations, sweating, and tremulousness. The most common sign is hypertension. Severe hypertension during anesthesia and surgical manipulations is a well-recognized manifestation of pheochromocytoma; 8% to 10% of tumors are asymptomatic.

The diagnosis is made by analyzing a 24-hour urine collection of catecholamine or catecholamine metabolite levels. (469-470)

52. The prevalence of pheochromocytomas and paragangliomas in the general population has been reported to be as high as 1 in 2000. (470)

53. For the perioperative management of pheochromocytomas and paragangliomas, the nonspecific α-blocking agent phenoxybenzamine might not be the agent of choice. Since α_2-agonists generally produce bradycardia, sedation, and lower blood pressure, phenoxybenzamine (with α_2-blocking properties) could increase blood pressure and increase pulse. Phenoxybenzamine, however, remains the agent most often recommended by authors of review articles and case series and is the agent with which there is the greatest clinical experience worldwide. It has a long pharmacologic half-life but is very expensive because it has no other clinical application. It is useful for the chronic treatment of patients with unresectable catecholamine secreting tumors.

Less costly alternatives prior to adrenalectomy include α_1-selective blockers (prazosin, doxazosin, and terazosin), calcium channel blockers, ACE inhibitors, angiotensin receptor blockers, β-blockers, and α_2-agonists.

Intraoperative hypertension and tachycardia may still require infusions of vasodilators, esmolol, and magnesium for treatment. Dexmedetomidine may be useful as well because of its α_2-agonist activity. (470)

MULTIPLE ENDOCRINE NEOPLASIA AND NEUROENDOCRINE TUMORS

54. Multiple endocrine neoplasia-1, described by Wermer in 1954, is characterized by a triad of tumors of the pancreas, parathyroid, and pituitary. Its inheritance is autosomal dominant. (470)

55. MEN-2 is characterized by autosomal dominant inherited medullary thyroid carcinoma and other associated tumors, including pheochromocytomas and parathyroid tumors. (471)

56. In MEN-1, pancreas tumors usually secrete gastrin (50%), insulin, glucagon, vasoactive intestinal polypeptide, or pancreatic polypeptide. Pituitary tumors are usually secreting adenomas (prolactin 60%, growth hormone 25%) although some are nonfunctioning adenomas. Parathyroid adenomas are present in 95%, are the most common tumor in the syndrome, and usually present as hypercalcemia. All four parathyroid glands usually must be removed surgically because all are involved by the disease. Other tumors may include adrenal cortical adenomas, carcinoids, neuroendocrine tumors, lipomas, angiofibromas, and collagenomas. (470)

57. There are two subtypes of MEN-2: MEN-2a, described by Sipple in 1961, and MEN-2b, described by Williams et al in 1966. MEN-2a includes pheochromocytoma, medullary thyroid carcinoma, and parathyroid adenoma. MEN-2b includes mucosal neuromas, pheochromocytoma, and medullary thyroid carcinoma. (471)

58. There are no specific anesthetic implications of MEN-1. Anesthetic implications of MEN-2 relate to its components and associated conditions. MEN-2 may be associated with pheochromocytomas or with Von Hippel-Lindau syndrome, which in turn may include cerebellar tumors. (470-471)

59. Carcinoids and neuroendocrine tumors are dispersed cells of neural crest embryologic origin. These tumors produce serotonin or other peptide hormones. When these tumors arise in the midgut, they are called carcinoid tumors; but when they arise elsewhere in the body, the current terminology is for them to be called neuroendocrine tumors. (471)

60. Midgut carcinoids are usually asymptomatic until they cause bowel obstruction or appendicitis because their venous drainage is via the portal vein to the liver, which detoxifies the excess serotonin they produce. (471)

61. Carcinoid syndrome is a constellation of systemic symptoms of serotonin excess. These include diarrhea, flushing, palpitations, and bronchoconstriction. It results from tumors outside the hepatic portal drainage field or when there is extensive metastatic liver disease. Octreotide may help ameliorate these symptoms. (471)

62. Perioperative considerations of carcinoid and neuroendocrine tumors result from the direct hemodynamic effects of serotonin. These are not problematic in the context of perioperative anesthetic care and an escalation of hemodynamic monitoring is seldom required as a consequence of the endocrine activity of the tumor. There should be a high index of suspicion in the face of right-sided valvular heart disease or right heart failure. Echocardiography should be considered as a diagnostic tool. Right heart failure is due to the sclerosing effect of serotonin on the tricuspid and pulmonic valves. It may be the cause of death in 50% of patients with carcinoid syndrome. (471)

ADRENAL INSUFFICIENCY AND STEROID REPLACEMENT

63. The principal hormones of the adrenal cortex are cortisol and aldosterone. (471)

64. Cortisol production in the adrenal cortex is stimulated by adrenocorticotropic hormone (ACTH) released from the pituitary gland. ACTH is secreted in response to hypothalamic corticotropin releasing hormone (CRH). Stress stimulates the hypothalamus to release CRH, which increases blood cortisol levels. Cortisol exerts negative feedback influence on the production of both CRH and ACTH. (471)

65. Cortisol is responsible for the conversion of norepinephrine to epinephrine in the adrenal medulla. It also maintains homeostasis of the cardiovascular system, especially in the presence of stress. It maintains vascular tone and endothelial integrity, preserving intravascular volume by reducing vascular permeability. It also potentiates the vasoconstrictor effects of catecholamines. When cortisol levels are deficient, systemic vascular resistance and myocardial contractility are decreased. Cortisol also plays an important role in gluconeogenesis, sodium retention, potassium excretion, and antiinflammatory effects. (471)

66. Addison's syndrome is chronic insufficient cortisol production and secretion, with or without aldosterone insufficiency. The symptoms of adrenal insufficiency are nonspecific. They include fatigue, malaise, lethargy, weight loss, anorexia, arthralgia, myalgia, nausea, vomiting, abdominal pain, diarrhea, and fever. (471)

67. Primary adrenocortical insufficiency is the nonfunctioning of the adrenal glands. Patients may also have hyponatremia and hyperkalemia along with aldosterone deficiency. Secondary adrenocortical insufficiency is the failure of the pituitary to stimulate the adrenals. Tertiary insufficiency is the failure of the hypothalamus to stimulate the pituitary, and thus the adrenals. (471)

68. The etiology of primary adrenocortical insufficiency is usually immunologic (an autoantibody), malignant, or infectious. Malignant causes are generally metastatic cancer, commonly from lung or breast. Infectious causes include tuberculosis. (471)

69. Secondary or tertiary adrenocortical insufficiency usually stems from exogenously administered steroids. Aldosterone production, under the stimulus of the renin-angiotensin system, is unimpaired. (471)

70. Acute adrenal failure (addisonian crisis) is circulatory shock caused by cortisol deficiency. It generally occurs in patients with primary adrenal insufficiency along with a superimposed acute stress, such as trauma, surgery, or infection. Symptoms include hyponatremia, hyperkalemia, hypovolemic shock, and myocardial and vascular unresponsiveness to catecholamines. (471)

71. Pituitary apoplexy generally occurs after acute pituitary hemorrhage, swelling, or infarction of a large pituitary adenoma. It may also occur following

cardiopulmonary bypass or postpartum hypotension (Sheehan's syndrome). It is also associated with diabetes, hypertension, sickle cell anemia, and acute shock.

Signs and symptoms of pituitary apoplexy may include sudden total loss of all anterior and posterior pituitary hormonal secretion, severe hypoglycemia, severe hypotension, central nervous system hemorrhage, cerebral edema, vision loss (often bitemporal hemianopsia), severe headache, meningeal irritation, ophthalmoplegia, cardiovascular collapse, or loss of consciousness. Diagnosis is made by computed tomography or magnetic resonance imaging. Corticosteroid replacement is the first line of treatment for both the resulting adrenal insufficiency and brain swelling. Acute surgical decompression of brain swelling may be necessary when there is significant visual loss and mental status alteration. (472)

72. Etomidate is associated with significant but transient (<24 hours) suppression of adrenal cortical function, even after a single dose of the drug. This is especially clinically significant in setting of CIRCI. (472)

73. Steroid-induced adrenal suppression is highly variable and its duration is unpredictable, from days to perhaps years. Since the consequences of a short course of steroids are minimal, anticipatory treatment is generally safe. The dosage for replacement therapy should be adequate but not excessive. The scientific foundation is based on surgical research in primates where administering supplements 10 times the normal cortisol production rates was not superior to simply replacing the normal daily production of cortisol. The daily cortisol production rate is between 20 and 30 mg/day. In surgical patients, the recommended approach is to begin at the time of surgery with a dose between 1 and 5 times the daily production, no more than 100 to 150 mg of cortisol equivalent per day with a tapered replacement over 48 to 72 hours. The potential risks of the administration of supplemental doses of corticosteroid to patients in the perioperative period are few. Of concern are impaired wound healing and an increased rate of infections. (472)

74. The term CIRCI recently has been applied to clinical situations where there is prior steroid treatment and the adrenal response to critical illness and other stresses is inadequate. The patient may not otherwise meet traditional criteria for adrenocortical dysfunction. One hundred to three hundred milligrams per day of IV hydrocortisone eliminates a preexisting need for vasopressors. Signs and symptoms include unexplained vasopressor-dependent refractory hypotension, a discrepancy between the anticipated severity of the patient's disease and the present state of the patient, or high fever without apparent cause or not responding to antibiotics. There may also be hypoglycemia, hyponatremia, hyperkalemia, neutropenia, or eosinophilia. (472)

CUSHING'S SYNDROME

75. Cushing's syndrome is the presence of elevated cortisol levels in the blood. Patients with Cushing's syndrome have a typical physical appearance characterized by rounding of the face, truncal obesity, thin extremities, an upper thoracic fat pad ("buffalo hump"), purple abdominal striae, and thinning of the skin. Physiologic effects of chronic elevated corticosteroid levels include weight gain, hypertension, hypercoagulability, muscle weakness, glucose intolerance, gonadal dysfunction, and osteoporosis. Diagnosis is confirmed by an elevated 24-hour urinary free cortisol. (472-473)

76. Primary Cushings is hypercortisolism independent of pituitary adrenocorticotropic hormone (ACTH) secretion, usually due to a hyperfunctioning adrenal gland or an adrenal adenoma. Secondary and tertiary disease occur from elevated circulating levels of ACTH or an ACTH-like substance. (472)

77. Cushings disease usually refers to one specific form of secondary Cushing's, that of adrenal cortical hyperfunction due to excess production of ACTH by a pituitary adenoma. This accounts for 60% to 70% of patients with Cushing's syndrome. (472)

78. After Cushing's disease, the remainder of secondary Cushing's syndrome patients have ectopic sources of ACTH. These may include primary cancers of the adrenal or metastatic cancers such as lung (usually small-cell), thyroid, prostate, pancreas, or intrathoracic neuroendocrine tumors. Secondary Cushing's may also occur with exogenous administration of cortisol-like medications or synthetic ACTH. (472-473)

79. Cushing's syndrome patients may be more susceptible to the effects of muscle relaxants than normal, leading to prolonged muscle relaxation and weakness. Because of this, Cushing's patients may be subject to unanticipated postoperative respiratory failure, even after laparoscopic surgery. (473)

Chapter

27 CENTRAL NERVOUS SYSTEM DISEASE

Alana Flexman, Pekka Talke

NEUROANATOMY

1. What is the arterial blood supply to the brain?
2. In what proportion of human brains is the classic depiction of the circle of Willis found?
3. What makes up the blood-brain barrier?
4. Name conditions in which the blood-brain barrier may be disrupted.

NEUROPHYSIOLOGY

5. Name some factors that influence cerebral blood flow.
6. What is normal cerebral blood flow?
7. What is the relationship between cerebral metabolic rate and cerebral blood flow?
8. For every 1° C decrease in temperature below normal body temperature, what is the corresponding decrease in cerebral blood flow?
9. Define cerebral perfusion pressure.
10. Within what range of mean arterial pressures will cerebral blood flow remain relatively constant?
11. What is the time course within which cerebral vasculature changes in response to alterations in mean arterial pressure? What is the clinical implication of this?
12. What are factors that impair the autoregulation of cerebral blood flow?
13. Describe the relationship between $Paco_2$ and cerebral blood flow.
14. How much does cerebral blood flow change for every 1 mm Hg increase or decrease in $Paco_2$ from 40 mm Hg?
15. What is a potential risk of prolonged, aggressive hyperventilation to a $Paco_2$ of less than 30 mm Hg?
16. Below what Pao_2 will cerebral blood flow increase?
17. What are the effects of volatile anesthetics on cerebral blood flow and intracranial pressure?
18. What are the effects of nitrous oxide on cerebral blood flow and intracranial pressure?
19. What are the effects of ketamine on cerebral blood flow and intracranial pressure?
20. What are the effects of thiopental on cerebral blood flow and intracranial pressure?
21. What are the effects of propofol on cerebral blood flow and intracranial pressure?
22. What are the effects of etomidate on cerebral blood flow and intracranial pressure?
23. What are the effects of dexmedetomidine and clonidine on cerebral blood flow and intracranial pressure?
24. What are the effects of benzodiazepines on cerebral blood flow and intracranial pressure?
25. What are the effects of opioids on cerebral blood flow and intracranial pressure?
26. What are the effects of neuromuscular blocking drugs on cerebral blood flow and intracranial pressure?

INTRACRANIAL PRESSURE

27. What is a normal intracranial pressure?
28. How does the body compensate for increasing intracranial pressure? What implications does this have clinically?
29. How do drug-induced increases in cerebral blood flow affect the intracranial pressures of normal patients and of patients with intracranial tumors?
30. Name some methods used to decrease elevated intracranial pressure.
31. Name some signs and symptoms that may be noted preoperatively that provide evidence that a patient may have an increased intracranial pressure.

NEUROPROTECTION

32. What is the current recommendation regarding the use of induced hypothermia for neuroprotection?
33. What is the current recommendation regarding the use of intravenous anesthetics for neuroprotection?

ANESTHESIA FOR NEUROSURGERY

34. What monitors are typically used for intracranial neurosurgery?
35. What two devices can be used to measure the intracranial pressure?
36. What measures can an anesthesiologist undertake to attenuate increases in arterial blood pressure and intracranial pressure during direct laryngoscopy?
37. How is maintenance anesthesia usually achieved in patients undergoing intracranial neurosurgery?
38. What minimum alveolar concentration (MAC) of volatile anesthetic should be administered when used for maintenance anesthesia in patients undergoing intracranial neurosurgery?
39. What is the desired range of $Paco_2$ to optimize cerebral blood flow intraoperatively?
40. What is a potential problem of the administration of positive end-expiratory pressure (PEEP) during mechanical ventilation of the lungs in patients undergoing intracranial neurosurgery?
41. How do peripheral vasodilators affect cerebral blood flow? What is the recommendation regarding the use of these drugs intraoperatively in patients undergoing intracranial neurosurgery?
42. Why might neuromuscular blockade be maintained throughout intracranial surgical procedures?
43. How can cerebral swelling be treated intraoperatively?
44. What are some potential problems that can occur with the administration of mannitol?
45. How should intravenous fluid administration be managed intraoperatively in patients undergoing intracranial neurosurgery?
46. Why should glucose-containing intravenous solutions be avoided in neurosurgical patients?
47. Why should coughing and straining by patients awakening from anesthesia be avoided after intracranial surgery? What are some methods by which these responses by the patient can be avoided?
48. Why is rapid awakening desirable in neurosurgical procedures?
49. How should delayed recovery after intracranial surgery be evaluated? When should tension pneumocephalus be considered as a possible cause of postoperative delayed recovery?
50. What drug is commonly used to treat hypertension on emergence from anesthesia for intracranial neurosurgery?
51. Why are patients undergoing neurosurgical procedures at an increased risk for venous air embolism?
52. Describe the pathophysiology of a venous air embolism. What percent of adult patients have a probe patent foramen ovale?
53. What are methods by which a venous air embolism can be detected? Which of these is the most sensitive?
54. What are some signs of a clinically significant venous air embolism?

55. What is the treatment for a venous air embolism?
56. Why should nitrous oxide administration be discontinued in the presence of a venous air embolism?
57. What are the advantages of a pulmonary artery catheter in the presence of a venous air embolism?
58. How efficacious is the use of PEEP in the prevention of a venous air embolism?
59. What typically causes death in a fatal venous air embolism?

INTRACRANIAL MASS LESIONS

60. What are some of the presenting signs and symptoms of patients with an intracranial tumor?
61. What are the anesthetic goals for patients undergoing surgical resection of an intracranial tumor?
62. Why is it important to limit drug-induced depression of ventilation with preoperative medicines in patients who are scheduled to undergo surgical resection of an intracranial tumor?
63. How is the induction of general anesthesia in patients undergoing surgical resection of an intracranial tumor achieved?
64. What are the advantages and disadvantages of the sitting position for the resection of intracranial tumors?
65. Name some anesthetic considerations that are unique to posterior fossa tumors.

INTRACRANIAL ANEURYSMS AND ARTERIOVENOUS MALFORMATIONS

66. How do patients with ruptured intracranial aneurysms usually present?
67. What is the goal of the anesthetic management of a patient undergoing resection of an intracranial aneurysm or arteriovenous malformation?
68. What are the major complications of intracranial aneurysm rupture?
69. How might the electrocardiogram of patients with a ruptured intracranial aneurysm appear?
70. When is vasospasm after cerebral aneurysm rupture most likely to occur? How is it diagnosed?
71. What is the treatment for vasospasm after cerebral aneurysm rupture?
72. What are the different treatment options for intracranial aneurysms?
73. What are the different treatment options for intracranial arteriovenous malformations?
74. What are special considerations during temporary clip placement during resection of intracranial aneurysms?

CAROTID DISEASE

75. What are the indications for carotid endarterectomy?
76. How should patients scheduled for a carotid endarterectomy be evaluated preoperatively?
77. What are the anesthetic goals for patients undergoing a carotid endarterectomy? What is the critical period during this surgery?
78. How should the arterial blood pressure be managed during a carotid endarterectomy?
79. How should the $Paco_2$ be managed during a carotid endarterectomy?
80. What is the purpose of intraoperative neurologic monitoring during a carotid endarterectomy? What are some methods of intraoperative neurologic monitoring?
81. Does local or general anesthesia have better outcomes for carotid endarterectomy?
82. How is local anesthesia for a carotid endarterectomy achieved? What is an advantage of local anesthesia for this procedure?
83. How is general anesthesia for a carotid endarterectomy usually achieved? What is an advantage of general anesthesia for this procedure?
84. What are some potential postoperative complications after carotid endarterectomy?
85. What are the consequences of postoperative hypertension after carotid endarterectomy?

ANSWERS*

NEUROANATOMY

1. The arterial blood supply to the brain is from three blood vessels, including the right and left internal carotids and the vertebrobasilar artery. Anastomoses between these vessels form the circle of Willis, and provide for a collateral blood supply for cerebral protection against ischemia. (476)
2. The classic depiction of the circle of Willis is found in less than half of human brains and collateralization may not be complete in all individuals. (476-477, Figure 30-1)
3. The blood-brain barrier is composed of capillary endothelial cells with tight junctions. This barrier allows the passage of lipid-soluble substances such as carbon dioxide, oxygen, and some anesthetic agents but prevents the passage of large macromolecules such as proteins. (476)
4. The blood-brain barrier may be disrupted in conditions such as acute systemic hypertension, head trauma, infection, arterial hypoxemia, severe hypercapnia, intracranial tumors, and sustained seizure activity. (476)

NEUROPHYSIOLOGY

5. Factors that influence cerebral blood flow include the cerebral metabolic rate, cerebral perfusion pressure and autoregulation, the Pa_{O_2}, the Pa_{CO_2}, and anesthetic drugs. (477)
6. Normal cerebral blood flow is 50 mL per 100 g of brain tissue per minute and represents approximately 15% of cardiac output. Although the brain is a very small percent of body weight, its high metabolic rate and inability to store energy account for the high percent of cardiac output it receives. (477)
7. The cerebral metabolic rate directly affects cerebral blood flow through cerebral flow-metabolism coupling. Increases or decreases in metabolic rate result in a proportional increase or decrease in cerebral blood flow. (477)
8. For every 1° C decrease in temperature below normal body temperature there is a corresponding decrease in cerebral blood flow by about 7%. This effect is due to the decrease in the cerebral metabolic rate caused by the decrease in temperature. (477)
9. Cerebral perfusion pressure is defined as the difference between mean arterial pressure and central venous pressure or intracranial pressure, whichever is greater. (478)
10. In healthy, normotensive individuals cerebral blood flow remains relatively constant between cerebral perfusion pressures of 50 to 150 mm Hg. Within this range the cerebral vasculature is able to vasodilate or vasoconstrict in response to changes in mean arterial blood pressure to maintain a constant cerebral blood flow. Below a cerebral perfusion pressure of 50 mm Hg (mean arterial pressure of about 65 mm Hg assuming an intracranial pressure of 15 mm Hg) cerebral blood flow decreases proportionally to mean arterial pressure. Above a cerebral perfusion pressure of about 150 mm Hg, cerebral blood flow increases proportionally to the mean arterial pressure. This response of the cerebral vasculature to alterations in the mean arterial pressure to maintain a constant cerebral blood flow is termed "autoregulation." (478)
11. The time course within which cerebral vasculature changes in response to alterations in mean arterial pressure is 1 to 3 minutes. That is, within 1 to 3 minutes of an alteration in the mean arterial pressure, the cerebral vasculature is able to

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

respond appropriately to maintain a constant cerebral blood flow. In the interim, with drastic increases or decreases in mean arterial pressure, there may be a brief period of respective cerebral hyperperfusion or hypoperfusion. (478)

12. Autoregulation of cerebral blood flow may be impaired in the presence of intracranial mass lesions, head trauma, intracranial surgery, subarachnoid hemorrhage, severe hypothermia, or volatile anesthetics. Chronic arterial hypertension or sympathetic nervous system stimulation results in a shift of the autoregulatory curve to the right, such that cerebral blood flow is maintained between pressures higher than 60 to 150 mm Hg. This effect is believed to occur after 1 to 2 months of hypertension. (478)

13. Cerebral blood flow is linearly related to the $Paco_2$, such that increases in the $Paco_2$ result in increases in cerebral blood flow and vice versa. This effect of the $Paco_2$ occurs as a result of the effect of the arterial carbon dioxide tension on the pH of the cerebrospinal fluid. An increase in $Paco_2$ leads to acidosis, which in turn leads to cerebral vascular vasodilation. The duration of this effect is 6 to 8 hours, after which cerebral blood flow normalizes through the transfer of bicarbonate out of the cerebrospinal fluid. This effect is only in response to respiratory acidosis. The cerebral vasculature is not affected by metabolic acidosis, owing to the blood-brain barrier protection against the diffusion of hydrogen ions from the vascular space. (477-478, Figure 30-2)

14. Cerebral blood flow increases by 1 mL/100 g of brain tissue per minute for every 1 mm Hg increase in the $Paco_2$ from 40 mm Hg. Conversely, cerebral blood flow decreases by 1 mL/100 g of brain tissue per minute for every 1 mm Hg decrease in the $Paco_2$ from 40 mm Hg. The impact of this can be marked, given that a decrease in the $Paco_2$ from 40 to 25 mm Hg can lead to approximately a 33% decrease in cerebral blood flow. (478)

15. A potential risk of prolonged, aggressive hyperventilation to a $Paco_2$ of less than 30 mm Hg is cerebral ischemia. Prolonged aggressive hyperventilation following traumatic brain injury has been shown to be associated with a poorer neurologic outcome. (478)

16. Cerebral blood flow increases dramatically when the Pao_2 falls below 50 mm Hg. (478, Figure 30-2)

17. Volatile anesthetics are potent cerebral vasodilators. At concentrations above 0.5 MAC, these anesthetic agents increase cerebral blood flow in a dose-dependent manner, most likely through the direct relaxation of vascular smooth muscle leading to vasodilation. In contrast, volatile anesthetics decrease the cerebral metabolic oxygen requirement profoundly. Normally, a reduction in cerebral metabolic rate would produce a reduction in cerebral blood flow through flow-metabolism coupling. However, the net effect of volatile anesthetics is to increase cerebral blood flow, particularly at high doses. Therefore, volatile anesthetics uncouple the normal physiologic relationship between cerebral blood flow and metabolism. These effects may lead to increases in intracranial pressure and cerebral edema. (478)

18. Nitrous oxide increases cerebral blood flow through cerebral vasodilation. The effect of nitrous oxide appears to be blunted in the presence of intravenous anesthetics and increases cerebral blood flow less than the volatile anesthetics. Limitation of the inspired concentration of nitrous oxide to less than 0.7 MAC minimizes its effect of cerebral vasodilation and intracranial pressure. (478)

19. The effect of ketamine on cerebral blood flow and intracranial pressure is controversial. In isolation, ketamine appears to increase $Paco_2$, cerebral blood flow, and intracranial pressure, limiting its use for patients with increased intracranial pressure. These effects appear to be attenuated, however, in the presence of other anesthetic agents and controlled ventilation. (478)

20. Thiopental decreases cerebral blood flow via cerebral vasoconstriction. It also decreases cerebral metabolic oxygen requirements and reliably decreases the intracranial pressure. (478)

21. Propofol decreases cerebral blood flow via cerebral vasoconstriction in a manner similar to thiopental. It also decreases cerebral metabolic oxygen requirements and reliably decreases the intracranial pressure. (478)

22. Etomidate decreases cerebral blood flow and cerebral metabolic oxygen requirements in the absence of myoclonus or seizure activity. (478)

23. Dexmedetomidine and clonidine decrease cerebral blood flow through reductions in mean arterial pressure and cerebral perfusion pressure. They have minimal effect on cerebral metabolic rate and intracranial pressure. (478)

24. Benzodiazepines minimally decrease cerebral blood flow and cerebral metabolic rate and do not appear to cause an increase in intracranial pressure. (478)

25. Studies evaluating the effects of opioids on cerebral blood flow and intracranial pressure have yielded inconsistent results. Opioids either very minimally decrease cerebral blood flow and intracranial pressure or produce no effect at all in the absence of respiratory depression and elevated $Paco_2$. (478)

26. Succinylcholine may increase intracranial pressure through stimulation of muscle spindles, which then increases cerebral metabolic rate and cerebral blood flow. These effects are not consistent, and may be attenuated through a deep level of anesthesia during the administration of succinylcholine. Nondepolarizing neuromuscular blocking drugs do not generally affect intracranial pressure except through the potential release of histamine, leading to cerebral vasodilation. (479)

INTRACRANIAL PRESSURE

27. Normal intracranial pressure is lower than 15 mm Hg. (478)

28. The intracranial pressure is determined by the intracranial contents occupying a fixed space. The intracranial compartment is composed of brain tissue, cerebrospinal fluid, and blood. Increases in brain tissue or fluid, such as by brain tumor and edema, are space occupying and could potentially increase the intracranial pressure. Initially, the displacement of cerebrospinal fluid from the cranium compensates for increases in the space-occupying mass, but as the mass enlarges an increase in intracranial pressure becomes apparent clinically. The relationship between the intracranial volume and intracranial pressure is such that after compensatory mechanisms are exhausted, minimal increases in the intracranial volume result in marked increases in the intracranial pressure. Increases in a patient's intracranial pressure can interfere with cerebral perfusion and result in cerebral ischemia. (478-479, Figure 30-3)

29. Although drug-induced increases in cerebral blood flow do not greatly affect the intracranial pressure of normal patients, patients with intracranial space-occupying lesions are not able to compensate for the changes in cerebral blood flow and are vulnerable to developing increased intracranial pressure. (478-479)

30. Reductions in elevated intracranial pressure are achieved through reductions in cerebral spinal fluid, cerebral blood volume, and cerebral edema. Cerebral spinal fluid may be drained through an external ventricular or lumbar drain, or its production decreased by drugs such as furosemide and acetazolamide. Methods of reducing cerebral blood volume include positioning of the head to facilitate venous drainage, avoidance of high ventilatory pressures and PEEP, avoidance of hypertension, and hyperventilation. Finally, osmotic diuretics such as mannitol, as well as surgical resection of space-occupying lesions and decompressive craniectomy, may reduce intracranial pressure from cerebral edema. (479, Table 30-1)

31. Signs and symptoms of an increased intracranial pressure include nausea and vomiting, hypertension, bradycardia, personality changes, altered levels of consciousness, altered patterns of breathing, papilledema, and seizures. (480, Table 30-2)

NEUROPROTECTION

32. The use of induced hypothermia in neurosurgical procedures was widespread based on laboratory studies. An international multicenter study in 2005 of 1001 patients did not show any benefit in neurologic outcome, however. Because there has been no verifiable benefit ascribed to hypothermia for neuroprotection in humans, the routine use of hypothermia in neurosurgery is no longer recommended. Indeed, the routine use of hypothermia in neurosurgery is unlikely to continue. (480)

33. Although intravenous anesthetics have been shown to decrease the cerebral metabolic rate and intracranial pressure, there has not been any evidence to prove that neurologic outcome is improved with their use. A concern with the use of intravenous anesthetics such as propofol or barbiturates for this purpose is that the moderate benefit they may provide for neuroprotection can be readily offset by alterations in the cardiovascular or hemodynamic status of the patient. When these drugs are being administered, vigilance is required to avoid exacerbation of cerebral injury, thus limiting their usefulness. Rather it is recommended that other physiologic parameters (cerebral perfusion pressure, oxygenation, normocapnia, temperature, and control of hyperglycemia) are attended to for maximal neuroprotection. (480)

ANESTHESIA FOR NEUROSURGERY

34. In addition to standard monitors, continuous monitoring of systemic blood pressure is commonly employed using a peripheral arterial catheter to monitor the hemodynamic changes that occur around induction of anesthesia, laryngoscopy, application of Mayfield head frame, surgery, and emergence from anesthesia. Abnormally low or high systemic blood pressure may compromise cerebral perfusion or increase cerebral swelling, respectively. In addition, these catheters permit blood sampling and accurate determination of $Paco_2$. Other monitors should include a peripheral nerve stimulator to monitor the level of paralysis and a bladder catheter, particularly if diuretics are used. Central venous catheters are not routinely employed but may be considered for patient or surgical indications. (480-481, Table 30-3)

35. An external ventricular device or a subdural bolt placed through a burr hole can be used to measure the intracranial pressure. The external ventricular device has the additional advantage of also allowing for drainage of cerebral spinal fluid. (480)

36. Before direct laryngoscopy and intubation of the trachea, there are several measures that can be taken to attenuate increases in arterial blood pressure and intracranial pressure. Neuromuscular blockade should be confirmed with a peripheral nerve stimulator. This ensures that dangerous rises in intracranial pressure due to coughing or bucking in response to direct laryngoscopy do not occur. The administration of an additional dose of propofol, thiopental, opioids, deeper levels of a volatile agent, a bolus of intravenous lidocaine, or a short-acting β-adrenergic antagonist (e.g., esmolol) prior to direct laryngoscopy are all methods that may be used to attenuate an increase in intracranial pressure. Finally, the duration of direct laryngoscopy should be minimized. (481)

37. Maintenance anesthesia in patients undergoing intracranial neurosurgery is often achieved with the administration of a low concentration of volatile anesthetic in conjunction with nitrous oxide and an opioid. The volatile anesthetic contributes to decreased awareness and the blunting of sympathetic nervous system responses. The disadvantage of volatile anesthetics during the resection of an intracranial tumor is its potential to increase cerebral blood flow. Alternatively, anesthesia may be maintained with a combination of intravenous anesthetic agents, most commonly propofol in conjunction with an opioid such as fentanyl or remifentanil.

The use of intravenous anesthesia may be preferred in patients with elevated intracranial pressure due to a reduction of cerebral blood flow associated with these agents, as well as their compatibility with intraoperative neuromonitoring with evoked potentials. (481-482)

38. To limit the degree of increase in cerebral blood flow associated with its administration, the MAC of volatile anesthetic administered should not exceed 0.5 MAC when administered for maintenance anesthesia in patients undergoing intracranial neurosurgery. It may be prudent to avoid the administration of volatile anesthetics altogether in patients with elevated intracranial pressure, since even slight increases in cerebral blood flow and intracranial pressure are potentially harmful. Likewise, the administration of a volatile anesthetic should be discontinued intraoperatively if cerebral swelling develops. (481)

39. The $Paco_2$ should be maintained between 30 and 35 mm Hg to optimize cerebral blood flow intraoperatively. Below a $Paco_2$ of 30 mm Hg there is no evidence of any additional benefit. (481)

40. Excessive use of PEEP during mechanical ventilation of the lungs in patients undergoing intracranial neurosurgery may lead to an increase in intracranial pressure by increasing the central venous pressure and impairing cerebral venous drainage. (481)

41. Peripheral vasodilators may increase cerebral blood flow by causing cerebral vascular vasodilation while simultaneously decreasing mean arterial blood pressure and cerebral perfusion pressure. Examples include nitroglycerin, nitroprusside, adenosine, calcium channel blockers, and hydralazine. The use of these drugs is not recommended for use in neurosurgical patients, particularly before the dura is open in patients with elevated intracranial pressure. (481)

42. Neuromuscular blockade is commonly maintained throughout intracranial surgical procedures to minimize the risk of patient movement, coughing, or bucking that may result in dangerous increases in intracranial pressure. Patient movement may also result in an increase in operative site bleeding and bulging of the brain into the operative site with difficult surgical exposure. (481-482)

43. Cerebral swelling occurring intraoperatively can be treated a number of ways. First, it should be confirmed that the maximal benefit is being derived from hyperventilation of the lungs with a $Paco_2$ between 30 and 35 mm Hg. Next, drugs that will cause cerebral dehydration may be administered. Mannitol at a dose of 0.25 to 1 g/kg or furosemide at a dose of 0.5 to 1 mg/kg is frequently used for this purpose. Intermittent injections of an intravenous anesthetic such as thiopental or propofol may also be administered. If surgically possible, placing the patient in a head-up position may improve venous drainage and reduce swelling. Discontinuing volatile anesthetic agents and using intravenous agents such as propofol should be considered to reduce cerebral blood flow. (482)

44. Mannitol is an osmotic diuretic whose onset of action is within 5 to 10 minutes, and whose maximum benefit lasts for 2 to 4 hours. There are some potential problems that can occur with the administration of mannitol, however. If given rapidly, hypotension through peripheral vasodilation combined with a short-term increase in intravascular fluid volume can lead to a decrease in the cerebral perfusion pressure. If large doses of mannitol are administered, there is a risk of acute mannitol toxicity, manifested by hyponatremia and a high measured serum osmolality. (482)

45. Maintenance of euvolemia with isotonic intravenous fluids, such as normal saline or lactated Ringer solution, during intracranial neurosurgery is recommended. Hypotonic solutions are not recommended due to increases in free water and possible cerebral edema. Colloids such as 5% albumin are acceptable but no improvement in outcome has been demonstrated. (482)

46. Glucose-containing solutions should be avoided as hyperglycemia augments ischemic neuronal cell damage in the brain. (482)

47. Coughing and straining in patients awakening from anesthesia after intracranial surgery can result in dangerous increases in the intracranial pressure, increases in cerebral edema, and precipitate postoperative bleeding. A small dose of opioid, intravenous lidocaine, or both at the conclusion of the procedure may decrease the likelihood of coughing during extubation. The emergence from anesthesia is better timed to follow placement of the head dressings because movement of the head at the conclusion of surgery in the lightly anesthetized patient can stimulate coughing on the endotracheal tube. (482)

48. Rapid awakening is desirable in neurosurgical procedures to allow for a timely assessment of neurologic status after surgery. (482)

49. Delayed recovery as well as worsening neurologic function after intracranial surgery without obvious cause warrant evaluation by computed tomography or magnetic resonance imaging. A tension pneumocephalus may be considered as a possible cause of postoperative delayed recovery when nitrous oxide was administered intraoperatively, particularly after posterior fossa surgeries in the sitting position. Tension pneumocephalus occurs as a result of air entering the subdural cavities and the treatment is burr hole removal of the gas. (482)

50. Labetalol is commonly used to treat hypertension on emergence from anesthesia for intracranial neurosurgery due to its ability to reduce mean arterial blood pressure without causing cerebral vasodilation and with rapid onset. (482)

51. Patients undergoing neurosurgical procedures are at an increased risk for a venous air embolism due to positioning of the patient's head above the level of the heart. In addition, veins that are opened intraoperatively in the cranial vault may remain tented open unlike in other body sites. Patients undergoing posterior fossa craniotomies in the sitting position are at particular risk of an intraoperative venous air embolism. For this reason, many neurosurgeons prefer to do posterior fossa craniotomies with the patient in the prone or park bench position. (480-481)

52. A venous air embolism is characterized by entry of air into the venous circulation and the right heart. After entry into the heart, the air may take three paths. First, it may stay in the right ventricle, interfering with blood flow into the pulmonary artery. Second, it may enter the pulmonary circulation and precipitate acute pulmonary hypertension as well as traverse the pulmonary circulation and enter the arterial circulation. Finally, from the right atrium it could enter the left atrium through a patent foramen ovale, which is present in approximately 25% of adults. Arterial emboli in the cerebral and coronary circulation can lead to neurologic and coronary infarctions, respectively. (482-483)

53. Methods by which a venous air embolism can be detected include transesophageal echocardiography, precordial Doppler ultrasound transducer, an acute decrease in the exhaled carbon dioxide concentration, increased end-tidal nitrogen concentration, and changes in pulmonary and systemic pressures. In response to a pulmonary embolus, patients may have bronchoconstriction, pulmonary edema, elevated right atrial or pulmonary artery pressure, and elevated peak inspiratory pressure. The most sensitive method to detect a venous air embolism is through the use of transesophageal echocardiography. It is also beneficial in that it allows for the identification of right-to-left air shunting. The drawbacks of routine transesophageal echocardiography monitoring for venous air embolism are its invasiveness, bulk, and cost. An acceptable alternative to transesophageal echocardiography for monitoring is through the combined use of a precordial Doppler transducer and monitoring exhaled concentrations of carbon dioxide. The transducer should be placed between the second or third intercostal spaces to the right of the sternum. The Doppler transducer is able to recognize small volumes

of intracardiac air, but it is not able to distinguish between small volumes and large volumes of air. (482)

54. Signs and symptoms of a clinically significant venous air embolism include a decrease in end-tidal carbon dioxide, hypotension, hypoxemia, tachycardia, cardiac dysrhythmias, cyanosis, and a characteristic "mill wheel" murmur. The awake patient may experience anxiety, chest pain, and coughing. (482-483)

55. The treatment for a venous air embolism includes the prompt administration of 100% oxygen and the discontinuation of nitrous oxide administration. The surgeons should be asked to irrigate the operative field with fluid and to occlude the bone edges to prevent the further entry of air. Lowering the operative field (Trendelenburg position) in conjunction with aggressive volume resuscitation may also prevent further entrainment of air and improve hemodynamics. Gentle compression of the jugular veins can be instituted. In addition, if a central venous catheter is in place, aspiration on the catheter to retrieve the air may be attempted to confirm the diagnosis. Other treatment methods of a venous air embolus are supportive as needed for hypotension, decreased cardiac output, bronchoconstriction, or other manifestations. (483)

56. Nitrous oxide administration should be discontinued in the presence of a venous air embolism. The diffusion of nitrous oxide into the air embolus could potentially increase its size and worsen its clinical effects. Some clinicians choose to avoid the administration of nitrous oxide in patients at risk for a venous air embolus. (482)

57. Although a pulmonary artery catheter is not useful for aspirating air from the venous circulation because of its small catheter size, it may detect increases in pulmonary artery pressure caused by a pulmonary air embolus. In practice, pulmonary artery catheters are rarely used. (483)

58. PEEP has not been shown to be efficacious in the prevention of a venous air embolism. (483)

59. Death occurring as a result of a venous air embolism is usually due to an obstruction of forward flow from the right side of the heart. Acute cor pulmonale, cardiovascular collapse, and arterial hypoxemia result. (483)

INTRACRANIAL MASS LESIONS

60. Presenting signs and symptoms of patients with an intracranial tumor are typically reflective of an elevated intracranial pressure due to a space-occupying mass. Manifestations of elevated intracranial pressure include nausea and vomiting, hypertension, bradycardia, personality changes, altered levels of consciousness, altered patterns of breathing, and papilledema. Patients may also present with seizures depending on the location of the tumor. New-onset seizures in a previously asymptomatic adult are suggestive of an intracranial tumor. (480, Table 30-2)

61. The anesthetic goals in patients undergoing surgical resection of an intracranial tumor are to reduce intracranial pressure using medications, and avoid drugs or events (e.g., hypercarbia) that will cause undesirable changes in cerebral blood flow or intracranial pressure. (483, Table 30-3)

62. Preoperative sedative medications may result in depression of ventilation and increases in $Paco_2$ in patients with an intracranial tumor. This in turn could lead to an increase in cerebral blood flow and a corresponding increase in the intracranial pressure. (480, Table 30-3)

63. The induction of general anesthesia in patients scheduled to undergo surgical resection of an intracranial tumor can be achieved with the administration of thiopental or propofol to produce adequate anesthesia and minimize increases in intracranial pressure with direct laryngoscopy. Cerebral perfusion pressure must be maintained, however, to prevent cerebral ischemia in compromised patients. Etomidate may be useful in situations in which patients have a suspected elevated

intracranial pressure but are also hemodynamically unstable or hypovolemic, such as trauma patients. (481, Table 30-3)

64. The sitting position facilitates surgical exposure of posterior fossa tumors and reduces retraction of brain structures, potentially preventing unwanted trauma. The high risk of venous air embolism (>25%), however, limits the use of the sitting position and many surgeons prefer the prone position instead. Other disadvantages of the sitting position include upper airway edema as a result of venous obstruction from cervical flexion and quadriplegia from spinal cord compression and ischemia. (481)

65. There are some anesthetic considerations that are unique to posterior fossa tumors. Posterior fossa tumors place the patient at a higher risk for venous air embolism. In addition, resection of tumors in this area may injure vital brainstem structures and result in intraoperative hemodynamic fluctuations as well as respiratory depression in the postoperative period. Finally, injury to the cranial nerves may result in a loss of protective airway reflexes that necessitates postoperative ventilation. (483)

INTRACRANIAL ANEURYSMS AND ARTERIOVENOUS MALFORMATIONS

66. Ruptured intracranial aneurysms have a mortality of 40% to 50%. Patients with ruptured intracranial aneurysms usually present with a sudden, severe headache, nausea, vomiting, focal neurologic signs, hypertension, and a depressed level of consciousness. Many of these symptoms are indications of an elevated intracranial pressure. The immediate management of patients with a ruptured intracranial aneurysm is to treat elevations in the intracranial pressure. (483, Table 30-4)

67. The goals of the anesthetic management of a patient undergoing resection of an intracranial aneurysm are (1) avoidance of sudden increases in systemic arterial blood pressure, and therefore transmural pressure of the aneurysm, which could result in rupture; and (2) facilitate surgical exposure and access to the aneurysm. Exaggerated increases in arterial blood pressure during direct laryngoscopy and surgical frame pinning must be attenuated. The anesthetic goals for resection or embolization of arteriovenous malformations are similar to those of aneurysms with a few distinct considerations. These vascular abnormalities are low pressure and high flow, and therefore increases in systemic blood pressure are less likely to result in rupture of the lesion. Hypertension should still be avoided, however, due to the high incidence of aneurysms associated with arteriovenous malformations. In addition, prolonged arteriovenous malformation resection has been associated with massive blood loss and severe cerebral swelling. (483-484, Table 30-4)

68. Major complications of intracranial aneurysm rupture include death, rebleeding, and vasospasm. Early treatment has been shown to reduce the incidence of rebleeding but may be technically more difficult due to swelling and inflammation. Other complications of aneurysm rupture include seizures, acute and chronic hydrocephalus, and systemic complications, such as neurogenic pulmonary edema and hyponatremia. (483)

69. The electrocardiogram of patients with a ruptured intracranial aneurysm often appears abnormal and may mimic myocardial ischemia. These changes are usually due to a neurologic mechanism and are not usually related to underlying coronary artery disease. Changes frequently seen on the electrocardiogram of these patients include arrhythmias, Q waves, U waves, T wave inversion, prolonged QT intervals, and ST segment depression or elevation. Mild elevations in cardiac enzymes are common but usually do not correlate with significant myocardial dysfunction. (483)

70. A major cause of mortality and morbidity after rupture of an intracranial aneurysm is vasospasm of the cerebral arteries. Vasospasm occurs in about 70% of these patients and typically has onset 3 to 5 days after rupture of an intracranial aneurysm, but may occur as late as 12 days after rupture. Drowsiness is the most common clinical sign of vasospasm, and transcranial Doppler ultrasound or radiologic studies can confirm its presence. (483)

71. Vasospasm that occurs after cerebral aneurysm rupture is treated with "Triple H" therapy (hypertension, hypervolemia, and hemodilution) through an increase in cardiac output and the administration of intravenous fluids. Administration of the calcium channel blocker nimodipine has been shown to decrease the morbidity and mortality from vasospasm. Finally, cerebral vasospasm may be treated using the selective injection of vasodilators into the cerebral circulation or angioplasty in the interventional radiology suite. (483)

72. Intracranial aneurysms may be treated using endovascular coiling or surgical resection. Outcomes are similar between patients treated surgically and with endovascular insertion of coils. Certain patients may be unsuitable candidates for endovascular coiling due to the anatomy and location of their aneurysms; these patients require surgery. (483)

73. Arteriovenous malformations may be treated expectantly, with open resection, endovascular embolization, or with stereotactic radiosurgery (gamma knife). Preoperative embolization is often used prior to open resection to reduce blood loss and facilitate surgical resection. (484)

74. Temporary clips are often applied to a major feeding artery of an aneurysm to facilitate resection and permanent clip placement. These clips may create regional hypoperfusion to the areas perfused by these vessels. Anesthetic management during temporary clip placement should involve maintenance of normal or slightly increased systemic arterial blood pressure to maintain perfusion through the collateral circulation. Drugs such as thiopental or propofol may be used to achieve burst suppression on the electroencephalogram in the hope that this provides some protection from ischemia. Rarely, hypothermic circulatory arrest may be required for very large or complex aneurysms. (484)

CAROTID DISEASE

75. Carotid endarterectomy is indicated in symptomatic patients with 70% to 99% stenosis of the carotid artery. Carotid endarterectomy may be beneficial in asymptomatic patients. However, the perioperative risk of stroke and death (approximately 4% to 7%) must be taken into account given a reduced benefit. Data suggest carotid endarterectomy should be optimally performed within 2 weeks of symptom onset. (484)

76. Patients undergoing a carotid endarterectomy often have coexisting coronary artery and other atherosclerotic disease. The perioperative risk of myocardial ischemia should be evaluated preoperatively and medically optimized. The range of normal blood pressures for the patient should be determined. Neurologic symptoms and deficits should be documented preoperatively to prevent any dysfunction noted postoperatively from being incorrectly attributed to the surgical procedure or intraoperative events. (484, Table 30-5)

77. The goals of the anesthetic management for patients undergoing a carotid endarterectomy include (1) prevention of cerebral ischemia through maintenance of adequate cerebral perfusion pressure and (2) prevention of myocardial ischemia through avoidance of acute peaks in blood pressure and heart rate. The critical period of the procedure occurs intraoperatively while the carotid artery is clamped. Mean arterial pressure should be maintained above the patient's baseline blood pressure (within 20%) to ensure adequate blood flow through the circle of Willis. Finally, rapid emergence from anesthesia is recommended to facilitate early neurologic assessment. (484, Table 30-5)

78. During a carotid endarterectomy procedure, the arterial blood pressure should be maintained in a normal or slightly elevated range specific to that patient. It may be helpful to blunt sympathetic nervous system responses to direct laryngoscopy to avoid acute hypertension. A high-normal range of mean arterial pressures should be maintained during carotid artery clamping to increase

collateral blood flow and prevent cerebral ischemia, particularly when there is no intraluminal shunt in place. Intraoperative hypotension is often treated with phenylephrine. (484, Table 30-4)

79. During a carotid endarterectomy the $Paco_2$ should be maintained near normal, between 35 and 40 mm Hg. Hypocarbia should be avoided given the risk of cerebral vasoconstriction and ischemia. (484)

80. The purpose of intraoperative neurologic monitoring during a carotid endarterectomy is to identify cerebral ischemia and the potential need for an intraluminal shunt placed for perfusion to the ipsilateral brain while the diseased carotid artery is clamped. Several methods of monitoring for cerebral ischemia have been used, including stump pressure measurement (blood pressure in the carotid artery distal to the placement of the surgical clamp as an indication of adequate collateral flow), electroencephalogram, and somatosensory evoked potentials, direct measurement of cerebral blood flow, and transcranial Doppler ultrasonography. Alternatively, an intraluminal shunt is routinely placed regardless of whether cerebral ischemia is detected. (484-485)

81. The administration of either local or general anesthesia for carotid endarterectomy is acceptable. Neither has been shown to have better outcomes or reduced morbidity or mortality. (484)

82. Local anesthesia for a carotid endarterectomy is achieved with the administration of a deep and superficial cervical plexus block. A deep cervical plexus block provides anesthesia to the C1-C4 nerve roots and blocks the greater auricular, lesser occipital, transverse cervical, and supraclavicular peripheral nerves. The superficial cervical plexus block anesthetizes the cutaneous nerves. The advantages of local anesthesia for this procedure include a more accurate assessment of the patient's neurologic status intraoperatively and improved hemodynamic stability. Neurologic status is typically monitored using the patient's contralateral grip strength, level of consciousness, and quality of prompted speech. Disadvantages of this technique include the need for a cooperative and motionless patient. (484)

83. The induction of general anesthesia for a carotid endarterectomy is usually achieved with the administration of an opioid, an intravenous induction agent, and a neuromuscular blocking drug. The maintenance of anesthesia is typically achieved by the administration of a volatile anesthetic in conjunction with nitrous oxide and an opioid. Neuromuscular blockade is usually maintained throughout the course of the procedure to minimize the risk of intraoperative movement. Advantages of general anesthesia include the ability to manipulate cerebral blood flow and the cerebral metabolic oxygen requirement, as well as the security of a protected airway. General anesthesia may also be advantageous when patients are unable to communicate or when their neck anatomy appears difficult for the administration of local anesthesia. Disadvantages include reliance on surrogate indicators to monitor neurologic status and greater hemodynamic instability. (484, Table 30-5)

84. Potential postoperative complications after a carotid endarterectomy include recurrent laryngeal nerve injury, hemodynamic instability, airway compression secondary to neck hematoma, loss of carotid body function, myocardial infarction, and neurologic dysfunction. Neurologic dysfunction after carotid endarterectomy is usually due to intraoperative embolization or hypoperfusion during carotid artery clamping. (485)

85. Postoperative hypertension is common after a carotid endarterectomy as the majority of patients undergoing carotid endarterectomy have chronic hypertension. Hypertension may also occur secondary to the loss of function of the carotid sinus or the loss of innervation to the carotid sinus during surgery. Hypertension may result in an increased incidence of postoperative complications such as neck hematoma, myocardial ischemia, and hyperperfusion syndrome, and should be strenuously avoided. (485)

Chapter

28 OPHTHALMOLOGY AND OTOLARYNGOLOGY

Steven Gayer, Howard D. Palte

OPHTHALMOLOGY

1. What is normal intraocular pressure (IOP)?
2. How is IOP created and maintained?
3. Why and to what extent does IOP increase during coughing or vomiting?
4. What factors during the course of a general anesthetic increase IOP?
5. What physiological factors (CO_2, temperature) during the course of a general anesthetic decrease IOP?
6. How does ketamine affect intraocular pressure? What other attributes of ketamine make it a less than ideal choice for anesthesia in patients undergoing ophthalmologic procedures?
7. How much does IOP increase with the intravenous administration of succinylcholine? What is the duration of this effect?
8. What is the mechanism for the increase in IOP following administration of succinylcholine?
9. What maneuvers may attenuate the rise in IOP associated with succinylcholine use for laryngoscopy and intubation?
10. How do paralyzing doses of nondepolarizing neuromuscular blocking drugs affect intraocular pressure?
11. How do inhaled anesthetics affect IOP? What is the effect on IOP of most intravenous anesthetics?
12. How do changes in arterial blood pressure affect IOP?
13. What topical ophthalmic medicines may be absorbed sufficiently to exert systemic effects?
14. What systemic effects have been attributed to the use of topical ophthalmic β-adrenergic blocking medications?
15. What are the systemic effects of topical phospholine iodide (echothiophate)?
16. Why is phenylephrine administered as a topical ophthalmic medicine? What systemic effect has been attributed to the topical ophthalmic application of this drug?
17. Why are carbonic anhydrase inhibitors, such as acetazolamide, administered as topical ophthalmic medicines? What systemic effects have been attributed to the topical ophthalmic application of this drug?
18. What is the oculocardiac reflex? What is its reported incidence? When is it most likely to occur?
19. When is the oculocardiac reflex most often encountered?
20. What cardiac rhythms are likely to result from the oculocardiac reflex?
21. How does arterial hypoxemia or hypercarbia affect the oculocardiac reflex? How does the depth of general anesthesia affect the oculocardiac reflex?
22. What is the first line of treatment of the oculocardiac reflex? What measures may be taken if the reflex persists?

23. Is prophylactic use of anticholinergics fully effective in preventing the oculocardiac reflex? What problems may arise from use of an anticholinergic?
24. What are some important demographic characteristics of patients scheduled for eye surgery?
25. Should antiplatelet or anticoagulant medications be discontinued prior to surgery?
26. What is a key anesthetic consideration for the patient scheduled for ophthalmic surgery with uncontrolled cough, untreated Parkinsonian tremor, severe claustrophobia, or pathological anxiety?
27. What are the anesthetic options for patients having eye surgery?
28. What is the significance of the extraocular muscle cone for eye blocks?
29. What is the ultimate needle tip position for a retrobulbar (intraconal) block?
30. What is the rationale behind extraconal (peribulbar) anesthesia? Where is the ultimate needle tip position?
31. What are some complications of a retrobulbar block?
32. What is the differential diagnosis of altered physiological status (blood pressure, heart rate) after a needle-based ophthalmic regional eye block?
33. How does a sub-Tenon block differ from a needle-based eye block?
34. Which patients are at high risk for retinal detachment?
35. What are the anesthetic considerations for patients undergoing surgery to repair a retinal detachment?
36. When must nitrous oxide be avoided as maintenance anesthetic for patients undergoing surgery to repair a retinal detachment? What is the risk associated with this?
37. What is glaucoma? What are its variants?
38. What are the anesthetic goals in the management of glaucoma patients?
39. What are some special anesthetic considerations in children undergoing strabismus surgery?
40. What is the most common reason for an inpatient admission for children following strabismus surgery?
41. What factors must be considered in the anesthetic management of patients with traumatic eye injuries?
42. Why is "awake" endotracheal intubation hazardous for patients with open globe injuries?
43. What anesthetic maneuvers may attenuate increases in IOP in traumatic eye injury?
44. Is regional anesthesia contraindicated in traumatic eye injuries?
45. What is the most common ocular complication following general anesthesia for non-ophthalmologic surgery? What other condition can mimic it?
46. Why are patients who are undergoing a surgical procedure via general anesthesia at risk for corneal abrasion?
47. What are clinical signs of corneal abrasion?
48. What are some measures that can be taken to reduce the risk of corneal abrasion in patients under general anesthesia? What are some of the potential problems with routine use of ophthalmic ointment?
49. Which surgical procedures are associated with increased risk of postoperative visual loss?
50. What action(s) should be taken if the patient complains of postoperative visual loss?

OTOLARYNGOLOGY

51. What special airway considerations pertain to ENT surgery?
52. Why are posterior pharyngeal packs used during ENT surgery and what precautions are required with their use?
53. What supplemental airway devices may be needed for a difficult airway during ENT surgery?
54. What is laryngospasm? How is the reflex mediated?

55. What is the treatment for laryngospasm?
56. Why are children at particular risk for laryngospasm?
57. Should scheduled ENT surgery be postponed if the child has an upper respiratory infection (URI)? What are the risks associated with proceeding with anesthesia in a child with an active upper respiratory infection?
58. What risks are associated with general anesthesia in a patient with massive epistaxis?
59. What are some symptoms that may alert the anesthesiologist to the presence of obstructive sleep apnea (OSA)?
60. What features may be noted in the airway examination of a patient with OSA?
61. What are the anesthetic implications of OSA?
62. What elements are necessary to generate an airway fire?
63. Are airway fires possible with monitored anesthesia care (MAC)?
64. What are the main anesthetic considerations for middle ear surgery?
65. What effects may nitrous oxide (N_2O) exert during ear surgery?
66. How is surgical identification of the facial nerve performed intraoperatively in patients undergoing otologic surgery? How might this affect the anesthetic management?
67. Why do otolaryngologists use epinephrine intraoperatively? What are the anesthesia implications of its use?
68. What concentration of epinephrine is considered safe in ear microsurgery?
69. During otolaryngology surgery how can bleeding in the surgical field be minimized?
70. What is an optimal anesthetic plan for emergence from general anesthesia in the patient who has undergone middle ear surgery?
71. Why are patients who have undergone middle ear surgery at risk for postoperative nausea and vomiting?
72. What anesthetic strategies minimize postoperative nausea and vomiting after ear surgery?
73. What factors contribute to airway obstruction in children undergoing tonsillectomy and adenoidectomy?
74. What is negative pressure pulmonary edema?
75. Why is blood loss often underestimated during and after tonsillectomy and adenoidectomy?
76. What are some considerations for the anesthetic management of patients who return to surgery because of significant bleeding after tonsillectomy and adenoidectomy?
77. What organism is frequently responsible for acute epiglottitis?
78. What are the clinical features of acute epiglottitis?
79. What anesthetic precautions are necessary in acute epiglottitis management?
80. What are the clinical features of foreign body aspiration into the airway?
81. What anesthesia precautions are necessary in addressing the patient with an airway foreign body?
82. What postoperative measures are necessary after the removal of a foreign body from the airway?
83. Why has cocaine been used for nasal surgery?
84. What are the disadvantages of using cocaine? Are there alternatives?
85. What considerations are important for general anesthesia emergence in nasal and sinus surgery?
86. What preoperative investigations may be useful in a patient undergoing endoscopic surgery?
87. What techniques may be used to maintain ventilation and oxygenation during airway endoscopy?
88. What risk is associated with the use of a manual high-pressure jet ventilator (Sanders' injector apparatus)?
89. What is a laser? What advantages does it offer for surgical procedures?
90. Name some hazards that are associated with laser surgery.

91. What is the purpose of a smoke evacuator used during laser surgery?
92. What measures can be taken during laser surgery to minimize the risk of an endotracheal tube fire?
93. Why should the ETT cuff be filled with saline or an indicator dye during laser surgery?
94. What medical issues are frequently encountered in patients undergoing radical neck dissection?
95. How does a history of radiation to the larynx, pharynx, or oral cavity affect anesthetic management?
96. What arrhythmias may be precipitated during radical neck dissection, and why?
97. What known injuries may be encountered postoperatively after radical neck dissection?
98. What catastrophic postoperative event may occur after neck surgery?
99. How may hypocalcemia present after thyroid surgery?
100. The patient is unable to grimace after a parotidectomy. Why? What monitor(s) may help prevent this complication?

ANSWERS*

OPHTHALMOLOGY

1. Intraocular pressure ranges between 10 to 22 mm Hg. In the intact normal eye there is a typical diurnal variation of 2 to 5 mm Hg. Small changes can occur with each cardiac contraction and with closure of the eyes, mydriasis, and changes in posture. (487)
2. Intraocular pressure is primarily a balance between the production of aqueous humor and its drainage. Aqueous humor is actively secreted from the posterior chamber's ciliary body and flows through the pupil into the anterior chamber where it becomes mixed with aqueous fluids, which are passively produced by blood vessels on the iris's forward surface. (487)
3. Any obstruction of venous return from the eye to the right side of the heart can raise IOP. Coughing or straining can increase intraocular pressure by 40 mm Hg or more. (487)
4. Any maneuver that increases venous congestion will increase IOP. These include: Trendelenburg positioning, tight cervical collar, straining, retching, vomiting, and coughing. Direct laryngoscopy and intubation also increase intraocular pressure. (487)
5. During general anesthesia hyperventilation and hypothermia decrease IOP. (487)
6. Ketamine can induce a rotatory nystagmus, cycloplegia, and blepharospasm (tight squeezing of the eyelids). Additionally, it is proemetic and increases secretions. Anticholinergic agents may be administered with ketamine to diminish secretions. There is controversy surrounding the effect of ketamine on IOP. (487)
7. Succinylcholine can produce an increase in intraocular pressure of about 9 mm Hg 1 to 4 minutes after intravenous administration. This effect can last up to 7 minutes. (487)
8. Increases in IOP secondary to the administration of succinylcholine are due to a number of mechanisms including tonic contraction of the extraocular muscles, relaxation of the orbital smooth muscle, choroidal vascular dilation, and cycloplegia, which impedes aqueous outflow. (487)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

9. Pretreatment with a small dose of nondepolarizing neuromuscular blocker, lidocaine, β-blocker, or acetazolamide may attenuate increases in IOP associated with use of succinylcholine prior to direct laryngoscopy and endotracheal intubation. (487)

10. Nondepolarizing neuromuscular blocking drugs will decrease IOP by relaxing the extraocular muscles. (487)

11. Both inhaled and most intravenous anesthetics produce dose-related reductions in intraocular pressure. This is probably due to multiple mechanisms including central nervous system depression, decreased production of aqueous humor, enhanced outflow of aqueous humor, and relaxation of the extraocular muscles. The effect of ketamine on IOP is controversial. (487)

12. Arterial hypertension has minimal influence on IOP. Venous drainage is the key factor affecting IOP. (487)

13. Topical ophthalmic agents can be absorbed systemically via the conjunctiva or drain down the nasolacrimal duct and be absorbed through the nasal mucosa. These agents include acetylcholine, anticholinesterases, cyclopentolate, epinephrine, phenylephrine, and timolol. (487, Table 31-1)

14. Topical ophthalmic β-adrenergic blocking medications may produce atropine resistant bradycardia and bronchospasm, and exacerbate congestive heart failure. (487, Table 31-1)

15. Phospholine iodide (echothiophate) is a miosis-inducing anticholinesterase that profoundly interferes with metabolism of succinylcholine. Patients with low levels of plasma cholinesterase are at risk for prolonged paralysis. (487, Table 31-1)

16. Phenylephrine is an α-adrenergic that causes mydriasis (pupil dilation). Systemic absorption of phenylephrine can induce transient malignant hypertension. (487, Table 31-1)

17. Acetazolamide inhibits the production of aqueous humor. Its systemic effects include diuresis and hypokalemic metabolic acidosis. (487, Table 31-1)

18. The oculocardiac reflex is a vagal-mediated response that manifests with an abrupt, profound decrease in heart rate. It occurs in response to extraocular muscle traction or external pressure on the globe. The reported incidence varies widely from 15% to 80%. (487)

19. The oculocardiac reflex is most often encountered during strabismus surgery. However, it can arise during any type of ophthalmic surgery as well as some otolaryngology procedures. A regional anesthetic eye block can ablate it. Paradoxically, it may be triggered during the administration of this block. (487)

20. The oculocardiac reflex can manifest as a variety of dysrhythmias including junctional or sinus bradycardia, atrioventricular block, ventricular bigeminy, multifocal premature ventricular contractions, ventricular tachycardia, and asystole. (487-488)

21. Hypercarbia, hypoxemia, and light planes of general anesthesia all augment the incidence and severity of the oculocardiac reflex. (488)

22. Prompt removal of the surgical stimulus often results in rapid recovery. At the first sign of any dysrhythmia, surgery must stop and all pressure on the eye or traction on extraocular muscles must be discontinued. Other measures that can be taken include the administration of a parasympatholytic such as atropine or glycopyrrolate. Consider increasing the depth of general anesthesia (provided that the patient is hemodynamically stable). Alternatively, infiltration of local anesthetic attenuates recurrence of the reflex. (488)

23. The prophylactic use of an anticholinergic is not 100% effective in preventing the oculocardiac reflex. Side effects that may result from the use of an anticholinergic include persistent tachycardia. This may have serious consequences in geriatric patients and those with a history of heart disease. (488)

24. Eye surgery patients are often at the extremes of age, and range in age from premature newborns to nonagenarians. Age-specific considerations such as altered pharmacokinetics and pharmacodynamics apply. The elderly, syndromic pediatric patients, and premature infants commonly have comorbidities that carry important anesthesia implications. (488)

25. The cessation of antiplatelet or anticoagulant drugs prior to ophthalmic surgery is controversial. One must weigh the risks of intraocular bleeding versus the risks of perioperative stroke, myocardial ischemia, or deep venous thrombosis. (488)

26. An important component of the preoperative assessment is to gauge the likelihood of patient movement during surgery. An inability to remain supine and relatively still during eye surgery under monitored anesthesia care may result in eye injury with devastating long-term visual consequences. (488)

27. The anesthetic options for ophthalmic procedures include general anesthesia, retrobulbar (intraconal) block, peribulbar (extraconal) anesthesia, sub-Tenon block, and topical analgesia. (488)

28. The extraocular muscle cone separates the intraconal from the extraconal space and determines whether the local anesthetic is delivered as a retro- or peribulbar block. (489, Fig. 31-1)

29. A retrobulbar block is accomplished by inserting a steeply angled needle into the muscle cone such that the tip of the needle is behind (retro) the globe (bulbar). (489, Fig. 31-1)

30. The boundary separating the intraconal from extraconal space is porous. Local anesthetics injected outside the muscle cone diffuse inward, resulting in anesthesia of the eye. An extraconal block is achieved by directing a needle with minimal angulation to a shallow depth, such that the tip remains outside the muscle cone. (489, Fig. 31-1)

31. Complications of needle-based ophthalmic regional anesthesia include superficial or retrobulbar hemorrhage, elicitation of the oculocardiac reflex, intraocular injection of local anesthetic, penetration or puncture of the globe, optic nerve trauma, intravenous injection of local anesthetic solution and resultant convulsions, central retinal artery occlusion, brainstem anesthesia, and blindness. (489, Table 31-3)

32. Intravenous sedation is the most common cause of altered physiologic status (blood pressure, heart rate, rhythm, ventilation) after a needle-based eye block. More sinister complications are brainstem anesthesia and local anesthetic toxicity secondary to intravascular injection. (489, Table 31-4)

33. A sub-Tenon block is performed using a blunt cannula inserted into the space between the globe's sclera and surrounding the Tenon capsule. Local anesthetic injected into this space blocks the optic and ciliary nerves as they penetrate the capsule. (490, Fig. 31-2)

34. Diabetics and patients with severe myopia are at particular risk for retinal detachment. (490)

35. Retinal surgery is often prolonged and associated with greater manipulation of the eye. Patients may require deeper planes of general anesthesia or a dense regional block. Perfluorocarbons such as sulfur hexafluoride are relatively insoluble gases that are surgically instilled in order to tamponade the retina; these may take up to 28 days to resorb. (490)

36. Nitrous oxide is 100 times more diffusible than sulfur hexafluoride and, therefore, can expand the size of a gas bubble. This will raise IOP and may result in retinal ischemia with permanent loss of vision. (490)

37. Glaucoma is a condition characterized by raised IOP, optic nerve injury, and gradual loss of vision. It is thought that a sustained increase in IOP results in diminished perfusion of the optic nerve. Variants include closed angle (or acute) glaucoma and open angle (or chronic) glaucoma. (491)

38. The key anesthetic goals in the management of glaucoma patients include avoiding mydriasis (by ensuring miotic drops are continued), understanding the interactions between glaucoma medications and anesthetic agents, and preventing increases in IOP associated with the induction, maintenance, and emergence from anesthesia. (491)

39. Special considerations for children undergoing strabismus surgery include an awareness of the high incidence of intraoperative oculocardiac reflex, an increased risk for malignant hyperthermia, and the high incidence of postoperative nausea and vomiting. (491)

40. The most common reason for pediatric inpatient admission following strabismus surgery is postoperative nausea and vomiting (PONV). (491)

41. The anesthetic plan for patients with traumatic eye injuries must balance the specific risks of increasing IOP and exacerbating the ocular insult versus anesthetizing a non fasted patient at risk for aspiration upon the induction of general anesthesia. Increasing IOP via a tightly applied facemask, laryngoscopy and intubation, or from coughing or bucking may result in extrusion of vitreous, and jeopardize ultimate visual outcome. A rapid sequence induction is indicated for the non fasted patient. (491)

42. Awake endotracheal intubation may be appropriate in patients with difficult airways. However, in the setting of a disruptive globe increases in IOP can lead to adverse visual outcomes. The risks associated with rises in IOP produced by an awake intubation must be weighed against the inherent dangers of the difficult airway. (491)

43. It is important to avoid maneuvers that increase IOP in patients with a traumatic eye injury. The patient should be positioned in a slight anti-Trendelenburg tilt. If no airway problems are anticipated, consider the rapid sequence induction of anesthesia with a large dose of nondepolarizing neuromuscular blocking agent. The systemic hypertension and rise in IOP that follows the administration of succinylcholine can be attenuated by the preinduction administration of intravenous medications such as lidocaine and opioids. Also, pretreatment with a small dose of a nondepolarizing neuromuscular blocking agents is useful. (491)

44. Regional anesthesia may be an option for select injuries, and in patients at higher risk from general anesthesia. (491)

45. The most common ocular complication following general anesthesia for non-ophthalmologic surgery is corneal abrasion. It is important to remember a painful eye may also be a manifestation of acute glaucoma.

46. Mechanical damage to the eye can occur during the induction of anesthesia. It can be caused by dangling eye tags, anesthesia masks, drapes, or other objects that come in contact with the open eye. Abrasions can also occur secondary to the loss of the blink reflex with subsequent drying from exposure to the atmosphere and diminished tear production. (491)

47. The clinical signs of corneal abrasion include conjunctivitis, tearing, and foreign body sensation. (491)

48. Preventative measures include gently taping the eyelid shut during mask ventilation, intubation, and thereafter. Ointments may cause an allergic reaction or blur post-emergence vision. Protective goggles may be beneficial. (491)

49. The risk of postoperative visual loss is higher in prolonged spine surgery in the prone position, and cardiac surgery. (492)

50. Early consultation with an ophthalmologist is essential when a patient complains of postoperative visual loss. Funduscopic and visual field examinations may aid in diagnosis. (492)

OTOLARYNGOLOGY

51. Since ENT surgery takes place around the head, the airway becomes relatively inaccessible to the anesthesia provider. Furthermore, there is a real possibility of encountering a difficult airway because of anatomic factors, surgical issues, or underlying pathology. Attention should be directed to establishing and securing the airway, preferably with an endotracheal tube. Also, the airway may become compromised in the perioperative period by undetected bleeding, edema, or surgical manipulation. (492)

52. Posterior pharyngeal packs minimize the risk of aspiration by sealing the larynx from blood that reaches the pharynx. It is vital to alert operating room personnel of their placement, and to confirm their removal prior to extubation. (492)

53. Supplemental airway devices include the video-laryngoscope or fiber-optic bronchoscope. A tracheostomy kit may be necessary for the gravely compromised airway. Ancillary equipment should be readied prior to the commencement of anesthesia. (492)

54. Laryngospasm is an abrupt, intense, and often prolonged closure of the larynx that leads to compromises in ventilation and oxygenation. The reflex is mediated through vagal stimulation of the superior laryngeal nerve. It may be precipitated by instrumentation of the endolarynx, blood or secretions on the vocal cords, and surgical manipulation at inadequate depths of anesthesia. (492)

55. Prompt recognition and intervention is key to the treatment of laryngospasm. Treatment modalities include administration of 100% oxygen via positive-pressure facemask ventilation, placement of oral or nasal airways, and deepening of anesthesia with intravenous or inhalational agents. In refractory cases, a small dose of succinylcholine may be required. (492)

56. In neonates, infants, and small children even brief laryngospasm is perilous. In this group peripheral oxygen saturation drops rapidly because of a small functional residual capacity and relatively high cardiac output. (492)

57. The child with an URI is at increased risk of airway issues, notably breath holding, oxygen desaturation, and postoperative croup. However, not all children with an URI need their ENT surgery postponed. An assessment of the benefits of surgery vs. the risk of airway compromise should be made. For example, the performance of a myringotomy with placement of ventilation tubes requires minimal airway manipulation. (492)

58. Massive epistaxis is often associated with ongoing hemorrhage and concealed swallowing of blood. These patients are at high risk for regurgitation and aspiration. Clinically, they are anxious, hypovolemic, and hypertensive. The preoperative placement of a large-bore peripheral intravenous cannula and adequate rehydration are vital. Hypertension and continued hemorrhage should be anticipated. (492)

59. OSA is characterized by upper airway obstruction and disordered breathing patterns during sleep. Symptoms include snoring, early morning headache, sleep disturbances, daytime somnolence, and personality changes. In children there may be behavioral and growth disturbances as well as poor school performance. (492-493)

60. Many patients with OSA are obese. The combination of limited mouth opening and a large tongue may make visualization of the pharynx difficult. In adult men the neck circumference is large, often exceeding 17 inches. (492-493)

61. One must anticipate difficult airway management in the OSA patient. Mask ventilation, laryngoscopy, and intubation are often challenging. Intraoperative hypertension is common. OSA patients are exquisitely sensitive to the effects of hypnotics and narcotics, and may require prolonged recovery room monitoring. (492-493)

62. There are three key elements needed to produce an airway fire:

- **a.** Heat or source of ignition (laser or electrosurgical unit)
- **b.** Fuel (paper drapes, gauze swabs)
- **c.** Oxidizer (O_2, air, N_2O) (493)

63. During monitored anesthesia care the danger of an airway fire exists because the heat and fuel elements are still present. It is important to remove the source of oxidation, and discontinue delivery of supplemental oxygen. (493)

64. There are five primary anesthetic concerns for middle ear surgery:

- **a.** N_2O—increases middle ear pressure and causes serous otitis
- **b.** Facial nerve monitoring—avoid intraoperative neuromuscular blockade
- **c.** Epinephrine—may precipitate acute hypertension and tachyarrhythmia
- **d.** Smooth emergence—avoid coughing, bucking, and acute hypertension
- **e.** Postoperative nausea and vomiting—institute prophylactic measures (493)

65. Nitrous oxide is more soluble than nitrogen in blood and diffuses into air-filled cavities. The increases in middle ear pressure may disrupt tympanoplasty grafts. Also, the acute discontinuation of N_2O may produce serous otitis. Nitrous oxide should be administered in moderate concentrations ($<50\%$), if at all. (493)

66. The surgeon frequently uses a facial nerve monitor to prevent trauma or accidental incision of the facial nerve and its branches. The use of neuromuscular blocking drugs should be curtailed in order to prevent attenuation of the monitor's twitch response. Succinylcholine or a single small dose of an intermediate-acting non depolarizing neuromuscular blocking agent is preferred. (493)

67. Epinephrine is injected during ear microsurgery to decrease bleeding and improve visualization within the surgical field. Systemic uptake may precipitate hypertension, tachycardia, and dysrhythmias. (493)

68. Epinephrine concentrations should be limited to 1:200,000 in ear microsurgery. (493)

69. Maneuvers to limit bleeding in the surgical field include use of topical or injected epinephrine, moderate reverse Trendelenburg (head-up) positioning, and volatile anesthetics to decrease arterial blood pressure (within an acceptable range). The use of potent vasoactive drugs and controlled hypotension is controversial. (493)

70. The risk of graft disruption or acute hemorrhage is minimized by the smooth emergence from general anesthesia. Episodic coughing and bucking will produce hypertension that may result in poor surgical outcome. In the uncomplicated airway, extubation of the trachea at a deep plane of anesthesia with spontaneous respiration may be beneficial. (493)

71. Postoperative nausea and vomiting is common after middle ear surgery because of manipulation of the vestibular apparatus. Factors that contribute to PONV include anesthesia technique (use of nitrous oxide and narcotics), inadequate hydration, and postoperative movement. (493)

72. The number of agents used to prevent PONV after ear surgery is guided by a relative risk analysis. Prophylactic agents include corticosteroids, 5HT3-receptor antagonists, neurokinin-1 receptor antagonists, scopolamine patches, and low-dose propofol. Gastric decompression is useful if blood has been swallowed. Scopolamine crosses the blood-brain barrier and may cause confusion, particularly in the elderly. (493)

73. Children undergoing tonsillectomy and adenoidectomy have upper airway obstruction that often only manifests during sleep. The routine use of premedication is controversial. Furthermore, airway obstruction is accelerated by large masses of tonsillar or adenoidal tissue, and loss of pharyngeal tone associated with the induction of anesthesia. Also, manipulation of the airway during light planes of anesthesia may result in acute airway obstruction. (493-494)

74. Negative pressure pulmonary edema clinically manifests when the patient inhales forcefully against a closed glottis. This effort generates marked negative intrathoracic pressures that are transmitted to the pulmonary interstitial tissue, and promotes fluid transition from the pulmonary circulation into the alveoli. (494)

75. Blood loss during tonsillectomy and adenoidectomy is either overt (into the suction bottle) or covert (swallowed). Blood loss is underestimated because the covert loss is not seen. (493-494)

76. Anesthesia considerations for the post-tonsillectomy bleed include the possibility of undetected and prolonged hemorrhage, concomitant hypovolemia, and regurgitation of blood swallowed into the stomach. Measures required include rehydration, rapid sequence induction of general anesthesia, protection of the airway with a cuffed endotracheal tube (minimize risk of aspiration), and drainage of gastric contents. (494)

77. Acute epiglottitis is an infectious disease caused by *Haemophilus influenzae* type B. It most often affects children between the ages of 2 and 7. (494)

78. There is a history of sudden onset of fever and dysphagia. Symptoms progress rapidly and the child may transition from an acute pharyngitis to complete airway obstruction and respiratory failure within a few hours. The clinical picture is of an agitated, drooling child leaning forward and holding the head in an extended position. The child becomes exhausted from the work of breathing against an almost fully occluded airway. (494)

79. Acute epiglottitis is an airway emergency. Direct visualization of the glottis should not be attempted because stimulation and struggling may produce acute airway obstruction. Emergency airway equipment should be readied. A surgeon adept at rigid bronchoscopy and tracheostomy should be present at the bedside. An inhaled induction of anesthesia maintaining spontaneous respiration is preferred. Atropine may dry secretions and prevent bradycardia. (494)

80. Tracheal aspiration of a foreign body is an airway emergency. Clinical features include sudden dyspnea, dry cough, hoarseness, and wheezing. (494)

81. A preoperative plan and mutual intraoperative cooperation between the anesthesia provider and surgeon are vital in order to avoid inadvertent distal displacement of the foreign body. Removal of the foreign body can be accomplished by either direct laryngoscopy or rigid bronchoscopy. The surgeon should be prepared for an emergency cricothyrotomy or tracheostomy in the event of acute airway occlusion. Total intravenous anesthesia with maintenance of spontaneous ventilation can eliminate operating room pollution. (494)

82. After the removal of a foreign body, postoperatively the patient should receive humidified oxygen and remain under close observation for development of airway edema. (494-495)

83. Cocaine is an effective topical anesthetic agent. Since it is also a potent vasoconstrictor, it reduces bleeding in the surgical field and shrinks the nasal mucosa. (495)

84. The disadvantages of cocaine include altered sensorium (euphoria and dysphoria) and untoward cardiac arrhythmias. For these reasons, cocaine has been surpassed by the "pseudo-cocaine" solution containing a local anesthetic and vasoconstrictor. (495)

85. The removal of posterior pharyngeal packs should be confirmed. Protective airway reflexes should be present prior to extubation because of possible airway edema and ongoing bleeding. (495)

86. Bronchoscopy, laryngoscopy, and microlaryngoscopy involve direct manipulation of the airway. In these procedures, the airway should be assessed carefully paying special attention to the presence of stridor (indicator of compromise). Preoperative investigations such as blood gas analysis, flow-volume loops, radiographic studies, and magnetic resonance imaging may be useful. (495)

87. A variety of techniques can be employed to provide oxygenation and ventilation during endoscopy. The trachea may be intubated with a small diameter pediatric endotracheal tube but this may impair visualization of the posterior commissure. An alternative technique, jet ventilation, utilizes high-flow oxygen insufflation through a small-gauge catheter placed in the trachea. (495)

88. The use of the manual high-pressure jet ventilator carries risks of pneumothorax and pneumomediastinum. (495, Fig. 31-4)

89. Laser is an acronym for *light amplification by stimulated emission of radiation*. It produces an intense focused light beam that allows for precise and controlled coagulation, incision, and vaporization of tissues. Advantages of laser include its ability to target difficult-to-reach lesions, provide hemostasis, produce minimal edema, and promote rapid healing. (495)

90. Hazards associated with laser surgery include atmospheric contamination by fine particles of vaporized tissues, misdirected laser energy, venous gas embolism, and ocular (retina) injury. There is also risk of endotracheal tube (ETT) fire during airway surgery. (495-496)

91. During laser surgery an efficient smoke evacuator, as well as special masks, is necessary because small, vaporized particles are easily inhaled. (495)

92. *Preoperative*:

a. Arrange surgical drapes to avoid accumulation of combustible gases
b. Use appropriate laser-resistant ETT
c. Moisten gauze and sponges in the vicinity of the laser

Intraoperative:

a. Alert surgeon and OR personnel to risk
b. Assign specific roles to each OR member in case of fire
c. Reduce inspired O_2 to minimal values
d. Replace N_2O with air
e. Wait a few minutes after changes in gas concentration before activating laser (495-496, Figure 31-5, Table 31-5)

93. The purpose of filling the ETT cuff with saline or an indicator dye during laser surgery is to help dissipate laser heat. Furthermore, leaking dye is an indicator of cuff rupture. (496)

94. Radical neck dissection is indicated for removal of a malignancy. These patients frequently have a history of tobacco and alcohol abuse. An extensive preoperative work-up is necessary because pulmonary and cardiac disease is prevalent. (496)

95. A history of prior radiation therapy to the larynx, pharynx, or oral cavity may produce marked tissue indurations, scarring, and limitation of mobility. These may cause difficulties with airway management, particularly endotracheal intubation. (496)

96. Traction or pressure on the carotid sinus may provoke acute arrhythmias. These include prolongation of the QT interval, bradydysrhythmias, and asystole. Treatment includes early detection, cessation of the surgical stimulus, and administration of an anticholinergic agent. Another option is local anesthetic infiltration of the carotid sinus. (496)

97. Injuries to the facial (VII) nerve, recurrent laryngeal nerve, and phrenic nerve may all be encountered postoperatively after radical neck dissection surgery. (496)

98. Hematoma formation in the neck may compress the airway leading to acute obstruction. If tracheotomy is not performed during the initial surgery, then the patient requires close monitoring (for laryngeal or upper airway obstruction) in the postoperative phase. (496)

99. Hypocalcemia after thyroid surgery may present in many forms. Clinical signs may include tetany (carpal spasm), peripheral and circumoral paresthesia, QT interval prolongation, and laryngospasm. (497)

100. The inability to perform a symmetrical grimace after parotid surgery is indicative of facial nerve injury or traction. Since the parotid gland is traversed by the facial nerve, it is customary to monitor the facial nerve function with a facial nerve monitor. Occasionally, the facial nerve may need to be sacrificed. It is then reconstructed with a graft from the greater auricular nerve. (497)

Chapter

29 ORTHOPEDICS

Andrew D. Rosenberg, Thomas J.J. Blanck

RHEUMATOLOGIC DISORDERS

1. Is rheumatoid arthritis (RA) just a disease of the joints and adjacent connective tissue?
2. What are some of the clinical manifestations of RA?
3. What are some airway abnormalities that can occur in patients with rheumatoid arthritis?
4. Why might the normal mouth opening be decreased in patients with rheumatoid arthritis?
5. What occurs to the developing mandible in patients with juvenile rheumatoid arthritis that makes it more difficult to intubate the trachea in this patient population?
6. What are some of the clinical manifestations of cricoarytenoid arthritis?
7. Can neck movement in patients with RA result in cervical spine injury? What is the clinical implication of this?
8. What percent of patients with RA have involvement of their cervical spine?
9. What are three abnormal movements of the cervical spine that may be manifest in patients with rheumatoid arthritis?
10. What is atlantoaxial subluxation?
11. What pathology in RA patients can lead to atlantoaxial subluxation?
12. How is the degree of atlantoaxial subluxation measured? What is this measurement called?
13. What test can be used to determine the atlas-dens interval?
14. What degree of motion between the atlas and dens, or at what atlas-dens interval, is the patient considered to be at risk for spinal cord injury?
15. In the case of pure transverse axial ligament disruption, does flexion or extension increase the atlas-dens interval?
16. If a patient is asymptomatic with neck flexion and extension preoperatively can the anesthesiologist be reassured of an atlas-dens interval of less than 4 mm?
17. What is subaxial subluxation? What is its clinical significance?
18. What is superior migration of the odontoid? What are the potential clinical manifestations?
19. What is the surgical treatment for superior migration of the odontoid?
20. What effect does rheumatoid arthritis have on the trachea?
21. What is the pathology in ankylosing spondylitis?
22. What is the hallmark neck position in patients with ankylosing spondylitis?
23. Ankylosing spondylitis is associated with which HLA type?
24. What are some considerations for the anesthetic management of patients with ankylosing spondylitis?

SPINE SURGERY

25. What are some considerations for the anesthetic management of patients undergoing spine surgery?
26. What are the various surgical approaches to spine surgery? What are the clinical implications of this?
27. What kind of endotracheal tubes can be employed to provide one-lung ventilation for thoracic spine surgery?
28. What is an advantage of a bronchial blocker to provide one-lung ventilation for thoracic spine surgery?
29. What newer technique do surgeons employ during thoracoscopic spine surgery to move the lung from the operative field that does not require one-lung ventilation?
30. Why is intraoperative awareness a possible complication of spine surgery?
31. Is it mandatory to employ a monitor for intraoperative awareness in patients undergoing spine surgery?
32. Name some methods to help decrease blood loss in patients undergoing spine surgery.
33. What pharmacologic methods exist to diminish blood loss in patients undergoing spine surgery? Why is aprotinin not used?
34. What are some considerations for patients placed in the prone position?
35. Why is spinal cord integrity monitored during spine surgery?
36. What are various methods used to monitor the spinal cord during spine surgery?
37. What are somatosensory evoked potentials (SSEPs)? What part of the spinal cord do they monitor?
38. What changes in latency and amplitude are considered abnormal when monitoring SSEPs during spine surgery?
39. What anesthetic technique should be employed in patients being monitored with somatosensory and/or motor evoked potentials?
40. What are some surgically related conditions that can interfere with spinal cord monitoring waveform acquisition?
41. Why are some areas of the spinal cord more prone to ischemia?
42. What are some factors that can affect intraoperative spinal cord monitoring waveform acquisition?
43. During spine surgery, what is the time course in which changes in the SSEP waveforms manifest after the loss of spinal cord integrity?
44. What is the appropriate management of a patient during spine surgery once significant changes are noted in the spinal cord monitoring waveforms?
45. What area of the spinal cord is monitored by transcranial motor evoked potentials?
46. How does paralysis with neuromuscular blocking drugs affect transcranial motor evoked potentials?
47. Why might masseter muscle contraction occur during transcranial motor evoked potentials monitoring? What is the clinical implication of this?
48. What special precautions should be taken for patients undergoing transcranial motor evoked potentials monitoring during spine surgery?
49. How are intraoperative electromyelograms used to determine if a pedicle screw has been placed too close to a nerve root?
50. Can neuromuscular blockade be in effect when electromyelograms are being obtained?
51. What is the role of the intraoperative wake-up test?
52. How is an intraoperative wake-up test performed?
53. Name potential complications of the intraoperative wake-up test.
54. What considerations are important at the conclusion of a spine procedure?
55. How can postoperative pain be managed in the patient after spine surgery?
56. Which patients are at the greatest risk of postoperative visual loss? What are some other possible factors that contribute to postoperative visual loss?
57. What are some aspects associated with the prone position that may contribute to postoperative visual loss?
58. How much of postoperative visual loss is due to ischemic optic neuropathy?
59. What are the determinants of the ocular perfusion pressure? What is the clinical implication of this?

60. What intraoperative factors has the American Society of Anesthesiologists (ASA) registry determined to be present in the vast majority of postoperative visual loss patients?
61. According to the ASA practice advisory regarding patients at high risk for postoperative visual loss during spine surgery, is the use of deliberate hypotension associated with postoperative visual loss?
62. According to the ASA practice advisory regarding patients at high risk for postoperative visual loss during spine surgery, what type of fluid should be administered with crystalloid in these cases?
63. According to the ASA practice advisory regarding patients at high risk for postoperative visual loss during spine surgery, is there a defined transfusion trigger at which the risk of postoperative visual loss is eliminated?
64. According to the ASA practice advisory regarding patients at high risk for postoperative visual loss during spine surgery, how should the patient's head and the operating room table be positioned when the patient is prone?

SURGERY IN THE SITTING POSITION

65. What neurologic postoperative complications have been noted in patients who undergo surgery in the sitting position?
66. When devastating neurologic postoperative complications occur after surgery in the sitting position, what is the implicated cause?
67. Is the systemic arterial blood pressure at the level of the heart the same as that at the level of the circle of Willis when patients are anesthetized and placed in the sitting position?
68. What calculation more accurately determines the arterial blood pressure at the level of the circle of Willis when one knows the arterial blood pressure at the level of the heart when patients are anesthetized and placed in the sitting position?
69. What superficial landmark correlates with the circle of Willis?
70. What is the potential risk of hypotension in patients that are anesthetized and placed in the sitting position?

FRACTURED HIP

71. Name several factors that predispose a person to a hip fracture.
72. What is the mortality rate associated with a hip fracture?
73. How do comorbidities in the patient with a fractured hip affect their postoperative outcome?
74. Does it make sense to delay surgery in a patient with a fractured hip and significant comorbidity to improve the patient's medical status prior to surgery?
75. When should patients with a recent myocardial infarction and a fractured hip be scheduled for surgery?
76. What are some considerations for the anesthetic management of patients undergoing hip surgery?
77. Does choice of anesthetic technique—spinal or general anesthesia—play a role in the outcome of patients who have fractured their hip?
78. What are the pros and cons of regional or general anesthesia in the patient with a fractured hip?
79. How are the elderly affected by the use of narcotics in the perioperative period?

TOTAL JOINT REPLACEMENT

80. Use of methylmethacrylate cement is associated with what side effects?
81. What is the etiology of the systemic reaction to methylmethacrylate cement?
82. Which patients are at high risk for a systemic reaction to methylmethacrylate cement?
83. What is an appropriate tourniquet inflation pressure for lower extremity surgery?
84. What is the upper limit of tourniquet time before it should be deflated?
85. If tourniquet time exceeds 2 hours and the procedure is not completed, then the tourniquet should be deflated for how long before it is reinflated and why?
86. What are some complications associated with tourniquet use?

87. When does the major amount of blood loss occur during total knee replacement surgery?
88. What are current recommendations for performing a neuraxial block in patients who received enoxaparin?
89. When can redosing of enoxaparin occur after removal of an epidural catheter?
90. What are the current recommendations for performing a neuraxial block in patients taking clopidogrel?

ANSWERS*

RHEUMATOLOGIC DISORDERS

1. RA is a chronic inflammatory disease, which initially destroys joints and adjacent connective tissue and then progresses to a systemic disease affecting major organ systems. (499, Figure 32-1)
2. Systemic manifestations of RA are widespread. They may include pulmonary involvement with interstitial fibrosis and cysts with honeycombing, gastritis and ulcers from aspirin and other analgesics, neuropathy, nephropathy, muscle wasting, vasculitis, and anemia. Ultimately the anatomy of the airway is damaged and altered in patients with rheumatoid arthritis. (499, Figure 32-1)
3. Some airway abnormalities that can occur in patients with rheumatoid arthritis include decreased mouth opening, a hypoplastic mandible, cricoarytenoid arthritis, and cervical spine abnormalities. (499-500)
4. Normal mouth opening may be decreased in patients with rheumatoid arthritis as a result of temporomandibular arthritis. (499)
5. The patient with juvenile rheumatoid arthritis often has a hypoplastic mandible as a result of early fusion. This results in the noticeable overbite in some patients with RA. (499)
6. As with other joints, the cricoarytenoid joint may be affected by rheumatoid arthritis. Cricoarytenoid arthritis may result in shortness of breath and snoring. RA patients have been misdiagnosed as having sleep apnea when in fact they have cricoarytenoid arthritis. Patients with cricoarytenoid arthritis may present with stridor on inspiration. This may present in the postanesthesia care unit (PACU) while the patient is recovering from anesthesia. Acute subluxation of the cricoarytenoid joint, as a result of tracheal intubation, can cause stridor as well, and it is not responsive to racemic epinephrine. (500)
7. Yes, movement of the neck in patients with RA can result in cervical spine injury. The patient must be carefully evaluated for both the complexity and the risk of endotracheal intubation because of difficulty in visualizing the airway as a result of the anatomic changes that occur. Normal endotracheal intubation maneuvers with neck movement may result in an increased risk of cervical spine injury due to destruction of the bones and ligaments of the cervical spine. These can place the cervical spinal cord at risk. Many cervical spine abnormalities may occur in patients with RA. (499)
8. The cervical spine is affected in up to 80% of patients with RA. (500)
9. Three abnormal movements of the cervical spine that may be manifest in patients with rheumatoid arthritis include atlantoaxial subluxation, subaxial subluxation, and superior migration of the odontoid. (500, Figure 32-2).

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

10. Atlantoaxial subluxation is the abnormal movement of the C1 cervical vertebra (the atlas) on C2 (the axis). (500)

11. Normally, the transverse axial ligament holds the odontoid process, (also referred to as the dens), which is the superior projection of the vertebra of C2, in place directly behind the anterior arch of C1. With destruction of the transverse axial ligament by RA, movement of the odontoid process is no longer restricted. As the neck is flexed and extended, the C1 vertebra can sublux on the C2 vertebra. This can result in impingement of the spinal cord, placing it at risk for damage. (500-501, Figure 32-3)

12. Subluxation of C1 on C2, referred to as atlantoaxial subluxation, can be quantified by a measuring the distance between the back of the anterior arch of C1 and the front of the dens or odontoid. This distance is referred to as the atlas-dens interval. (501)

13. Flexion and extension radiographs of the cervical spine are obtained to determine the distance between the atlas and dens, or the atlas-dens interval, and thus the degree of subluxation. (501, Figure 32-4)

14. If the atlas-dens interval is 4 mm or more atlantoaxial instability is present, the amount of subluxation is considered significant, and the patient is considered to be at risk for spinal cord injury. (501)

15. In a situation in which the transverse axial ligament is disrupted, extension of the neck minimizes the atlas-dens interval and increases the safe area for the spinal cord. Conversely, flexion of the neck increases the atlas-dens interval and decreases the safe area for the spinal cord, making flexion a more frequent risk position. Still, rheumatoid arthritis affects more than just the transverse axial ligament; therefore, all neck movements in patients with rheumatoid arthritis have to be evaluated carefully as extension of the neck can also lead to problems. (501, Figure 32-5)

16. Patients with rheumatoid arthritis can be asymptomatic with neck flexion and extension preoperatively while awake, and still have an atlas-dens interval of greater than 4 mm and be at risk for cervical spine injury. These patients are able to compensate for their cervical spine instability through local muscle. Once anesthetized and the muscles are relaxed, atlantoaxial subluxation may occur. Therefore the anesthesiologist should not be falsely reassured by asymptomatic flexion and extension in the awake patient. (502)

17. Subaxial subluxation is the subluxation of 15% or more of one cervical vertebra on another at any level below C2. Subaxial subluxation most commonly occurs at the C5-C6 level. Patients with subaxial subluxation are at risk for spinal cord impingement with neck movement. Minimal neck movement is recommended in these patients. (502)

18. Superior migration of the odontoid is a condition where an intact odontoid process projects up through the foramen magnum and into the skull. This occurs because of inflammation and bone destruction that results in cervical spine collapse with sparing of the odontoid process. This can occur because not all areas of the cervical spine are equally affected in any given patient. If the odontoid is spared, the intact odontoid can impinge on the brainstem and patients may suffer neurologic symptoms including quadriparesis or paralysis. (502, Figure 32-6)

19. Surgical treatment for superior migration of the odontoid involves removal of the odontoid to decompress the spinal cord and brainstem. A complicated surgical procedure, referred to as a transoral odontoidectomy, may be performed to accomplish this and involves an incision in the posterior pharyngeal wall, followed by removal of the arch of C1 and then removal of the odontoid and pannus, to relieve neurologic symptoms. With completion of the transoral portion of the procedure, the cervical spine is very unstable, necessitating a posterior spinal fusion. (503)

20. Although the cervical spine is affected by rheumatoid arthritis and may collapse from bone destruction, the trachea is usually spared. This results in the trachea twisting in a characteristic manner as the cervical spine collapses, only serving to increase the difficulty of intubating the trachea of these patients. Tracheal intubation aids such as a fiber optic bronchoscope, Glidescope, Airtraq, or intubating LMA should be available for assistance in endotracheal intubation of these patients should it be required. (503)

21. Ankylosing spondylitis is a rheumatologic disorder in which repetitive minute bone fractures followed by healing results in the characteristic bamboo spine, disease of the sacroiliac joint, fusion of the posterior elements of the spinal column, and fixed neck flexion that is characteristic of this patient population.

22. The hallmark of patients with ankylosing spondylitis is a fused neck in flexion. (503)

23. There is an association between ankylosing spondylitis and HLA-B27, although not all HLA-B27 positive patients are affected with ankylosing spondylitis. (503)

24. Patients with ankylosing spondylitis typically have a rigid cervical spine and neck fused in flexion, which makes endotracheal intubation difficult. Airway manipulation should be performed only after careful assessment, and an intubation assist device can help secure the airway. Patients with ankylosing spondylitis may also develop thoracic and costochondral involvement, which may result in a rapid shallow breathing pattern. (503)

SPINE SURGERY

25. There are several considerations for the anesthetic management of patients undergoing spine surgery, and much depends on the level of the spine in which the surgery will take place, as well as the surgical approach. Preoperative assessment of the patient for underlying neurologic deficits and chronic pain issues are important. For patients in whom the approach may be thoracic, pulmonary function tests may be indicated. In general, spine surgery can be long and complex with significant blood loss and hemodynamic alterations. Intravascular access and intraoperative monitoring should be adjusted accordingly, and blood products may need to be ordered. In the event that there will be intraoperative monitoring of the spinal cord with evoked potentials, the anesthesia administered for the surgery may need to be modified so as not to interfere with the acquisition of waveforms. (503-504)

26. Spine surgery may have anterior, posterior, lateral, and thoracic approaches. In some cases, two approaches may be used during the same surgery. Preoperative discussion with the surgeon is crucial: (1) to determine the surgical approach as it may influence the location of intravascular access and monitoring placement, (2) to ensure proper positioning and padding accessories, and (3) because there may be a need to provide lung isolation and one-lung ventilation. A thoracic surgical approach may involve open thoracotomy or thoracoscopic techniques. High thoracic and thoracoscopic procedures frequently require one-lung ventilation to ensure adequate visualization. (503)

27. A double-lumen endotracheal tube or a bronchial blocker can be employed to provide one-lung ventilation for thoracic spine surgery. (503)

28. A bronchial blocker can be used with a single-lumen endotracheal tube to provide one-lung ventilation for thoracic spine surgery. An advantage of the bronchial blocker is the avoidance of the need to change the tube between different stages of the procedure or at the end of the operation. With the bronchial blocker, deflating the cuff and withdrawing the catheter back into its casing and recapping the proximal end returns the endotracheal tube to its single-lumen tube characteristics. If extubation of the trachea at the end of the surgical procedure is not indicated, the endotracheal tube does not have to be changed, thereby avoiding the issue of changing an endotracheal tube in the presence of potentially significant airway

edema. Make certain that the PACU staff is properly educated as to the various ports of the bronchial blocker. (503, Figure 32-7)

29. Some surgeons are using carbon dioxide insufflation as the sole means of moving the lung away from the surgical field even in high thoracic spine surgical procedures. This obviates the need for one-lung ventilation, and allows for the use of a single-lumen endotracheal tube for the entire procedure. (504)

30. Patients undergoing spine surgery appear to be at an increased risk for intraoperative awareness as a result of the requirement that the anesthetic technique administered to them be modified to allow for obtaining adequate intraoperative neurophysiologic monitoring waveforms to assess spinal cord integrity. Therefore, some advocate the use of brain function monitoring in these patients to help avoid intraoperative awareness. (504)

31. Awareness monitoring is not a standard and, as noted in the Practice Advisory for Intraoperative Awareness and Brain Function Monitoring, a decision should be made on a case-by-case basis by the individual practitioner for selected patients (e.g., light anesthesia). There was a consensus in the advisory that brain function monitoring is not routinely indicated for patients undergoing general anesthesia as the "general applicability of these monitors in the prevention of intraoperative awareness had not been established." In fact, Avidan and associates demonstrated that awareness is not decreased with use of brain function monitoring. The need for brain monitoring is still not clear. (504)

32. Methods to decrease blood loss in spine surgery patients include predonation, hemodilution, wound infusion with a dilute epinephrine solution, hypotensive anesthesia techniques, red blood cell salvage, positioning to diminish venous pressure, careful surgical hemostasis, and the administration of antifibrinolytics. (504)

33. Medications to decrease blood loss during surgery include the antifibrinolytics aprotinin, tranexamic acid, and ϵ-aminocaproic acid. Aprotinin, a serine protease inhibitor, effectively decreased blood loss in cardiac patients and has been demonstrated to be efficacious in patients undergoing spine surgery as well. The negative side effects of aprotinin in cardiac patients include an increased risk of myocardial infarction (MI) or heart failure by approximately 55%, nearly double the risk of stroke, increased risk of long-term mortality, and a higher death rate in patients receiving aprotinin as demonstrated in a study over a 5-year period comparing aprotinin and lysine analogs in high-risk cardiac surgery. The study was terminated early and resulted in relabeling and ultimately withdrawing aprotinin from the market so that it is no longer available. The synthetic lysine analogs, tranexamic acid and ϵ-aminocaproic acid, have also been employed in spine surgery as well as in patients undergoing orthopedic surgery. Tranexamic acid can be administered by an initial bolus injection of 10 mg/kg over 30 minutes followed by a continuous infusion of 1 mg/kg/hr. (504)

34. Spine surgery is often performed with the patient in the prone position. Careful positioning is crucial to avoid patient injury. Movement to the prone position should be performed in a carefully coordinated manner with the surgical team. The neck should not be hyperextended or hyperflexed but placed in the neutral position. The endotracheal tube is positioned so it is not kinked, contact areas are padded, and the face and eyes are protected. Pressure and stretch on nerves is avoided by proper padding and avoiding any extension over 90 degrees. The abdomen needs to be hanging free to avoid increased venous pressure and thereby increased venous bleeding. The prone position alters pulmonary dynamics, so pulmonary function must be reassessed in this position. (504)

35. Monitoring spinal cord integrity is an important component of major surgical procedures involving distraction and rotation of the spine such as occurs with major

anteroposterior spinal fusions and scoliosis surgery. Spinal cord monitoring is employed to detect, and hopefully reverse in a timely manner, any adverse effects on the spinal cord noted during the operative period. (505)

36. There are a variety of methods to monitor the spinal cord during spine surgery. These include SSEPs; motor evoked potentials, including transcranial motor evoked potentials, electromyograms (EMGs), or a wake-up test. (505)

37. SSEPs are sensory evoked potential waves generated in the extremities by repetitive stimulation that propagate up through the dorsum or sensory portion of the spinal cord and into the brain, where these signals or waveforms are detected via electrodes placed over the scalp. Specific areas on the scalp coincide with the brain's sensory areas for the upper and lower extremities and proper signal acquisition obtained over these sites indicates an intact sensory or dorsal portion of the spinal cord. The SSEP waveform generated from multiple repetitive stimulations is analyzed for its latency and amplitude (505, Figure 32-8)

38. An increase in latency of greater than 10% or a decrease in amplitude of 60% or more, as well as the inability to obtain a proper waveform or signal, may be indicative of spinal cord dysfunction or disruption. (505)

39. If SSEPs alone are being monitored, an inhaled anesthetic, equivalent to a small percentage of 1 MAC, can be administered. Volatile anesthetics may interfere with signal acquisition in patients monitored with transcranial motor evoked potentials and may have to be discontinued, if used at all, if adequate signals cannot be obtained. Intravenous anesthetics will need to be administered in these surgical cases. While neuromuscular blockade may be used to facilitate tracheal intubation, paralysis should not be maintained if transcranial motor evoked potentials are being continuously monitored. If the patient is having pedicle screws placed, then the neuromuscular blockade needs to be terminated before the EMGs are obtained so that testing can be properly performed. A small dose of ketamine can be given in the perioperative period as an additional pain relief modality to provide analgesia for major surgery including spine surgery. (504)

40. Surgically related conditions that can result in interference of waveform acquisition during spinal cord monitoring include direct injury or trauma to the cord or impairment of the blood supply. Distraction, rotation, excessive bleeding, and severing or clamping of arterial blood supply can result in ischemia to the cord and neurologic injury. (505)

41. Some areas of the spinal cord are more vulnerable and therefore more prone to ischemia because their blood supply is dependent on watershed blood flow. (505)

42. Many factors can alter intraoperative spinal cord monitoring waveforms unrelated to surgery. These should be properly detected and eliminated. These may include hypotension, hypothermia, high concentrations of volatile anesthetics, benzodiazepines, hypercarbia or hypocarbia, and anemia. Only a small concentration of volatile anesthetic should be employed when SSEP monitoring is used. Midazolam and other benzodiazepines are avoided because they may interfere with obtaining a waveform. Some anesthesiologists even avoid nitrous oxide and use a combination of air in oxygen. (505)

43. Direct injury to the spinal cord results in immediate changes in SSEP waveforms. In contrast, if surgery impairs blood supply and thus renders the spinal cord ischemic, the change in SSEP waveforms may take up to half an hour to manifest. (505)

44. Once a significant change in intraoperative spinal cord monitoring waveforms is noted, specific maneuvers should be used to restore spinal cord blood flow, such as releasing the rotation and distraction of the spine if applicable. In addition, as a result of spinal cord manipulation there may be insufficient blood supply to the spine. Therefore the mean arterial blood pressure should be increased in an effort

to restore adequate blood flow to the spine. All variables such as hemoglobin, temperature, arterial carbon dioxide concentration, and arterial blood pressure should be considered. Once these are all evaluated, a wake-up test may be necessary if the waveforms do not improve. (506)

45. Transcranial motor evoked potentials allow for monitoring the patient's spinal cord motor pathways throughout the entire procedure. Stimulation over the motor cortex of the brain generates a waveform, which is propagated down the motor pathways and detected distally in the arm or leg. This stimulation results in a characteristic waveform. (506, Figure 32-9)

46. To generate transcranial motor evoked potentials, the patient cannot have residual neuromuscular blockade. (506)

47. The electrical current causing the stimulus over the motor cortex during transcranial motor evoked potentials monitoring also stimulates muscles directly in the area of the electrodes placed in the scalp—the masseter muscle and muscles of mastication. This muscle contraction may result in a strong bite, which can potentially injure the tongue, lip, and endotracheal tube. Instances of significant tongue lacerations and damage to endotracheal tubes can occur and this can develop into emergency situations, especially with the patient in the prone position. (506)

48. Special precautions should be taken for patients undergoing transcranial motor evoked potentials monitoring during spine surgery. The tongue should not protrude through the teeth. Placing a bite block made of tongue depressors and gauze in the back of the mouth along the teeth line bilaterally will help prevent injury. In the prone position, any motion may allow for the tongue to slip and fall between the teeth, rendering it vulnerable to laceration. Each stimulus is associated with a masseter muscle contraction, so the patient is at risk as long as waveforms are being generated. (506)

49. Intraoperative electromyelograms are used to determine if a pedicle screw has been placed too close to a nerve root. An electric current is sent through the screw and the electromyelogram is measured distally. If a low milliamp current can stimulate the nerve root, then the screw is too close to the nerve root. In general, a current greater than 7 mA is considered safe enough to know that the pedicle screw is not too close to the nerve root. (506)

50. For accurate electromyelogram testing, residual neuromuscular blockade must be terminated or reversed. (506)

51. The wake-up test was traditionally used to assess spinal cord integrity in many scoliosis cases. Development of sophisticated spinal cord monitoring is now standard in many hospitals and the wake-up test is generally reserved for those situations in which monitoring is unobtainable or a significant intraoperative change in spinal cord monitoring waveforms is noted. (506)

52. The intraoperative wake-up test is performed as follows: turn off all inhaled anesthetics, reverse any neuromuscular blocking drug present, and stop infusions such as dexmedetomidine, propofol, narcotics, or ketamine. If spontaneous respirations do not begin, inject naloxone, 0.04 mg at a time, to reverse any residual narcotic effect. The patient's head should be held to reduce the risk of self-extubation. Prior to assessing lower extremity function, there should be confirmation of upper extremity function. Patient compliance denotes adequate recovery from general anesthesia. Then, while someone is observing the feet, ask the patient to wiggle his or her toes. A rapid-acting anesthetic such as propofol should be ready to be administered as soon as the assessment is complete, so the patient can rapidly be reanesthetized. If the wake-up test is not successful in demonstrating adequate motor movement, further surgical intervention may be warranted and the patient may require transport to the radiology suite for additional imaging studies. (507)

53. There are some potential complications of an intraoperative wake-up test. These include increased bleeding, venous air embolism, and even inadvertent extubation of the trachea in the prone position with the wound exposed. (506)

54. At the conclusion of a spine procedure, the patient is placed in the supine position. All lines and tubes are secured so that intravenous line, arterial line, and airway access are not lost at this crucial time. Carefully reassess the patient for hemodynamic status, intravascular fluid volume status, hematocrit, blood loss, degree of fluid and blood replacement, temperature, and the potential for airway edema. Premature extubation must be avoided. Also, facial edema, respiratory effort, the amount of pain medication, and the presence of splinting and pain should be evaluated before extubating the trachea. After tracheal extubation, the patient may be transported to the PACU. Supplemental oxygen should be administered in the PACU. Electrolytes, hemoglobin, and clotting studies should be ordered as indicated. (507)

55. Postoperative pain management may prove complicated after spine surgery because some patients may have been taking pain medications preoperatively, particularly opioids. Patient-controlled analgesia (PCA) may be effective, with the dose tailored to the patient's needs. Some centers use ketamine as an analgesic adjunct. The use of nonsteroidal antiinflammatory drugs (NSAIDs), particularly ketorolac, needs careful consideration because it is a medication that interferes with bone formation and therefore should be avoided in patients who just underwent spinal fusion. NSAIDs may be appropriate when bone healing is not a factor. Other oral medications that are helpful may include acetaminophen, anticonvulsants (e.g., gabapentin and pregabalin), antispasmodics that work at the spinal cord level (e.g., baclofen, tizanidine), antiinflammatory medications, and opioids. (507)

56. Although its etiology is unclear, patients undergoing prolonged spine surgery (>6 hours) in the prone position who have large blood loss (>1 L) are particularly at risk. Yet, patients with small blood loss and short procedures also have had visual loss. Perioperative factors such as anemia, hypotension, prolonged surgery, blood loss, increased venous pressure from positioning in the prone position, edema, a compartment syndrome within the orbit, and resistance to blood flow, such as from direct pressure on the eye, as well as systemic diseases such as diabetes, hypertension, and vascular disease, are all possible etiologic factors. One recent study entitled Risk Factors Associated with Ischemic Optic Neuropathy (*Anesthesiology* 2012;116:15-24) has reported that that male sex, obesity, use of a Wilson frame, longer cases, greater estimated blood loss, and a decreased percent of colloid are associated with an increased incidence of postoperative visual loss. (507)

57. There are several aspects of the prone position that may contribute to postoperative visual loss. These include increased venous pressure from positioning in the prone position, edema, a compartment syndrome within the orbit, and resistance to blood flow such as direct pressure on the eye. (507)

58. Ischemic optic neuropathy is a major cause of postoperative visual loss. Variations in the blood supply to the optic nerve may play a role in the development of ischemic optic neuropathy including reliance on a watershed blood supply to critical areas of the optic nerve.

59. Ocular perfusion pressure (OPP), or the blood pressure supplying blood flow to the optic nerve, is a function of the mean arterial pressure (MAP) and intraocular pressure (IOP) such that $OPP = MAP - IOP$. Increases in IOP or decreases in MAP can have a negative impact on the ocular perfusion pressure. The prone position is associated with increases in intraocular pressure, which can decrease the ocular perfusion pressure and lead to ischemia. The prone position allows edema to develop in the orbit and this increase in venous pressure may impact arterial blood flow. (507)

60. A visual loss registry has been established by the ASA to facilitate establishing the etiology of postoperative visual loss. Also, an ASA practice advisory points to ischemic optic neuropathy as the most likely cause of postoperative visual loss.

Of the 93 cases reported in the registry publication, 83 resulted from ischemic optic neuropathy, with the remainder attributed to central retinal artery occlusion. Central retinal artery occlusion may be embolic in nature or the result of direct pressure on the eyeball and tends to be unilateral. Most patients in the registry were healthy and positioned prone for spine surgery. Blood loss of more than 1 L and procedures of 6 hours or longer were present in 96% of cases. (507, Table 32-1)

61. According to the ASA practice advisory regarding patients at high risk for postoperative visual loss during spine surgery, the use of deliberate hypotension has not been shown to be associated with postoperative visual loss. (507, Table 32-1)

62. According to the ASA practice advisory regarding patients at high risk for postoperative visual loss during spine surgery, colloid should be administered in addition to crystalloid to maintain intravascular volume. (507, Table 32-1)

63. According to the ASA practice advisory regarding patients at high risk for postoperative visual loss during spine surgery, there is no defined transfusion trigger at which the risk of postoperative visual loss is eliminated. (507, Table 32-1)

64. According to the ASA practice advisory regarding patients at high risk for postoperative visual loss during spine surgery, when in the prone position the patient's head should be positioned level with or higher than the heart when possible. Also, when possible, maintain the head in a neutral forward position without significant neck flexion, extension, lateral flexion, or rotation. (507, Table 32-1)

SURGERY IN THE SITTING POSITION

65. Postoperative complications that have been noted in the patient undergoing surgery in the sitting position are rare but significant and devastating. These neurologic complications include stroke, ischemic brain injury, and vegetative states. (507)

66. When devastating neurologic postoperative complications occur after surgery in the sitting position, the implicated cause is a decrease in cerebral perfusion pressure resulting in insufficient blood supply to the brain. (508)

67. No, the systemic arterial blood pressure is not the same at the level of the heart as it is at the level of the circle of Willis when patients are anesthetized and placed in the sitting position. This is due to the arterial blood pressure gradient that develops between the heart and brain in this position. (508)

68. When patients are anesthetized and placed in the sitting position, one can more accurately determine the arterial blood pressure at the circle of Willis through the following calculation: for each centimeter of head elevation above the level of the heart there is a decrease in arterial blood pressure of 0.77 mm Hg. Therefore, arterial blood pressure measured at the level of the heart is not the blood and perfusion pressure at the brain. Indeed, a 20-cm difference in height between the heart and the circle of Willis calculates to approximately a 15- to 17-mm Hg gradient. (508)

69. A convenient point for measuring height difference between the heart and brain is the external auditory meatus, which is at the same level as the circle of Willis. Even so, there is still a significant amount of brain tissue above this level. (508)

70. When patients are anesthetized and placed in the sitting position, the mean arterial blood pressure should be maintained to avoid decreases in the cerebral perfusion pressure and to potentially avoid devastating neurologic injury. Thus, hypotension in these patients should be avoided. This is particularly true in the elderly or in patients with chronic hypertension in whom the cerebral autoregulatory curve is altered. (508)

FRACTURED HIP

71. Factors predisposing a person to a hip fracture include medical comorbidities, osteoporosis, lower limb dysfunction, visual impairment, increasing age, Parkinson's disease, previous fracture, stroke, female gender, dementia, institutionalized patients, excess alcohol or caffeine consumption, cold climate, and use of psychotropic medications. (508)

72. Mortality rates can range up to 14% to 36% in the first year after fracture. (508)

73. Medical status affects morbidity and mortality. One example is the number of comorbidities from which the patient suffers, as in one study the presence of four to six comorbidities is associated with increased mortality rate when compared to patients with less comorbidity. Roche and associates, in studying 2448 patients, reported that the presence of three or more comorbidities was a strong preoperative risk factor with the postoperative development of chest infection or heart failure being associated with a high mortality rate. White and associates reported that ASA I and II patients had mortality rates equal to age-matched control subjects, but ASA III and IV patients had higher mortality rates (49% vs. 8%) after a hip fracture. Moran and colleagues, in a study of 2660 hip fracture patients with an overall mortality rate of 9% at 30 days, 19% at 90 days, and 30% at 12 months, noted that healthy patients did well as long as surgery was performed within 4 days. Patients with comorbidities had a nearly 2.5 times increased mortality rate at 30 days as compared with healthy patients. (508)

74. Generally, when significant comorbidities that need correction exist, patients benefit from a delay in surgery while their medical status improves. The mortality rate in high-risk patients in one study decreased from 29% to 2.9% when time was taken to correct physiologic abnormalities. This was also demonstrated by Kenzora and co-workers, who noted a higher mortality rate (34% vs. 6.9%) in patients who went immediately into surgery as compared to those who were delayed 2 to 5 days to improve their medical status. Also, patients admitted to the hospital immediately after fracture did better than those admitted more than a day later. (508)

75. The management of a patient with a recent myocardial infarction (MI) and hip fracture illustrates how evaluations and management have changed. Previously, surgery was delayed up to 6 months following a myocardial infarction, but now the tendency is to risk-stratify patients based on the severity of their myocardial infarction to determine wait time until surgery. The recent MI needs to be evaluated on a risk-benefit ratio comparing the risk of surgery after a recent MI with the negative side effects of keeping a patient bed bound with its attendant risks of pneumonia, pulmonary embolism, pain, loss of ability to walk, and decubitus ulcers. Factors to consider are the extent of the MI, additional myocardium that may be at risk, if the patient suffers from postinfarct angina, and the presence of congestive heart failure (CHF). Although ongoing angina or the presence of CHF may preclude early surgery, a small subendocardial MI with a minimal increase in cardiac enzymes and normal echocardiogram and stress test would allow consideration for an earlier intervention. A fractured hip usually prevents the patient from undergoing a normal exercise stress test. Therefore, if indicated, a pharmacologic stress test may be needed. (508)

76. Considerations for the anesthetic management of patients undergoing hip surgery include the patient's intravascular fluid volume status and the potential for significant perioperative blood loss, patient positioning and proper padding on the fracture table, maintaining normothermia, and whatever additional comorbidities may be present as these patients are typically elderly. (509)

77. For patients undergoing hip surgery, there is no clear advantage of one anesthetic technique over another. Therefore, choice of spinal or general anesthesia should be made on a case-by-case basis taking the patient's specific medical issues into consideration. (508-509)

78. Although no one anesthetic technique has proven to be superior, the pros and cons of both spinal and general anesthesia must be considered when choosing the anesthetic technique for a given patient. Advantages of regional anesthesia, such as provided by a spinal anesthetic, are that (1) it avoids endotracheal intubation and airway manipulation and the medications that need to be administered to

accomplish this, (2) it decreases the total amount of systemic medication the patient receives throughout the procedure, and (3) it may play a role in decreasing the risk of thromboembolism. The vasodilatory effect of the spinal anesthetic may help the patient with CHF. However, intravascular fluid still should be given cautiously because CHF may worsen as the intravascular vasodilatory effect of the spinal anesthesia recedes. General anesthesia, in contrast, is easy to administer, particularly in patients in whom movement and positioning for a regional anesthetic may be painful. In addition, in a patient who may be hypovolemic, general anesthesia may be preferred to avoid a precipitous decrease in arterial blood pressure that may occur as a result of the decrease in systemic vascular resistance that accompanies regional anesthesia. (509)

79. The dose and frequency of pain medication given to elderly patients in the perioperative period may need to be decreased, and should be given cautiously because of an increased circulation time, and the cumulative effect of administered opioids may become evident when not expected. (509)

TOTAL JOINT REPLACEMENT

80. The use of methylmethacrylate cement is associated with cardiopulmonary side effects such as hypoxia, bronchoconstriction, hypotension, cardiovascular collapse, and even death. (510)

81. The systemic reaction to methylmethacrylate cement may result from the liquid methylmethacrylate cement monomer itself, which is used in producing the cement for cementing the prosthesis, or may be due to air, fat, or bone marrow elements being forced into the circulation. The higher the liquid content of the liquid monomer in the mix with the polymer methylmethacrylate cement at the time of insertion, which occurs from not adequately mixing or not waiting long enough for mixing to occur, the more frequently side effects are noted. (510)

82. Patients who are at high risk for a reaction to methylmethacrylate cement include those who are hypovolemic at the time of cementing, hypertensive patients, and patients with significant preexisting cardiac disease. (510)

83. In the lower extremity surgery, the tourniquet is inflated to approximately 100 mm Hg above the systolic blood pressure, as this will prevent arterial blood from entering the exsanguinated limb. (510)

84. As tourniquets render the limb ischemic, there is a limit to inflation time before the ischemia can result in permanent limb damage. The safe upper limit of ischemia time is considered to be 2 hours. The surgeon should be informed of tourniquet inflation time at 1 hour and then as the tourniquet approaches the 2-hour limit so it can be deflated in a timely manner. (511)

85. If the total tourniquet time will exceed the 2-hour limit, the tourniquet should be deflated at 2 hours for a period of at least 15 to 20 minutes before it is reinflated. This will allow for the "wash-out" of acidic metabolites from the ischemic limb as the limb is reperfused with oxygenated blood. Recirculation of the ischemic limb with release of the tourniquet is noted by a decrease in blood pressure and an increase in end-tidal carbon dioxide as the acid products recirculate. The hypotension usually responds to intravascular fluid administration and vasopressors if necessary. (510)

86. Complications associated with tourniquet use include nerve damage, vessel damage especially in patients with atherosclerosis, pulmonary embolism, and skin damage. One source of skin damage is the antiseptic prep solution, if it is allowed to seep under the tourniquet and tourniquet padding at the time of skin prep, causing a chemical burn. Additional concerns at the time of tourniquet deflation are pulmonary embolism and a decrease in core temperature as the isolated extremity is reperfused. (510)

87. During total knee replacement surgery a tourniquet is used, and in the operating room blood loss is usually not significant. However, if much blood loss occurs into drains in the PACU, hypotension may result. Some surgeons do not deflate the tourniquet until the wound is closed and the dressing is on the patient. In this situation blood loss is usually less but there is a risk of bleeding. (510)

88. Consensus statements from the American Society of Regional Anesthesia and Pain Medicine (ASRA) addressed the issue. Recommendations included waiting at least 10 to 12 hours before neuraxial needle placement in a patient who received a preoperative dose of enoxaparin. (511)

89. Consensus statements from the American Society of Regional Anesthesia and Pain Medicine recommend waiting 2 hours prior to dosing enoxaparin after an epidural catheter is removed. Patients on warfarin should have their catheter removed only when the international normalized ratio (INR) is below 1.5, and care should be taken to avoid other anticoagulants and antiplatelet medications when low-molecular-weight heparin is being used and an epidural catheter is in place. (511)

90. Current recommendations in the ASRA Practice Advisory, Anticoagulation, 3rd edition, 2010, suggest that clopidogrel be discontinued for 7 days prior to performing a neuraxial block. However, the article quotes labeling as recommending this while the PDR section for clopidogrel actually recommends that for elective surgery it only be discontinued for 5 days. The executive summary for the Anesthetic Management of the Patient Receiving Antiplatelet Medication, as part of the third edition, states, "On the basis of labeling and surgical reviews, the suggested time interval between discontinuation of thienopyridine therapy and neuraxial blockade is 14 days for ticlopidine and 7 days for clopidogrel. If a neuraxial block is indicated between 5 and 7 days of discontinuation of clopidogrel, normalization of platelet function should be documented." In patients who need to be maintained on clopidogrel or who have not discontinued it for an adequate time period, other anesthetic techniques should be considered. The guidelines for some of the antiplatelet medications will probably undergo revision as physicians gain experience with the use of medications such as clopidogrel in the perioperative period. (511)

Chapter

30 OBSTETRICS

Mark Rollins, Jennifer Lucero

PHYSIOLOGIC CHANGES IN PREGNANT WOMEN

1. How do the maternal intravascular fluid, plasma, and erythrocyte volumes change during pregnancy?
2. How does the coagulation status change during pregnancy?
3. What is the average maternal blood loss during the vaginal delivery of a newborn? What is the average maternal blood loss during cesarean delivery?
4. How does the maternal cardiac output change from nonpregnant levels?
5. In an uncomplicated pregnancy, what changes occur in blood pressure, systemic vascular resistance, and central venous pressure?
6. What is the supine hypotension syndrome? What symptoms accompany the syndrome?
7. What compensatory mechanisms do most women have that prevents them from experiencing supine hypotension syndrome and how can maternal hypotension be minimized?
8. What are some aspects of the upper airway that undergo physiologic change in pregnancy? What are the clinical implications of these changes?
9. How is minute ventilation changed during pregnancy from nonpregnant levels? How does the resting maternal $Paco_2$ change as a result of the change in minute ventilation?
10. How do the binding characteristics of hemoglobin change during pregnancy?
11. What are the changes in maternal lung volumes that occur with pregnancy? What are the anesthetic implications of these changes?
12. How does maternal Pao_2 change during pregnancy?
13. What are the gastrointestinal changes in pregnancy that render the woman vulnerable to regurgitation of gastric contents? What clinical implication does this have?
14. How do the epidural and subarachnoid spaces change in pregnancy? How is the sensitivity to local anesthetics different in the pregnant versus nonpregnant patient? How are the dosing requirements for neuraxial anesthesia affected by these changes?
15. How do renal blood flow and glomerular filtration rate change in pregnancy? At what gestational month of pregnancy is this change at a maximum? How does this affect the normal upper limits of creatinine and blood urea nitrogen in pregnant patients?
16. Does hepatic blood flow change during pregnancy? How are plasma protein concentrations and plasma cholinesterase activity altered by pregnancy?

PHYSIOLOGY OF UTEROPLACENTAL CIRCULATION

17. How are maternal and fetal blood delivered to the placenta?
18. What is uterine blood flow (UBF) at term?
19. What are the determinants of UBF?
20. What factors affect the transfer of oxygen between the mother and fetus?
21. What factors affect placental exchange of drugs and other substances? What is the most reliable way to minimize fetal transfer of a drug?
22. What common drugs used in anesthesia have limited ability to cross the placenta? Which readily cross the placenta?

FETAL UPTAKE AND DISTRIBUTION OF DRUGS

23. How does the pH of fetal blood affect the transfer of drugs? What is ion trapping?
24. What characteristics of the fetal circulation are protective against the distribution of large doses of drugs to vital organs?

STAGES OF LABOR

25. Name the stages of labor and what events define each stage.
26. What is an "active phase arrest"? What is an "arrest of descent"?

ANATOMY OF LABOR PAIN

27. In the first stage of labor, describe the associated sensory levels and where the end organ afferent nerve impulses are initiated.
28. In the second stage of labor, describe the associated sensory levels and where the end organ afferent nerve impulses are initiated.
29. For each stage of labor, describe which analgesic techniques benefit the pregnant woman and why.

METHODS OF LABOR ANALGESIA

Nonpharmacologic Techniques and Systemic Medications

30. Describe the different nonpharmacologic techniques used for labor and the efficacy of each.
31. List the different systemic medications used for labor analgesia and their active metabolites, if any.
32. What is "morphine sleep"?
33. How is remifentanil used as a labor analgesic and what are the indications for its use?
34. Are benzodiazepines used in pregnancy and if so, when?
35. When is ketamine used in labor and delivery and what additional benefits does it provide for pain control?

Neuraxial Analgesia and Neuraxial Techniques

36. List the different types of neuraxial analgesia?
37. When would you use each type of neuraxial analgesia for labor pain?
38. Should laboring women remain "nothing per oral (NPO)" after placement of an epidural or combined spinal and epidural (CSE)?
39. What is a walking epidural and what are the associated risks?
40. What drugs are used or being evaluated as adjuvant neuraxial drugs for labor analgesia?
41. Name the tissue layers and ligaments encountered when placing an epidural and in what order the anesthesiologist encounters each.
42. The American Society of Anesthesiologists (ASA) recommendations regarding aseptic technique for placement of neuraxial block include what specific precautions?

43. What are the interspaces where the neuraxial block for labor analgesia is placed and what are the risks of placing the neuraxial block higher or lower than this range of interspaces?
44. What is a "test dose" and what does it assess?
45. Can a test dose be used with a CSE?
46. What type of needle is used in placement of spinal analgesia and why?
47. What is a "saddle block" and when is it used during labor and delivery?

CONTRAINDICATIONS AND COMPLICATIONS OF NEURAXIAL ANESTHESIA

48. What are the contraindications to neuraxial procedures?
49. Is known infection with human immunodeficiency virus (HIV) a contraindication to epidural placement?
50. List the potential complications of a neuraxial block.
51. What is the occurrence rate of postdural puncture headache (PDPH)? What are the treatment options for PDPH?
52. What is the treatment for systemic local anesthetic toxicity of bupivacaine?
53. What physiologic effects do you expect to see with a high spinal or high epidural?
54. What are the important differences in performing advanced cardiac life support (ACLS) for a pregnant woman compared to a nonpregnant patient?
55. What is the rate of hypotension after neuraxial blockade?
56. What is the first-line pharmacologic treatment of hypotension after a neuraxial block?
57. How does epidural analgesia affect maternal body temperature?

OTHER TECHNIQUES FOR LABOR ANALGESIA

58. Where is local anesthetic injected to achieve a paracervical block? What are the disadvantages of a paracervical block?
59. When is the pudendal block useful? What are the disadvantages of this type of block?
60. Can inhaled nitrous oxide be administered safely for labor and delivery analgesia?

ANESTHESIA FOR CESAREAN DELIVERY

61. What are some benefits of regional anesthesia over general anesthesia for cesarean delivery?
62. What are the benefits of general anesthesia over regional anesthesia for cesarean delivery?
63. What are some advantages and disadvantages of spinal anesthesia for cesarean delivery compared to an epidural block?
64. What dermatome level of spinal anesthesia ensures patient comfort adequate for cesarean delivery? How can this be achieved?
65. What are some advantages and disadvantages of epidural anesthesia for cesarean delivery compared to spinal anesthesia?
66. Which local anesthetics, and corresponding doses, are typically administered to achieve an adequate density and dermatomal level of epidural anesthesia for cesarean delivery?
67. What is the advantage of the administration of morphine into the epidural space for cesarean delivery? What are some of the negative side effects that may accompany this route of morphine administration?
68. What are some indications for general anesthesia for cesarean delivery? What are some benefits of general anesthesia for cesarean delivery?
69. What are the main causes of increased morbidity and mortality associated with general anesthesia during pregnancy?
70. How should difficulty with endotracheal intubation be managed by the anesthesiologist?
71. What is the level of exposure of the fetus to thiopental after the administration of induction doses for general anesthesia? Is there an advantage to using propofol for the induction of general anesthesia?

72. What are some of the advantages and disadvantages of inducing general anesthesia for cesarean delivery with etomidate?
73. What are the effects of using volatile anesthetics for cesarean delivery on the fetus?
74. What neuromuscular agents are typically used for cesarean delivery with general anesthesia? Do they result in neuromuscular blockade of the fetus or relaxation of the uterus?

ABNORMAL PRESENTATIONS AND MULTIPLE BIRTHS

75. What percent of live births are twins and why is the number increasing? What are the complications that develop with multiple gestations?
76. What are the modes of delivery for twin pregnancies? What anesthetic techniques can be used to optimize delivery?
77. Describe external cephalic version and the associated risks.
78. What is a shoulder dystocia? What are the risk factors associated with the development of a shoulder dystocia? What are the risks to the fetus during a shoulder dystocia?

HYPERTENSIVE DISORDERS OF PREGNANCY

79. At what gestational age does gestational hypertension present?
80. What is the percent of preeclampsia in the general population? What are the risk factors for developing preeclampsia?
81. What are the criteria for the diagnosis of preeclampsia?
82. What are the criteria for severe preeclampsia?
83. What is HELLP syndrome?
84. What is the mechanism of preeclampsia?
85. How should patients with preeclampsia be managed for labor? What is the definitive treatment of preeclampsia?
86. How is magnesium sulfate infusion used and why? What are the signs of and treatment of magnesium sulfate toxicity?
87. What are the typical antihypertensive drugs used in preeclampsia?

HEMORRHAGE IN PREGNANT WOMEN

88. What are some causes of hemorrhage in the pregnant patient? When do these typically manifest?
89. What is placenta previa? What are the associated risk factors?
90. If a massive postpartum hemorrhage is not controlled with standard measures (i.e., uterine massage, uterotonics), what invasive options can be considered by the obstetrician?
91. What is abruptio placentae? What are some risk factors for abruptio placentae?
92. What are some risk factors for uterine rupture? What is the incidence of uterine rupture associated with vaginal birth after a previous cesarean delivery?
93. What approximate percent of vaginal deliveries are associated with some amount of retained placenta? What are some options for the anesthetic management of patients with retained placenta?
94. What are some risk factors for uterine atony?
95. What medications are used to manage uterine atony? What are their side effects?
96. Define placenta accreta, increta, and percreta.
97. In a patient with known placenta previa, how does the risk of placenta accreta change with the number of prior cesarean deliveries?

AMNIOTIC FLUID EMBOLISM

98. What is the clinical presentation of an amniotic fluid embolism? What are some conditions that may mimic amniotic fluid embolism and must therefore be ruled out?
99. How is the definitive diagnosis of an amniotic fluid embolism made? What is the treatment of an amniotic fluid embolism?

ANESTHESIA FOR NONOBSTETRIC SURGERY DURING PREGNANCY

100. What are common nonobstetric surgeries that occur during pregnancy?
101. When should nonobstetric surgeries be performed during pregnancy?
102. What anesthetics are teratogenic?
103. How can intrauterine fetal hypoxia and acidosis be prevented?
104. When should fetal heart rate monitoring be done during nonobstetric surgery?
105. What is the usual etiology of premature labor that presents in the pregnant patient after having undergone nonobstetric surgery? How can premature labor be treated?
106. Can laparoscopic surgery be performed safely during the third trimester?

DIAGNOSIS AND MANAGEMENT OF FETAL DISTRESS

107. Describe the frequency of normal uterine contractions and tachysystole. What is the treatment for tachysystole?
108. What is the normal baseline fetal heart rate (FHR)?
109. Define FHR variability in terms of absent, minimal, moderate, and marked.
110. What is the definition of a FHR acceleration?
111. What are late decelerations indicative of in the fetus?
112. What is a variable deceleration indicative of in the fetus?
113. What was fetal heart rate monitoring designed to assess?

EVALUATION OF THE NEONATE AND NEONATAL RESUSCITATION

114. Define the values of each Apgar score category.
115. What are normal blood gas values for the umbilical artery and vein?
116. During neonatal evaluation and resuscitation, when is it appropriate to give positive pressure ventilation?
117. What is the dose of epinephrine given for neonatal resuscitation?
118. Should naloxone be given in the delivery room for neonatal resuscitation?
119. In neonates delivered with meconium-stained amniotic fluid, when should suctioning below the cords be instituted?
120. What have been significant advances in the prevention of meconium aspiration syndrome?

ANSWERS*

PHYSIOLOGIC CHANGES IN PREGNANT WOMEN

1. During pregnancy the maternal intravascular fluid volume increases from its prepregnancy volume. The increase in intravascular volume begins in the first trimester of pregnancy. By term, the intravascular fluid volume has increased by about 35% above the prepregnancy state. The plasma volume increases by approximately 45% at term. The erythrocyte volume in the pregnant patient increases by approximately 20%. Because the plasma volume increases by over twice as much as the erythrocyte volume, the woman has a relative physiologic anemia. That is, the hematocrit of the pregnant patient is relatively less than her prepregnancy state. This is termed the *physiologic anemia of pregnancy*. **(515, Table 33-1)**

2. The pregnant woman at term is in a hypercoagulable state secondary to increases in factors I, VII, VIII, IX, X, and XII, and decreases in factors XI, XIII, and Antithrombin III. This results in an approximately 20% decrease in prothrombin time (PT) and partial thromboplastin time (PTT). Platelet count may remain normal or decrease 10% by term. (515)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

3. The average maternal blood loss during vaginal delivery of a newborn is 300 to 500 mL. The average maternal blood loss during the delivery of a newborn by cesarean delivery is 800 to 1000 mL, but blood loss during a cesarean delivery is greatly variable. The increase in intravascular fluid volume and the hypercoagulable state of the mother help to counter the blood losses incurred during this time. The contracted uterus after either type of delivery creates an autotransfusion of approximately 500 mL of blood, which decreases the overall effect of the blood loss on the mother. (515)

4. Maternal cardiac output increases 10% by the tenth week of gestation, and at term pregnancy increases by approximately 40% to 50% of its prepregnancy value. Cardiac output is equal to the product of stroke volume and heart rate. The increase in cardiac output is primarily due to an increase in stroke volume. The increase in heart rate during pregnancy is less and is therefore only a minimal contributor to the increase in cardiac output. Labor is associated with further increases in cardiac output with output above prelabor values by 10% to 25% during the first stage and 40% in the second stage. The greatest increase in cardiac output occurs just after delivery, when it increases by as much as 80% above prelabor values. This is the maximal change in cardiac output in the woman. Cardiac output decreases substantially toward prepregnant values by 2 weeks postpartum. (515, Table 33-1)

5. The systolic blood pressure of the woman having an uncomplicated pregnancy does not exceed her prepregnancy blood pressure and typically decreases secondary to a 20% reduction in systemic vascular resistance at term. Systolic, mean, and diastolic blood pressure may all decrease 5% to 15% by 20 weeks gestational age and gradually increase toward prepregnant values as the pregnancy progresses towards term. Central venous pressure does not change during pregnancy despite the increased plasma volume because venous capacitance increases. (515-516, Table 33-1)

6. Supine hypotension syndrome, as the name implies, is the decrease in blood pressure seen when the pregnant patient lies in the supine position after midgestation. The supine hypotension syndrome occurs because of a decrease in cardiac output by approximately 10% to 20%. When the pregnant woman is in the supine position, the gravid uterus compresses the inferior vena cava, resulting in decreased venous return and decreased preload for the heart. Symptoms that accompany the hypotension include diaphoresis, nausea, vomiting, and possible changes in cerebration. Symptoms must be present for the patient to be considered susceptible to supine hypotension syndrome. (516, Figure 33-1)

7. Most pregnant women, when lying in the supine position, are able to compensate for the possible decrease in blood pressure that results from the compression of the inferior vena cava by the gravid uterus. One compensatory mechanism includes maintaining venous return by diverting blood flow from the inferior vena cava to the paravertebral venous plexus. The blood then goes to the azygos vein and returns to the heart via the superior vena cava. Dilation of the epidural veins may make unintentional intravascular placement of an epidural catheter more likely. A "test dose" is given before dosing an epidural catheter to decrease the likelihood of an unrecognized intravascular placement before initiating neuraxial blockade.

   Another compensatory mechanism is an increase in peripheral sympathetic nervous system activity. This increases peripheral vascular tone and helps to maintain venous return to the heart. Regional anesthesia, however, can interfere with these compensatory mechanisms by causing sympathetic nervous system blockade, rendering the pregnant woman at term more susceptible to decreases in blood pressure. The gravid uterus can also compress the lower abdominal aorta and lead to arterial hypotension in the lower extremities, but maternal symptoms

or decreases in systemic blood pressure as measured in the arms are often not reflective of this decrease. The major clinical significance of the aortocaval compression is the decrease in placental and uterine blood flow that results. The decrease in blood flow through the uteroplacental unit leads to a decrease in blood flow to the fetus. The aortocaval compression can be minimized by having the woman lie in the lateral position. Uterine displacement can also be used, typically with displacement being to the left because the inferior vena cava sits just to the right of and anterior to the spine. Left uterine displacement is easily accomplished by table tilt or the placement of a wedge or folded blanket under the right hip, elevating the hip by 10 to 15 cm. (516-517, Figures 33-1 and 33-2)

8. There is significant capillary engorgement of the mucosal layer of the upper airways and increased tissue friability during pregnancy. There is increased risk of obstruction from tissue edema and bleeding with instrumentation of the upper airway. Additional care is needed during suctioning, placement of airways (avoid nasal instrumentation if possible), direct laryngoscopy, and intubation. In addition, because the vocal cords and arytenoids are often edematous, smaller-sized cuffed endotracheal tubes (6.0 to 6.5 mm internal diameter) may be a better selection for intubation of the trachea for these patients. The presence of preeclampsia, upper respiratory tract infections, and active pushing with associated increased venous pressure further exacerbate airway tissue edema, making both intubation and ventilation more challenging. (517)

9. During pregnancy, the minute ventilation increases to about 50% above prepregnancy levels. This change occurs in the first trimester of pregnancy and remains elevated for the duration of the pregnancy. An increase in tidal volume is the main contributor to the increase in minute ventilation seen, with only small increases in respiratory rate from prepregnancy. During the first trimester, as a result of the increase in minute ventilation, the resting maternal $Paco_2$ decreases from 40 mm Hg to about 30 or 32 mm Hg. Arterial pH, however, remains only slightly alkalotic (7.42 to 7.44) secondary to increased renal excretion of bicarbonate ions. (517, Table 33-1)

10. Maternal hemoglobin has less of an affinity for binding oxygen during pregnancy, which facilitates downloading oxygen to the tissues and the fetus. The hemoglobin dissociation curve is thus shifted to the right with the P-50 increasing from 27 to approximately 30 mm Hg. (517)

11. Maternal lung volumes start to change in the second trimester. This is a result of mechanical compression by the gravid uterus as it enlarges and forces the diaphragm cephalad. This leads to a decrease in the woman's functional residual capacity by approximately 20% at term. This decrease is a result of approximately equal decreases in both the expiratory reserve volume and residual lung volume. This can result in a functional residual capacity less than closing capacity and increased atelectasis in the supine position. There is no significant change in vital capacity seen during pregnancy. The rates of change in the alveolar concentration of inhaled anesthetics during induction and emergence from anesthesia are both increased secondary to the increase in minute ventilation and decrease in functional residual capacity. Clinically this, along with the decrease in MAC that accompanies pregnancy, leads to a more rapid achievement of an anesthetized state than when the patient is not pregnant. Apnea in the woman rapidly leads to arterial hypoxemia. There are at least two explanations for this. First, a decreased functional residual capacity and subsequent decreased oxygen reserve are contributors. Second, aortocaval compression and decreased venous return leading to decreases in cardiac output may also contribute. The decrease in cardiac output would lead to an increase in overall oxygen extraction and therefore decrease the level of oxygenation of blood returning to the heart. Third, maternal oxygen consumption is increased by 20% at term, with further

increases noted during labor. Because of the rapid decrease in maternal Pa_{O_2} with apnea or hypoventilation, preoxygenation with 100% O_2 for 3 minutes or four maximal breaths over the 30 seconds just prior to the induction of emergent general anesthesia is recommended. (517, Table 33-1)

12. Maternal Pa_{O_2} changes during the progression from early gestation to term. Early in gestation, the Pa_{O_2} in the mother is slightly increased over prepregnancy values to over 100 mm Hg breathing room air. This is secondary to maternal hyperventilation and subsequent decreased Pa_{CO_2} during this time. As the pregnancy progresses, the Pa_{O_2} is normal or even slightly decreased. The decrease in Pa_{O_2} during the course of pregnancy likely results from airway closure and associated intrapulmonary shunt. (517)

13. There are at least four gastrointestinal changes in pregnancy that render the woman significantly vulnerable to the regurgitation of gastric contents beyond midgestation. The enlarged uterus acts to displace the stomach and pylorus cephalad from its usual position. This repositions the intraabdominal portion of the esophagus into the thorax and leads to relative incompetence of the physiologic gastroesophageal sphincter. The tone of the gastroesophageal sphincter is further reduced by the higher progesterone and estrogen levels of pregnancy. Gastric pressure is increased by the gravid uterus. Gastrin secreted by the placenta stimulates gastric hydrogen ion secretion. The pH of the woman's gastric fluid is predictably low as a result. Reflux and subsequent esophagitis are common during pregnancy. During labor, gastric emptying is delayed and intragastric fluid volume tends to be increased as a result. (Epidural analgesia alone does not alter gastric emptying.) Anxiety, pain, and the administration of opioids can further decrease gastric emptying. Clinically, this means that the pregnant patient must always be treated as if she has a full stomach. Regardless of what amount of time has elapsed since her last ingestion of solids, she is at increased risk of regurgitation and aspiration of gastric contents. This includes the routine use of nonparticulate antacids, rapid sequence induction, cricoid pressure, and cuffed endotracheal intubation as part of general anesthesia induction sequence in a pregnant woman after approximately 20 weeks gestational age.

    Pharmacologic interventions that are recommended in the woman to help minimize the risks of pulmonary aspiration are aimed at decreasing the severity of acid pneumonitis should aspiration occur. The administration of antacids to pregnant women before the induction of anesthesia is common practice. This is as an attempt to increase the pH of gastric contents. Sodium citrate is the antacid commonly used. Of note, the antacid must be nonparticulate, because aspiration of particulate matter contained in some antacids is in itself a hazard. Metoclopramide can be useful for decreasing the gastric fluid volume of pregnant women in active labor who require general anesthesia. It can significantly decrease gastric volume in as little as 15 minutes, although gastric hypomotility associated with prior opioid administration reduces the effectiveness of metoclopramide. H_2 receptor antagonists increase gastric fluid pH in pregnant women approximately one hour after administration without producing adverse effects, and are additionally recommended by some. (517-518)

14. During pregnancy, both the epidural and intrathecal spaces are decreased in volume from their prepregnancy state. This occurs because of the engorgement of epidural veins and the increased intraabdominal pressure resulting from the progressive enlargement of the uterus. However, CSF pressure does not increase with pregnancy. The decrease in the epidural space decreases the required volume of local anesthetic necessary to achieve a particular level of anesthesia by facilitating its spread in the epidural space. The decreased intrathecal space also facilitates the spread of spinal anesthetic and decreases the dose required from prepregnancy values.

There appears to be an increased sensitivity to local anesthetics by women who are pregnant. The decreased local anesthetic requirement in pregnant women appears to have a biochemical component to it as well as a mechanical one. This is based on the observation of decreased neuraxial local anesthetic doses as early as the first trimester, before significant uterine enlargement.

15. Renal blood flow and glomerular filtration rate in the woman are both increased. By the third month of pregnancy the increase is about 50% to 60%. This results in a decrease in what is considered the normal upper limit of both the blood urea nitrogen and serum creatinine concentrations during pregnancy to about 50% of what it was in the prepregnancy state. (518)

16. Liver blood flow does not change significantly with pregnancy. Plasma protein concentrations are reduced in pregnancy secondary to dilution. The decreased albumin levels can create increased blood levels of highly protein bound drugs. Plasma cholinesterase, or pseudocholinesterase, decreases in activity by about 25% during pregnancy. This decrease in activity is first noted by about the tenth week of gestation and persists for as long as 6 weeks postpartum. There is no clinical manifestation of this change in plasma cholinesterase activity, and no significant change in the duration of action of succinylcholine. (518)

PHYSIOLOGY OF UTEROPLACENTAL CIRCULATION

17. The function of the placenta is to unite maternal and fetal circulations. The union allows for the physiologic exchange of nutrients and waste. Maternal blood is delivered to the placenta by the uterine arteries. Fetal blood is delivered to the placenta by the two umbilical arteries. Nutrient rich blood is returned from the placenta to the fetus via a single umbilical vein. The two most important determinants of placental function are uterine blood flow and the characteristics of the substances to be exchanged across the placenta. (519)

18. Uterine blood flow increases during gestation from approximately 100 mL/min before pregnancy to 700 mL/min at term. Adequate uterine blood flow must be maintained to ensure placental circulation is adequate and therefore guarantee fetal well-being. About 80% of the uterine blood flow perfuses the placenta and 20% supports the myometrium. (519)

19. During pregnancy uterine blood flow has limited autoregulation, and the uterine vasculature is essentially maximally dilated under normal pregnancy conditions. Uterine blood flow is proportional to the mean blood perfusion pressure to the uterus and inversely proportional to the resistance of the uterine vasculature. Decreased perfusion pressure can result from systemic hypotension secondary to hypovolemia, aortocaval compression, or decreased systemic resistance from either general or neuraxial anesthesia. Uterine blood flow also decreases with increased uterine venous pressure. This can result from vena caval compression (supine position), uterine contractions (particularly uterine tachysystole as may occur with oxytocin administration), or significant abdominal musculature contraction (Valsalva during pushing). Additionally, extreme hypocapnia ($Paco_2 < 20$ mm Hg) associated with hyperventilation secondary to labor pain can reduce UBF to the point of fetal hypoxemia and acidosis. Epidural or spinal anesthesia does not alter UBF as long as maternal hypotension is avoided. Endogenous catecholamines induced by stress or pain and exogenous vasopressors have the capability of increasing uterine arterial resistance and decreasing UBF, although both ephedrine or phenylephrine are used clinically in moderate amounts to maintain uterine perfusion pressure when the pregnant patient is hypotensive. (519)

20. Transfer of oxygen to the fetus is dependent on a variety of factors including the ratio of maternal to fetal umbilical blood flow, the oxygen partial pressure gradient, the respective hemoglobin concentrations and affinities, the placental

diffusing capacity, and the acid-base status of the fetal and maternal blood (Bohr effect).

21. Transfer of drugs and other substances less than 1000 Da from the maternal circulation to the fetal circulation and vice versa is primarily by diffusion. Some factors that affect the exchange of substances from the maternal circulation to the fetus include the concentration gradient of the substance across the placenta, maternal protein binding, molecular weight, lipid solubility, and degree of ionization of the substance. The most reliable way to minimize the amount of drug that reaches the fetus is by minimizing the concentration of the drug in the maternal blood. (519)

22. Nondepolarizing neuromuscular blocking drugs have a high molecular weight and low lipid solubility. These two characteristics together limit the ability of nondepolarizing neuromuscular blocking drugs to cross the placenta. Succinylcholine is highly ionized, preventing it from diffusing across the placenta despite its low molecular weight. Additionally, both heparin and glycopyrolate have significantly limited placental transfer. Placental transfer of barbiturates, local anesthetics, and opioids is facilitated by the relatively low molecular weights of these substances. (519)

FETAL UPTAKE AND DISTRIBUTION OF DRUGS

23. Fetal blood is slightly more acidic than maternal blood, with a pH about 0.1 unit less than maternal blood pH. The lower pH of fetal blood facilitates the fetal uptake of drugs that are basic. Weakly basic drugs, such as local anesthetics and opioids that cross the placenta in the nonionized state, become ionized in the fetal circulation. This results in an accumulated concentration of drug in the fetus for two reasons. First, once the drug becomes ionized it cannot readily diffuse back across the placenta. This is known as *ion trapping.* Second, a concentration gradient of nonionized drug is maintained between the mother and the fetus. In the case of lidocaine administration, this may mean that if the fetus was distressed and acidotic and lidocaine was given in sufficient doses to the woman, lidocaine may accumulate in the fetus. (519)

24. First, about 75% of the blood that is coming to the fetus via the umbilical vein passes through the liver. This allows for a significant amount of metabolism of the drug to take place before going to the fetal arterial circulation and delivery to the heart and brain. Second, drug contained in the umbilical vein blood enters the inferior vena cava via the ductus venosus. This blood is diluted by drug-free blood returning from the lower extremities and pelvic viscera of the fetus, resulting in a decrease in the concentration of the drug that is in the inferior vena cava. In addition, despite decreased liver enzyme activity in comparison to adults, fetal/neonatal enzyme systems are adequately developed to metabolize most drugs. (520)

STAGES OF LABOR

25. Labor is a continuous process divided into three stages. The first stage is the onset of labor until the cervix is fully dilated. This first stage is further divided into the latent and active stage. The active phase begins at the point when the rate of cervical dilation increases (often between 3 and 5 cm.). The second stage of labor begins when the cervix is fully dilated and ends when the neonate is born. This stage is referred to as the "pushing and expulsion" stage. The third and final stage begins once the neonate is delivered and is completed when the placenta is delivered. (520)

26. If a woman fails to dilate adequately in the active phase despite pharmacologic interventions, it is considered *active phase arrest* and will result in cesarean delivery. During the second stage of labor, the patient may not be able to "push" the neonate out of the pelvis. This is termed *arrest of descent.* If the neonate is low enough in the pelvis, the obstetrician can perform an instrumented vaginal delivery via vacuum or forceps, otherwise a cesarean delivery is required. (520)

ANATOMY OF LABOR PAIN

27. During the first stage of labor (cervical dilation), the majority of painful stimuli result in afferent nerve impulses from the lower uterine segment and cervix. This pain is typically visceral in nature (dull, aching, poorly localized). The nerve cell bodies are located at the dorsal root ganglia of T10 to L1 level. (520, Figure 33-3)

28. In the second stage of labor, afferents innervating the vagina, perineum, and pelvic floor travel primarily via the pudendal nerve to the dorsal root ganglia of the S2 to S4 levels. This pain is typically somatic in nature (sharp and well localized). (520, Figure 33-3)

29. The first and second stages of labor can employ neuraxial techniques such as an epidural or combined spinal epidural (CSE). Although used less frequently, a paracervical block can also be used during the first stage of labor. A single shot spinal or pudendal block can be used for the second stage of labor. Typically, the obstetrician performs both the paracervical and pudendal block. (520)

METHODS OF LABOR ANALGESIA

Nonpharmacologic Techniques and Systemic Medications

30. A variety of nonpharmacologic techniques for labor analgesia exist. These include hypnosis, the breathing techniques described by Lamaze, acupuncture, acupressure, the LeBoyer technique, transcutaneous nerve stimulation, massage, hydrotherapy, vertical positioning, presence of a support person, intradermal water injections, biofeedback, and many others. A meta-analysis reviewing the effectiveness of a support individual (e.g., doula, family member) noted that women with a support individual used less pharmacologic analgesia methods, had a decreased length of labor, and a lower incidence of cesarean delivery. In a 2006 retrospective survey, nonpharmacologic methods of tub immersion and massage were rated more or equally effective in relieving pain compared to use of opioids in labor. (521)

31. Fentanyl is commonly used for labor analgesia because it is short acting with no active metabolite. Morphine was used more frequently in the past, but currently is rarely used. Its active metabolite (morphine-6-glucuronide) has a prolonged duration of analgesia, the half-life is longer in neonates compared to adults, and it produces significant maternal sedation. Meperidine is still one of the most frequently used opioids worldwide. Maternal half-life of meperidine is 2 to 3 hours with half-life in the fetus and newborn significantly greater (13 to 23 hours) and more variable. In addition, meperidine is metabolized to an active metabolite (normeperidine) that can significantly accumulate after repeated doses. With increased dosing and shortened time between doses, there are increased neonatal risks. (521-522)

32. In latent labor, obstetrical providers may use intramuscular morphine combined with phenergan for analgesia, sedation, and rest termed “morphine sleep.” This produces analgesia for approximately 2.5 to 4 hours with an onset of 10 to 20 minutes. (521)

33. Remifentanil patient controlled analgesia (PCA) has been considered for women who have contraindications to neuraxial blockade. Although pain was improved with remifentanil compared to those without pharmacologic intervention, a randomized control trial comparing epidural analgesia to remifentanil PCA had overall pain scores that were lower in the epidural group. More sedation and hemoglobin desaturation were noted during remifentanil analgesia, but there was no difference between groups in fetal and neonatal outcome measures. (522)

34. Diazepam is used in obstetrics; however, it will readily cross the placenta and yield roughly equal maternal and fetal blood levels. Since neonates have a limited ability to excrete the active metabolites, use of diazepam has been associated with neonatal respiratory depression. Midazolam is a shorter acting anxiolytic, but also rapidly crosses the placenta, and large induction doses have been associated with profound neonatal hypotonia. Their use has been controversial given

their amnestic properties. In specific obstetrical situations, use of midazolam in small doses may be beneficial. (522)

35. During labor ketamine can be administered for urgent situations in divided IV doses (10 to 20 mg) totaling less than 1 mg/kg. Ketamine in these doses will provide rapid analgesia, and is useful for vaginal delivery and episiotomy. It has a rapid onset (30 seconds) and minimal duration of action (<5 minutes). When given with opioids, ketamine can act synergistically to reduce the amount of opioid necessary to produce adequate analgesia. (522)

Neuraxial Analgesia and Neuraxial Techniques

36. Neuraxial analgesia typically involves the administration of local anesthetics, often with the coadministration of opioid analgesics or other adjunctive analgesics. Bupivacaine and ropivacaine are the most commonly used local anesthetics. Epidural, spinal, and combined spinal and epidural (CSE) are the techniques typically used for labor analgesia. (522)

37. Anytime a woman in labor without contraindications requests neuraxial analgesia, regardless of the stage of her labor, a neuraxial blockade may be placed. The timing of placement does not depend on an arbitrary cervical dilation. A single shot spinal analgesic has a finite analgesic duration depending on the local anesthetic and this should be taken into account when using this technique. For example, a single shot spinal analgesic is ideal if an obstetrician is performing an instrumented vaginal delivery in a woman without previous neuraxial block. The other neuraxial techniques employ catheter delivery techniques and can be extended throughout the length of the labor. (523)

38. Otherwise healthy women in labor may have modest amounts of clear liquids. However, in a complicated labor (e.g., by morbid obesity, difficult airway, concerning fetal status), the decision to restrict oral intake should be individualized. (523)

39. Placing opioids alone in the epidural or intrathecal space (if placing a CSE) is considered a walking epidural. The local anesthetic solution, while providing analgesia, has minimal effects on sympathetic or motor nerves. This allows the woman to ambulate after tests for motor blockade indicate that she is not at risk of falling. Even so, the woman should be closely monitored and ideally should only ambulate when accompanied because proprioception and balance may be impaired. Use of neuraxial opioids is associated with dose-related maternal side effects including pruritus, sedation, and nausea. In addition, the administration of intrathecal opioids can result in fetal bradycardia independent of hypotension. The mechanism for fetal bradycardia is unclear, but may result from uterine hyperactivity following the rapid onset of analgesia. (522)

40. Clonidine and neostigmine are epidural adjuncts to local anesthetics and have been evaluated for use in neuraxial blockade. They prolong the blockade and limit the dose of local anesthetic infusion. Neostigmine is still undergoing evaluation for its use in obstetric anesthesia and currently is not recommended for standard practice. It increases acetylcholine binding within the spinal cord stimulating nitric oxide to produce analgesia. Neostigmine also produces refractory nausea and vomiting if given intrathecally, but minimal nausea and vomiting if given epidurally. Clonidine inhibits the release of substance P in the dorsal horn and produces analgesia. It also increases the level of acetylcholine in the cerebral spinal fluid. Intrathecal clonidine can produce excellent analgesia, but sedation and hypotension are common. (522-523)

41. When placing an epidural, the needle traverses the skin and subcutaneous tissues, supraspinous ligament, interspinous ligament, the ligamentum flavum, and is advanced into the epidural space. (523, Figures 33-4 and 33-5)

42. Aseptic technique should be used during neuraxial procedures, including (1) jewelry removal (e.g., rings and watches), hand washing, and use of caps, masks, and sterile gloves; (2) use of individually packaged chlorhexidine (preferred) or povidone-iodine (preferably with alcohol) for skin preparation, allowing for adequate drying time; (3) sterile draping; and (4) use of sterile occlusive dressings at the catheter insertion site. (523)

43. For neuraxial analgesia the needle is normally inserted between L1 and L4. If the needle is placed too high, there is a risk of puncturing the conus medullaris if the needle inadvertently punctures the dura. In addition, coverage of sacral roots needed during the second stage may be inadequate. If the catheter is placed lower than L4, the neuraxial block may not adequately cover the nerves that innervate the uterus and may not provide the necessary labor analgesia for uterine contractions and cervical dilation. (523)

44. Prior to the infusion of local anesthetic through an epidural catheter a test dose typically composed of 3 cc of 1.5% lidocaine with 1:200,000 epinephrine is administered. The anesthesia provider waits 3 minutes to confirm that the needle is not intravascular with no increase in heart rate or blood pressure, and no systemic symptoms of lidocaine infusion have resulted such as tinnitus or perioral tingling. Additionally, the patient is asked to move her lower extremities to confirm that the bolus was not placed intrathecally, which would result in motor blockade. (524-526)

45. A test dose can and should be used with the CSE. The test dose will both confirm whether the catheter is intravascular by changes in heart rate and blood pressure, and unintended intrathecal catheter placement can still be assessed as the patient should still be able to move her lower extremities after typical spinal local anesthetic doses in the spinal portion of the CSE. (524-526)

46. A 24 to 26-gauge "pencil point" spinal needle is commonly selected for CSE to reduce the risk of a postdural puncture headache. (526)

47. If primarily perineal anesthesia is needed (i.e., forceps delivery, perineal laceration repair), the patient may be left in the sitting position for 2 to 3 minutes after intrathecal injection with hyperbaric local anesthetic to concentrate the sensory block in the perineal region ("saddle block"). A true saddle block anesthetic (requiring more time in the sitting position) does not produce complete uterine pain relief because the afferent fibers (extending to T10) from the uterus are not blocked. (526)

CONTRAINDICATIONS AND COMPLICATIONS OF NEURAXIAL ANESTHESIA

48. Certain conditions contraindicate neuraxial procedures. These include: (1) patient refusal, (2) infection at the needle insertion site, (3) significant coagulopathy, (4) hypovolemic shock, (5) increased intracranial pressure from mass lesion, and (6) inadequate provider expertise. Other conditions such as systemic infection, neurologic disease, and mild coagulopathies are relative contraindications and should be evaluated on a case-by-case basis. (526)

49. Neither HIV nor hepatitis virus infection are contraindications to placement of neuraxial anesthesia. (526)

50. Possible complications of a neuraxial block include inadequate block, hypotension, intravascular catheter placement, systemic toxicity of local anesthetic, unintentional intrathecal catheter placement, excessive blockade, postdural puncture headache, epidural hematoma, epidural abscesses, meningitis, and nerve or spinal cord injury. Other side effects include pruritus, nausea, shivering, urinary retention, motor weakness, low back soreness, and a prolonged block. (526)

51. The rate of accidental dural puncture during epidural catheter placement is approximately 1% to 2%, and approximately half of these will result in a severe headache. PDPH are typically managed with analgesics, hydration, rest, caffeine, and an epidural blood patch, if necessary. (526)

52. If a local anesthetic overdose occurs, in addition to following standard ACLS algorithms for pregnancy, consider use of a 20% IV lipid emulsion to decrease toxicity. (527)

53. A high spinal (total spinal) can result from an unrecognized epidural catheter placed subdural, migration of the catheter during its use, or an overdose of local anesthetic in the epidural space (i.e., high epidural). Both high spinals and high epidurals can result in severe maternal hypotension, bradycardia, loss of consciousness, and blockade of the motor nerves to the respiratory muscles. (526-527)

54. ACLS guidelines for pregnancy include use of left uterine displacement, avoidance of lower extremity vessels for drug delivery, chest compressions positioned slightly higher on the sternum, and no modifications to the defibrillation protocol except removal of fetal and uterine monitors prior to shock. In any situation of maternal cardiac arrest with unsuccessful resuscitation, the fetus should be emergently delivered if the mother is not resuscitated within 4 minutes of the arrest. This guideline for emergent cesarean delivery increases the chances of survival for both the mother and neonate. Typically, at 20 weeks or greater gestational age, an emergent cesarean delivery will be performed to help save the life of the mother. Less than 24 to 25 weeks gestational age, the fetus is not viable, but in the setting of ACLS the delivery of the fetus regardless of viability improves the chances of survival for the woman. (527)

55. Hypotension (decrease in systolic BP $>$20%) secondary to sympathetic blockade is the most common complication of neuraxial blockade for labor analgesia with rates between 10% and 24%. Left uterine displacement and hydration are used to decrease hypotension associated with the initiation of neuraxial blockade. (527)

56. Small vasopressor boluses of either phenylephrine or ephedrine can be used to treat hypotension after a neuraxial block. Although ephedrine was historically used primarily, phenylephrine is now preferred as first-line treatment because it is associated with less fetal acidosis. If treated promptly, maternal hypotension does not lead to fetal depression or neonatal morbidity. (527)

57. During the first 5 hours of epidural analgesia, there is no significant rise in body temperature. Temperature increases at about 0.10° C/hr, and may reach 38° C in as many as 15% of women with a labor epidural compared with 1% without an epidural. Although the etiology of the maternal temperature rise remains uncertain, it does not increase the rate of neonatal sepsis and need not affect neonatal septic workup. (527)

OTHER TECHNIQUES FOR LABOR ANALGESIA

58. For achievement of a paracervical block, local anesthetic must be injected submucosal, lateral and posterior to the uterocervical junction bilaterally. Sensory fibers that come from the uterus, cervix, and upper vagina travel through this area. Therefore, this block is most effective to help provide analgesia during the first stage of labor and is usually not effective for the second stage of labor. The major disadvantage of a paracervical block is potential fetal bradycardia. In approximately 15% of laboring women who receive this block, fetal bradycardia develops 2 to 10 minutes after the local anesthetic solution is injected. Although the definitive cause of the bradycardia is not known, it is often associated with fetal acidosis. The bradycardia is normally limited to less than 15 minutes with supportive treatment as needed. (527)

59. A pudendal nerve block is useful for anesthesia of the lower vagina and perineum as needed for delivery with an episiotomy or low forceps delivery. The obstetrician

typically performs this block, which is done transvaginally with the woman in the lithotomy position. The failure rate is high and complications include local anesthetic toxicity, ischiorectal or vaginal hematoma, and rarely, fetal injection of local anesthetic. (527)

60. The inhaled anesthetic that is most often used for analgesia in the pregnant woman is 50% nitrous oxide administered in a blend with oxygen. The other inhaled anesthetics are rarely used for this purpose. The inhalation of nitrous oxide for analgesia during labor and delivery should be self-administered after appropriate patient instruction. Optimal results from the administration of nitrous oxide during labor are obtained by having the woman inhale the nitrous oxide between contractions, so that an effective concentration of nitrous oxide is achieved for the uterine contraction. About 45 seconds of continuous breathing of the nitrous oxide are necessary for optimal labor analgesia with contractions. Maternal cardiovascular and respiratory depression is minimal, uterine contractility is not affected, and neonatal depression does not occur regardless of the duration of nitrous oxide administration. (527-528)

ANESTHESIA FOR CESAREAN DELIVERY

61. Benefits of regional anesthesia over general anesthesia for cesarean delivery include the avoidance of the risks of general anesthesia, such as a decreased risk of pulmonary aspiration, difficult airway, decreased fetal depression from and exposure to anesthetic agents, the placement of neuraxial opioids for postoperative pain, and the maintenance of maternal awareness. No differences in neonatal outcome after cesarean delivery with regional anesthesia or general anesthesia have been shown. (528)

62. Benefits of general anesthesia over regional anesthesia for cesarean delivery include rapid and dependable onset, secure airway, controlled ventilation, and the potential for less hemodynamic instability. (528)

63. Advantages of spinal anesthesia for cesarean delivery include its technical ease of administration, low levels of systemic medication that decrease the risk of systemic toxicity and fetal drug levels, its low failure rate, and its rapid onset time. Disadvantages of spinal anesthesia for cesarean delivery include the finite duration of anesthesia provided, and its higher incidence of hypotension. It can be safely used in preeclamptic patients. (528)

64. Spinal anesthesia with a sensory level of T4 is usually sufficient for patient comfort during cesarean delivery. Exteriorization of the uterus or traction of the abdominal viscera may still lead to discomfort in the woman. A T4 sensory level can be achieved with the administration of hyperbaric bupivacaine 10 to 15 mg. The medication will flow with the spinal curvature to a position near T4. (528)

65. Advantages of epidural anesthesia for cesarean delivery include the ability to extend the duration of anesthesia if necessary, to control block height, and to slowly titrate the dose to avoid precipitous maternal hypotension. Disadvantages of epidural anesthesia for cesarean delivery include the potential for intravascular injection of toxic levels of local anesthetic and its technical difficulty, longer onset time, less reliability, and increased perception of visceral pain with peritoneal manipulation. (528)

66. An approximate volume of 15 to 20 mL of local anesthetic solution must be delivered in the epidural space to achieve the T4 sensory level of anesthesia necessary for cesarean delivery. Before the administration of such high volumes of local anesthetics a test dose for epidural catheter placement should be administered. Local anesthetics that can be administered for cesarean delivery by epidural catheter placement include 2% lidocaine, 0.5% bupivacaine, 0.5% ropivacaine, and 3% 2-chloroprocaine. Each of these should be administered in increments to further minimize the risk of accidental intravenous administration

of toxic levels of local anesthetic. Addition of epinephrine (1:200,000) or fentanyl (50 to 100 μg) can enhance the intensity and duration of the block. For the rapid onset of analgesia with a lumbar epidural catheter, as in an urgent cesarean delivery, 2-chloroprocaine 3% has the most rapid onset. (528)

67. The administration of preservative-free morphine into the epidural space during cesarean delivery extends the duration of analgesia by up to 24 hours into the postoperative period. The dose of morphine commonly administered is 3 to 5 mg. Some negative effects of morphine that may accompany this route of administration include pruritus, nausea and vomiting, and, on rare occasions, delayed respiratory depression. (522, 528)

68. Indications for general anesthesia for cesarean delivery include fetal distress and required emergent delivery to prevent poor fetal outcome, maternal hemorrhage, and contraindications to regional anesthesia such as maternal coagulopathy or maternal refusal. Benefits of general anesthesia for cesarean delivery include a more reliable and rapid onset of anesthesia, less hypotension and hemodynamic instability than regional anesthesia, and control of the airway and ventilation. (529)

69. The main cause of maternal morbidity and mortality with general anesthesia are an eightfold increased risk of failed endotracheal intubation (approximately 1 in 500) and a threefold increased risk of pulmonary aspiration (1 in 650) compared with nonpregnant patients undergoing general anesthesia. Appropriate airway examination, preparation, and familiarity with techniques and an algorithm for the difficult airway are critical for providing a safe anesthetic. (528, Figure 33-6)

70. A major cause of morbidity and mortality for the woman with regard to general anesthesia is failed or difficult intubation of the trachea. Contributing factors include inadequate time for preoperative evaluation of the airway, unpredicted airway edema, and emergency situations. If a difficult airway is suspected preoperatively, an awake fiberoptic intubation of the trachea should be considered. The anesthesiologist must have a difficult airway algorithm to follow should she or he be confronted with a difficult or failed intubation. There should be equipment immediately available for the difficult airway, such as a variety of functioning laryngoscope blades, several sizes of endotracheal tubes, laryngeal mask airways, a fiberoptic bronchoscope, and the means to perform a cricothyrotomy. Extra help should be solicited. Numerous attempts at laryngoscopy should be avoided to prevent increasing airway edema and bleeding. If hypoxia should occur during attempted laryngoscopy, the patient should be hand ventilated with bag and mask while cricoid pressure is maintained. If intubation attempts fail, the cesarean delivery may proceed if the anesthesiologist communicates that she or he can reliably ventilate the mother with either facemask or laryngeal mask airway (LMA). Other options may include allowing the patient to resume spontaneous ventilation, waking the patient and doing an awake fiberoptic intubation of the trachea, or, in dire circumstances of inadequate ventilation and hypoxemia, proceeding to a surgical airway. (529, Figure 33-6)

71. The level of exposure of the fetus to thiopental after the administration of thiopental for the induction of general anesthesia is generally low as long as the dose administered to the woman is less than 6 mg/kg. It peaks in the umbilical vein blood in 1 minute and in the umbilical artery blood in 2 to 3 minutes, and has no significant clinical effect on neonatal well-being. The lack of neonatal effects in standard doses is unclear, but may be due to first pass metabolism as (1) the drug is partially cleared as it passes through the liver of the fetus before reaching the fetal heart, (2) there is rapid redistribution into maternal vascular rich tissue beds, (3) there is higher fetal brain water content, and (4) there is additional dilution by the fetal circulation as the blood reaching the fetal heart from the placenta is diluted by the blood from the fetal viscera and lower extremities. However, doses of 8 mg/kg can result in neonatal depression. Propofol is not

superior to thiopental in maternal or neonatal outcome. Induction doses of 2.5 mg/kg have no significant effect on neonatal behavior scores, while larger doses (9 mg/kg) are associated with neonatal depression. (529)

72. Like thiopental, etomidate has a rapid onset because of its high lipid solubility, and redistribution results in a relatively short duration of action. At typical induction doses (0.3 mg/kg), unlike thiopental and propofol, etomidate has minimal cardiovascular effects, but is painful on injection, can cause muscle tremors, has higher rates of nausea and vomiting, and has increased risk of seizures in patients with decreased thresholds. (529)

73. Maintenance of anesthesia for cesarean delivery often includes the inhalation of a low concentration (<0.75 MAC) of halogenated anesthetic in combination with either nitrous oxide or propofol. The volatile anesthetic is an important component to decrease the incidence of maternal recall. Uterine tone after delivery is maintained when the concentration of volatile anesthetic used is low. Maternal blood loss is minimized, the uterine response to oxytocin is not altered, and little neonatal depression is seen. Placental transfer of volatile anesthetics is rapid because they are nonionized, highly lipid-soluble substances of low molecular weight. Fetal concentrations depend on the concentration and duration of anesthetic administered to the mother. There is no evidence to show that neuraxial anesthesia is superior to general anesthesia for neonatal outcome. However, emergent delivery of a depressed fetus often results in a depressed neonate. A long time from induction to delivery may result in a lightly anesthetized, but not an asphyxiated neonate. If excessive concentrations of volatile anesthetics are administered for prolonged periods, neonatal effects of these drugs, as evidenced by flaccidity, cardiorespiratory depression, and decreased tone, may be anticipated. It is important to recognize that if neonatal depression is due to transfer of anesthetic drugs, the infant is merely anesthetized and should respond easily to simple treatment measures such as assisted ventilation of the lungs to facilitate excretion of the volatile anesthetic. Rapid improvement of the infant should be expected, and if it does not occur, it is important to search for other causes of depression. (530-531)

74. Succinylcholine remains the neuromuscular blocking drug of choice for obstetric anesthesia because of its rapid onset and short duration of action. Because it is highly ionized and poorly lipid soluble, only small amounts cross the placenta. It is normally hydrolyzed in maternal blood by the enzyme pseudocholinesterase and does not generally interfere with fetal neuromuscular activity. If large doses are given (2 to 3 mg/kg), it results in detectable levels in umbilical cord blood, and extreme doses (10 mg/kg) are needed for the transfer to result in neonatal neuromuscular blockade. Rocuronium is an acceptable alternative. It provides adequate intubating conditions in approximately 60 seconds at doses of 1.2 mg/kg. Unlike succinylcholine it has a much longer duration of action, potentially decreasing maternal safety in the event the anesthesiologist is unable to intubate or ventilate the patient. Uterine smooth muscle is not affected by neuromuscular blockade. Under normal circumstances, the poorly lipid-soluble, highly ionized, nondepolarizing neuromuscular blockers do not cross the placenta in amounts significant enough to cause neonatal muscle weakness. This placental impermeability is only relative and when large doses are given over long periods, neonatal neuromuscular blockade can occur. (531)

ABNORMAL PRESENTATIONS AND MULTIPLE BIRTHS

75. Currently twin pregnancy accounts for 3.4 % of the live births in 2006. The vast majority of multiple gestations are twin (97% to 98%). Higher order multiples account for only 0.1% to 0.03% of the births. Multiple pregnancies account for a significant risk to both the mother and the fetuses, with a higher rate of preterm labor, preeclampsia, gestational diabetes, preterm premature rupture of

membranes, intrauterine growth restriction, and intrauterine fetal demise. The United States is seeing an increase in multiple gestations with the expanded use of artificial reproductive technologies. (531-532)

76. The majority of twin pregnancies have vertex-vertex positioning of the fetuses, and can be delivered vaginally. If the second twin is breech, it is important to discuss the mode of delivery with the obstetricians and perinatologists as an emergent cesarean delivery might be required if the second twin changes position after delivery of the first or develops fetal bradycardia. Placement of an epidural can facilitate delivery and extraction of the second twin if it becomes necessary for the obstetrician to perform an instrumented delivery of the second twin. At the late second stage of delivery, a more concentrated local anesthetic will optimize the perineal anesthesia and relaxation during this critical portion of the delivery. At this time, the potential for head entrapment or fetal bradycardia is highest and a denser block allows for possible transition to cesarean delivery. (532)

77. Singleton breech presentation occurs in about 3% to 4 % of all pregnancies. External cephalic version (ECV) has a mean success rate of approximately 60%. The procedure involves rotating the fetus via external palpation and pressure of the fetal parts. Neuraxial analgesia may improve success of the ECV. The risks of ECV include placental abruption, fetal bradycardia, and rupture of membranes. The anesthesia provider should be immediately available if an ECV is performed in case an urgent or emergent cesarean delivery is needed. (532)

78. A shoulder dystocia is an obstetric emergency analogous to a difficult airway in anesthesia. After delivery of the fetal head, further expulsion of the infant is prevented by impaction of the fetal shoulders with the maternal pelvis. It occurs in approximately 1% to 1.5% of all deliveries. Risk factors include: macrosomia, diabetes, obesity, history of dystocia, labor induction, and instrumented delivery. Fetal pH declines 0.04 units/min between delivery of the head and trunk. Cases of shoulder dystocia 7 minutes or longer are associated with a significant increase in risk of neonatal brain injury. The final maneuver of the obstetrician is to push the fetus back into the uterus and proceed to emergent cesarean delivery. Among the fetal injuries and sequelae of shoulder dystocia are brachial plexus injury, neurologic injury from asphyxia, and broken clavicle. Often these neurologic injuries improve over time with roughly less than 10% having a permanent Erb's palsy. (532)

HYPERTENSIVE DISORDERS OF PREGNANCY

79. Gestational hypertension is diagnosed in previously normotensive women who develop elevated blood pressure (SBP >140 or DBP >90) after 20 weeks gestational age without evidence of proteinuria. (532)

80. Preeclampsia affects 5% to 7% of pregnant women. Risk factors include primigravida, chronic hypertension, gestational/preexisting diabetes, obesity, preeclamptic family history, multiple gestation, and use of assisted reproductive technology. (532-533)

81. The diagnosis of preeclampsia requires both of the following: a blood pressure of 140 mm Hg systolic or higher, or 90 mm Hg diastolic or higher that occurs after 20 weeks of gestation in a woman with previously normal blood pressure, and proteinuria defined as urinary excretion of 0.3 g protein or higher in a 24-hour urine specimen ($\geq 1+$ urine dip). (533, Table 33-3)

82. Preeclampsia is considered severe if one or more of the following criteria are present:

- Blood pressure of 160 mm Hg systolic or higher or 110 mm Hg diastolic or higher on two occasions at least 6 hours apart while the patient is on bed rest.
- Proteinuria of 5 g or higher in a 24-hour urine specimen or 3+ or greater on two random urine samples collected at least 4 hours apart.

- Oliguria of less than 500 mL in 24 hours
- Cerebral or visual disturbances
- Pulmonary edema or cyanosis
- Epigastric or right upper quadrant pain
- Impaired liver function
- Thrombocytopenia
- Fetal growth restriction (533, Table 33-3)

83. A subcategory of severe preeclampsia is HELLP syndrome, which is a constellation of Hemolysis, Elevated Liver enzymes, and Low Platelet count. (533)

84. Although the exact cause remains unknown, preeclampsia begins with the pathogenic maternal/fetal interface. During placental formation there is failure of complete trophoblast cell invasion of the uterine spiral arteries. The failure of spiral artery remodeling creates decreased placental perfusion, which may ultimately lead to early placental hypoxia. Ultimately there is upregulation of cytokines and inflammatory factors as seen in sepsis. (533)

85. The American College of Obstetricians and Gynecologists prefer neuraxial analgesia for labor in preeclamptics. Special concerns for neuraxial analgesia in this patient population include maintaining the uterine perfusion pressure through the avoidance of hypotension, and evaluation of the patient's coagulations status and platelet levels both with the placement of the epidural and prior to pulling out the epidural catheter. Currently, the definitive treatment of preeclampsia is delivery. If the pregnancy is remote from term in the presence of severe preeclampsia, a determination must be made whether to deliver or expectantly manage. This requires repeated evaluation of the mother and fetus. It is critical for the anesthesiologist on labor and delivery to be aware of these patients and their clinical course, as they can rapidly deteriorate and require urgent or emergent delivery. (533)

86. Magnesium sulfate is used for seizure prophylaxis in preeclamptic women. The infusion usually is performed by loading 4 to 6 g over 20 to 30 minutes then continued magnesium sulfate infusion of 1 to 2 g/hr until 12 to 24 hours after delivery. The therapeutic blood level range for seizure prophylaxis is between 6 to 8 mg/dL. Monitoring for magnesium sulfate toxicity is important in all patients, but is especially important in patients with impaired renal function, since magnesium sulfate is renally excreted. Loss of deep tendon reflexes occurs at 10 mg/dL with prolonged PQ intervals and widening QRS on ECG. Respiratory arrest occurs at 15 to 20 mg/dL, and asystole occurs when the level exceeds 20 to 25 mg/dL. If toxicity occurs, IV calcium chloride (500 mg) or calcium gluconate (1 g) should be administered. (533)

87. Initial antihypertensive therapy for preeclampsia normally includes hydralazine and labetalol. In refractory severe hypertension, nitroglycerin and sodium nitroprusside may be used in the acute situation to prevent intracerebral hemorrhage. Current guidelines recommend treating SBP >160. (533-534)

HEMORRHAGE IN PREGNANT WOMEN

88. Placenta previa, abruptio placentae, and uterine rupture are major causes of bleeding in the third trimester and during labor. Postpartum hemorrhage occurs in 3% to 5% of all vaginal deliveries and is typically due to uterine atony, retained placenta, placenta accreta, or lacerations involving the cervix or vagina. (534)

89. Placenta previa is an abnormal uterine implantation of the placenta in front of the presenting fetus. The incidence is approximately 1 in 200 pregnancies. Risk factors include advanced age, multiparity, assisted reproductive techniques, prior hysterotomy, and prior placenta previa. Placenta previa classically presents as painless vaginal bleeding. This usually occurs around the thirty-second week

of gestation when the lower uterine segment is beginning to form. The diagnosis of placenta previa can be confirmed by ultrasound examination of the placenta. (534)

90. If hemorrhage is not controlled with standard measures, the obstetrical team can consider (1) uterine artery ligation, (2) B-Lynch sutures, (3) an intrauterine balloon, (4) use of arterial embolization by interventional radiology if the patient is stable for transport, or (5) hysterectomy. (534)

91. Abruptio placentae is separation of the placenta after 20 weeks of gestation, but before delivery. The incidence is approximately 1 in 100 pregnancies. Risk factors include advanced age, hypertension, trauma, smoking, cocaine use, chorioamnionitis, premature rupture of membranes, and history of prior abruption. The woman often has painful, frequent uterine contractions. The separation can involve only the placental margin, presenting as vaginal bleeding. Abruptio placentae can also occur without vaginal bleeding. In these cases, blood can accumulate in large volumes and be entirely sequestered within the uterus. Therefore, the degree of vaginal bleeding may not reflect the total amount of blood loss from the placenta. (535)

92. Risk factors for uterine ruptures include prior uterine scar, rapid spontaneous delivery, motor vehicle trauma, trauma from instrumented vaginal delivery, large or malpositioned fetus, and excessive oxytocin stimulation. After previous cesarean delivery, vaginal birth is associated with a 0.4% to 1% incidence of uterine rupture. The presentation is variable, but may include vaginal bleeding, cessation of contractions, FHR deceleration, and abdominal pain normally not masked by neuraxial analgesia. Unfortunately, pain is not always a diagnostic finding. (535)

93. Retained placenta occurs when some portion of the placenta has not been spontaneously delivered within 1 hour of delivery of the fetus. Uterine bleeding continues due to the inability of the uterus to contract around adherent placenta. Approximately 1% of all vaginal deliveries are associated with some retained placenta. The treatment involves manual exploration of the uterus for the removal of retained placental parts. The anesthetic management of patients with retained placenta has as its goal uterine relaxation, as well as decreasing the pain and anxiety of the patient. Anesthetic methods that may be used to initially accomplish this typically include intravenous sedation (keeping airway reflexes intact) or dosing of a preexisting epidural catheter. If uterine relaxation is necessary, nitroglycerin (50 to 150 μg IV) is normally effective. Additionally, relocation to the operating room and placement of neuraxial analgesia may be beneficial for thorough evaluation. Rarely, induction of general anesthesia with endotracheal intubation and administration of a volatile anesthetic to provide uterine relaxation will be necessary. (535)

94. Risk factors for postpartum uterine atony include retained products, long labor, high parity, macrosomia, polyhydramnios, excessive oxytocin augmentation, and chorioamnionitis. (535)

95. The treatment of uterine atony is by the administration of agents that increase uterine tone. Oxytocin (20 to 40 U/L) is normally the initial treatment. This dilute solution of oxytocin exerts minimal cardiovascular effects, but rapid intravenous injection is associated with tachycardia, vasodilation, and hypotension. Methylergonovine (0.2 mg IM) is an ergot derivative. Due to the significant vasoconstriction, it is relatively contraindicated in preeclamptics and patients with cardiac disease. The prostaglandin F2α (0.25 mg IM) is associated with nausea, tachycardia, pulmonary hypertension, desaturation, and bronchospasm. It should be avoided in asthmatics. Prostaglandin E1 (600 μg oral/sublingual/rectal) has no significant cardiac effects, but may cause hyperthermia. (535)

96. Placental implantation beyond the endometrium gives rise to (1) placenta accreta vera, which is implantation and adherence onto the myometrium;

(2) placenta increta, which is implantation into the myometrium; and (3) placenta percreta, which is penetration through the full thickness of the myometrium. With placenta percreta, implantations may occur onto bowel, bladder, ovaries, or other pelvic organs and vessels. (535-536, Figure 33-7)

97. In patients with placenta previa and no previous cesarean delivery, the incidence of accreta is approximately 3%. However, the risk of placenta accreta associated with placenta previa increases with the number of previous cesarean deliveries. With one previous uterine incision, the incidence of placenta accreta has been reported to be 11%, with two previous uterine incisions the rate is 40%, and with three or more prior uterine incisions, the incidence rises to more than 60%. (536)

AMNIOTIC FLUID EMBOLISM

98. The incidence of amniotic fluid embolism (AFE) is estimated between 1:20,000 and 1:80,000. Clinical features of AFE include the sudden onset of hypotension, respiratory distress, hypoxia, disseminated intravascular coagulopathy, altered mental status, and eventual maternal collapse. These signs must be differentiated from other more common morbidities of pregnancy and delivery, such as inhalation of gastric contents, air embolism, pulmonary thromboembolism, high spinal, anaphylaxis, and local anesthetic toxicity. (536)

99. The exact cause and pathogenesis of AFE remains uncertain, but it is thought to be a type of anaphylactoid reaction. The diagnosis of AFE is a clinical diagnosis of exclusion. Although in the past it had been believed that aspirating amniotic fluid debris such as fetal squamous cells from the maternal pulmonary circulation was diagnostic, the presence of fetal squames has been demonstrated in asymptomatic pregnant women, and no diagnostic laboratory test for AFE currently exists. Definitive diagnosis is extremely difficult or impossible, even with postmortem examination. There is no treatment of AFE other than supportive. (536)

ANESTHESIA FOR NONOBSTETRIC SURGERY DURING PREGNANCY

100. The overall incidence of nonobstetric surgery during pregnancy is 1 in 50 to 1 in 100, with trauma, appendicitis, and cholecystitis being the most frequent causes. (536)

101. Elective procedures should be delayed until 6 weeks postpartum. When possible, nonelective operations should be delayed until after the first trimester to minimize teratogenic effects on the fetus or spontaneous abortion. The second trimester is considered the optimal time for surgical intervention, because the risk of preterm labor is lowest. In the case of acutely urgent surgical procedures, their timing should mimic that of nonpregnant patients. (536-537)

102. The critical gestational period for organogenesis occurs between 15 and 56 days of gestation. This is important because drugs that are teratogenic will exert their most disastrous effects when they are administered to the pregnant woman during this period. Most data regarding the administration of anesthetics to pregnant women in the first trimester are retrospective. There is no evidence that any of the currently used anesthetics, administered during pregnancy, are teratogenic with the exception of cocaine. Neurodegeneration and widespread apoptosis following exposure to anesthetics has been clearly established in developing animals, and a few studies demonstrate cognitive impairment in adult animals after neonatal anesthetic exposure. Currently there are no data to extrapolate these animal findings to humans, and this phenomenon is difficult to study in humans as clinical evidence is still scarce and amounts to an associative and not causal relationship. (537)

103. Intrauterine fetal hypoxia and acidosis has been associated with maternal hypotension, arterial hypoxemia, and excessive changes in the $Paco_2$. Both

hypercapnia and hypocapnia result in reduced uterine blood flow and fetal acidosis. During surgery, normocarbia should be maintained (30 mm Hg end-tidal CO_2), adequate uterine perfusion pressure maintained using fluids and vasopressors, and uterine displacement maintained if after 20 weeks gestational age to optimize uterine blood flow and fetal well-being. It is recommended that the maternal inhaled concentration of oxygen should be at least 50%. High oxygen consumption of the placenta plus the uneven distribution of maternal and fetal blood flow in the placenta prevent fetal Pao_2 from exceeding about 60 mm Hg even with high maternal arterial oxygen levels. (537)

104. FHR monitoring via Doppler is possible at 16 to 18 weeks gestational age, but variability as a marker of well-being is not established until 25 to 27 weeks. Fetal monitoring can display fetal compromise and allows further optimization of the maternal and fetal condition with in utero resuscitation maneuvers. Currently there is no evidence for the efficacy of FHR monitoring. In addition, interpretation is difficult since most anesthetics reduce FHR variability, placement and signal acquisition may be challenging, and a trained person is needed for interpretation. The decision of whether or not to monitor the fetal heart rate during nonobstetric surgery should be individualized case by case in discussion with an obstetrician and other perioperative team members. (537)

105. The usual cause of premature labor that presents in the pregnant woman after having nonobstetric surgery is the underlying pathologic process that led to the need for surgery and not the anesthetic technique. Postoperative monitoring that should be done in these circumstances, in addition to the routine monitoring, includes continuous fetal heart rate monitoring and monitoring of maternal uterine activity. Premature labor can be treated through the administration of tocolytics in consultation with an obstetrician. Common tocolytics include terbutaline, magnesium, indomethacin, and nifedipine. (537)

106. Laparoscopic surgery is as safe as an open approach during any trimester, and the indications for its use are the same as nonpregnant patients. A recent review which compared laparascopic surgery to open surgery found that the trimester did not influence the complication rate, the conversion to open was low (1%), there was a slightly higher fetal loss rate, but there was a lower preterm delivery rate. Most studies comparing laparoscopic to open techniques note no difference in fetal or maternal outcomes. (538)

DIAGNOSIS AND MANAGEMENT OF FETAL DISTRESS

107. Normal uterine activity is five contractions or less in 10 minutes, averaged over a 30-minute window. Tachysystole while tachysystole is defined as more than five contractions in 10 minutes, averaged over a 30-minute window. If a tonic contraction or period of tachysystole occurs during labor, treatment with either sublingual or IV nitroglycerin can briefly relax the uterus and restore fetal perfusion. In addition, the obstetrician can give subcutaneous terbutaline. (538, Table 33-4)

108. The normal baseline FHR is between 110 and 160 beats/min.

109. Baseline variability is determined by examining fluctuations that are irregular in amplitude and frequency during a 10-minute window excluding accelerations and decelerations. Variability is classified as follows:

- Absent FHR variability: amplitude range undetectable.
- Minimal FHR variability: amplitude range greater than undetectable and 5 beats/min or less.
- Moderate FHR variability: amplitude range 6 to 25 beats/min.
- Marked FHR variability: amplitude range more than 25 beats/min. (538)

110. A FHR acceleration is an abrupt increase in FHR defined as an increase from the acceleration onset to the peak in greater than 30 seconds. In addition, the peak

must be 15 beats/min or greater, and last 15 seconds or longer from the onset to return. Before 32 weeks of gestation, accelerations are defined as having a peak of 10 beats/min or more and a duration of 10 seconds or longer. (538)

111. Late decelerations are a result of uteroplacental insufficiency, causing relative fetal brain hypoxia during a contraction. The change results in sympathetic response and increased peripheral vascular resistance in the fetus, elevating the fetal blood pressure, which is detected by the fetal baroreceptors and results in slowing in the FHR. (539; Table 33-5)

112. Variable decelerations are generally synonymous with umbilical cord compression. (539; Table 33-5)

113. Intrapartum fetal monitoring was designed to detect hypoxia in labor and allow the clinicians to intervene prior to acidosis and long-term fetal CNS damage. The fetal brain responds to peripheral and central stimuli: (1) chemoreceptors, (2) baroreceptors, and (3) direct effects of metabolic changes within the CNS. FHR monitoring was developed as a crude, nonspecific method of tracking fetal oxygenation and distress. (538)

EVALUATION OF THE NEONATE AND NEONATAL RESUSCITATION

114. Apgar scoring system:

Characteristic	*Score = 0*	*Score = 1*	*Score = 2*
Heart rate (beats/min)	Absent	<100	>100
Breathing	Absent	Slow	Irregular, crying
Reflex irritability	No response	Grimace	Cry
Muscle tone	Limp	Flexion of the extremities	Active
Color	Cyanotic	Body pink Extremities cyanotic	Pink

(539-541, Table 33-6)

115. Umbilical cord blood gas values:

	Mean Artery	*Mean Vein*
pH	7.27	7.34
P_{CO_2}	50	40
P_{O_2}	20	30
Bicarbonate	23	21
Base excess	−3.6	−2.6

(539, Table 33-6)

116. When evaluating the neonate, if breathing and crying does not occur, then clearing of the airway (mouth then nose) and repeated stimulation should be performed. Following this, the 1-minute Apgar score is determined with evaluation of the respirations, heart rate, and color. In the event of apnea or heart rate less than 100, positive pressure hand ventilation should be provided with 21% or up to 100% oxygen using a properly fitted facemask (avoiding excessive inspiratory pressure >30 cm H_2O). Based on the current 2005 neonatal resuscitation

guidelines, if the clinician begins with room air, it is recommended that supplemental oxygen be given if no improvement is seen within 90 seconds after birth. (540-541, Figure 33-9)

117. The dose of epinephrine for neonatal resuscitation is 0.1 to 0.3 mL/kg of a 1:10,000 solution given rapidly intravenously through an umbilical artery catheter inserted just below the abdominal skin (preferred) or via the trachea. The dose may be repeated every 3 to 5 minutes, if necessary. (541)

118. Naloxone is no longer recommended for use in newborns in the delivery room. Should the newborn manifest respiratory depression in the delivery room, appropriate ventilation should be maintained until the neonate is transported to the intensive care nursery, where naloxone can be given if determined to be necessary. (542)

119. Currently, neonates at delivery with meconium-stained amniotic fluid (MSAF) who are at term and vigorous should not be suctioned at the perineum, and once delivered do not require intubation. Intubation and suctioning should be performed in MSAF neonates if they are not vigorous (heart rate <100, decreased muscle tone, and ineffectual respirations). (542)

120. The most significant advances in the prevention of meconium aspiration syndrome are improved estimation of gestational age and use of an earlier gestational age for postdates induction. (542)

Chapter

31 PEDIATRICS

Erin A. Gottlieb, Dean B. Andropoulos

DEVELOPMENTAL PHYSIOLOGY

1. How does the oxygen consumption of a neonate compare with that of an adult?
2. How does the cardiac output of a neonate compare with that of an adult?
3. Are changes in the cardiac output of a neonate more dependent on changes in the heart rate or stroke volume?
4. How does the position of the oxyhemoglobin dissociation curve in a neonate compare with that of an adult? Describe how this affects the affinity of oxygen for hemoglobin. At what age does the curve approximate that of an adult?
5. How does the hemoglobin level of a neonate compare with that of an adult? How does the hemoglobin level change as the infant progresses to 2 years old?
6. What hemoglobin level is worrisome in the newborn? What hemoglobin level is worrisome in infants older than 6 months of age?
7. At what age does the foramen ovale close? What percent of adults have a probe patent foramen ovale?
8. How well do neonates reflexively respond to hemorrhage as compared with adults?
9. How does alveolar ventilation in neonates compare with that of adults?
10. How does the tidal volume per weight in neonates compare with that of adults?
11. How does the respiratory rate in neonates compare with that of adults?
12. How does carbon dioxide production in neonates compare with that of adults? How does the $Paco_2$ in neonates compare with that of adults?
13. How does the Pao_2 change in the first few days of life?
14. How predictable is the neonate's response to hypoxia?
15. What percent body weight in neonates is contributed by the extracellular fluid volume? How does this compare with an adult?
16. What are some ways in which infants and children maintain normal body temperature? Why is maintenance of normal body temperature more difficult in neonates and children than in an adult?
17. How effective is kidney function at birth? When does kidney function become approximately equivalent to that of an adult?
18. After fluid restriction, what is the maximum urine osmolarity possible for term neonates at birth? At what age are adult levels of urine concentrating abilities achieved?

PHARMACOLOGIC DIFFERENCES

19. What are some physiologic characteristics of neonates that explain the pharmacologic differences between pediatric and adult responses to drugs?
20. How is the uptake and distribution of inhaled anesthetics different in neonates and infants when compared with adults?
21. How does the minimum alveolar concentration (MAC) of inhaled anesthetics change from birth to puberty?

22. What is the effect of intracardiac shunting on the rapidity of anesthesia induction with halogenated anesthetic gases?
23. What physiologic factors increase the sensitivity of neonates to the effects of intravenous anesthetics?
24. How does the dose of thiopental change between neonates and adults?
25. How does the rate of plasma clearance of opioids differ between neonates and adults?
26. Are neonates more or less sensitive to nondepolarizing neuromuscular blocking drugs than adults? How does the initial drug dose differ between these two groups?
27. How does the duration of action of nondepolarizing neuromuscular blocking drugs differ between neonates and adults?
28. How does the dose of neostigmine necessary to antagonize neuromuscular blockade in the neonate compare with the dose necessary in the adult? How does this affect clinical practice?
29. How does the dose of succinylcholine necessary to produce neuromuscular blockade in the infant and neonate compare with the dose necessary in the adult?

FLUIDS AND ELECTROLYTES

30. What is the recommendation for fluid maintenance and replacement in the pediatric population?
31. What is the goal for urine output when monitoring the intraoperative volume status of the pediatric patient?
32. When should glucose administration be considered in the pediatric population?
33. What is the preferred crystalloid fluid to replace intraoperative losses and compensate for any preoperative fluid deficit?
34. What is a reasonable approach to replace preoperative fluid deficits in pediatric patients?
35. How are third-space losses and fluid replacement estimated according to the degree of invasiveness of the surgery? How does this contribute to an overall fluid management strategy for pediatric patients?

TRANSFUSION THERAPY

36. What formula can be used to help guide the anesthesiologist with blood loss replacement?
37. What is the transfusion threshold for packed red blood cells (PRBC) in pediatric patients? What is the expected hemoglobin increase with PRBC transfusion? What special precautions are needed for PRBC transfusion in neonates and young infants?
38. What is the indication for a platelet transfusion in pediatric patients, and what is the expected response to platelet transfusion?
39. What is the usual indication for transfusion of fresh frozen plasma (FFP) in pediatric patients? What is the expected response to FFP administration?
40. What is the usual indication for administration of cryoprecipitate in pediatric patients? What is the expected response to cryoprecipitate administration?
41. What are some other pharmacologic agents that will either reduce blood loss or help achieve hemostasis with major blood loss surgery in pediatric patients?

THE PEDIATRIC AIRWAY

42. What is the leading cause of difficult airway management in infants and young children? What are some genetic syndromes that cause this condition?
43. What is the general approach to the difficult pediatric airway, and how does it differ from the adult difficult airway?

PREANESTHETIC EVALUATION AND PREPARATION

44. What history should be obtained from a preoperative evaluation of a pediatric patient? What are some considerations that are specific to the pediatric population with regard to the history and physical examination?

45. What preoperative laboratory data may be important in the pediatric population?
46. What are the recommendations for the preoperative ingestion of solids and clear liquids for pediatric patients?
47. What are some considerations regarding the choice of premedicant in the pediatric patient? What are some drugs and their routes of administration for preoperative medication in the pediatric population?

INDUCTION AND MAINTENANCE OF ANESTHESIA

48. How can the induction of anesthesia be achieved in pediatric patients without an intravenous catheter in place?
49. What are some risks of an inhaled induction of anesthesia?
50. What is the indication for the placement of an intravenous catheter in the pediatric patient undergoing a surgical procedure?
51. How can the anesthesiologist regulate the intravenous fluids to be administered in the pediatric patient?
52. How can the induction of anesthesia be achieved in pediatric patients with an intravenous catheter in place?
53. How can the induction of anesthesia be achieved in pediatric patients without an intravenous catheter in place and in whom an inhalation induction is not possible?
54. What is the concern regarding the use of succinylcholine in pediatric patients? What are some alternatives that may be used?
55. Under what circumstances is succinylcholine accepted for use for neuromuscular blockade in the pediatric population?
56. What are some physiologic characteristics of the pediatric airway that differ from the adult airway?
57. Why has the classic teaching that uncuffed endotracheal tubes should be used for intubating the trachea of pediatric patients under the age of 8 years changed?
58. What is the benefit of the administration of heated and humidified gases or using a condenser humidifier in children undergoing prolonged operations?
59. What are some signs the clinician may use to determine the adequacy of the depth of anesthesia for surgery in the pediatric population?
60. When hypotension accompanies the administration of volatile anesthetics to neonates, what is it likely to be indicative of?
61. How does intraoperative monitoring in the pediatric population differ from intraoperative monitoring in the adult population?
62. What problem may be encountered with the monitoring of end-tidal carbon dioxide concentrations in pediatric patients?
63. How should the size of a blood pressure cuff be selected? What errors in blood pressure measurement may be encountered with an erroneously sized cuff?
64. What veins may be used to monitor the central venous pressure in the neonate? In infants? In children?
65. What are some regional anesthetic blocks that can be administered in the pediatric population?
66. What local anesthetic and what dose is commonly used in a caudal anesthetic? What is the approximate duration of the postoperative pain relief obtained from this caudal anesthetic? How is the length of the dural sac different in children and adults?

THE POSTANESTHESIA CARE UNIT

67. Are most pediatric patients extubated “awake” or “deep”? What are some of the clinical implications of awake and deep extubation techniques?
68. What is emergence delirium?
69. How can pain be assessed in pediatric patients in the postanesthesia care unit?
70. What are some risk factors for postoperative nausea and vomiting in the pediatric population?

MEDICAL AND SURGICAL DISEASES THAT AFFECT PEDIATRIC PATIENTS

71. What is respiratory distress syndrome?
72. What are some physiologic complications that result from respiratory distress syndrome?
73. How should neonates with respiratory distress syndrome be managed intraoperatively?
74. What is bronchopulmonary dysplasia? What are some characteristic findings in these patients?
75. What is retinopathy of prematurity? What is another name for this pathologic finding?
76. What is a risk factor for retinopathy of prematurity? At what age does the risk of retinopathy of prematurity become negligible?
77. What Pa_{O_2} should be maintained during anesthesia in the premature neonate to minimize the risk of retinopathy of prematurity?
78. Patients of what age are at risk of apnea spells in the postoperative period? What is the recommendation for these patients in the postoperative period?
79. Which pediatric patients are at risk of hypoglycemia?
80. What are some manifestations of hypoglycemia in this population? How do these manifestations change with general anesthesia? What is the immediate treatment of hypoglycemia in these patients?
81. Which pediatric patients are at risk of hypocalcemia?
82. When might hypocalcemia occur intraoperatively? How might intraoperative hypocalcemia manifest?
83. What is the incidence of malignant hyperthermia in the pediatric population? What is the incidence in the adult population?
84. What is the association between malignant hyperthermia and the calcium ion channel?
85. What are some anesthetic triggering drugs for malignant hyperthermia?
86. What are some clinical signs of malignant hyperthermia?
87. What is the treatment of malignant hyperthermia?
88. How can the patient at risk for malignant hyperthermia be identified preoperatively?
89. Which anesthetic regimen is reliably safe for patients susceptible to malignant hyperthermia? Name some drugs used in anesthesia that have not been shown to trigger malignant hyperthermia.
90. What preparations must take place before the administration of anesthesia to patients susceptible to malignant hyperthermia?
91. Is regional anesthesia considered safe for patients at risk for malignant hyperthermia?
92. What is a congenital diaphragmatic hernia? How is a congenital diaphragmatic hernia manifest in the neonate at birth?
93. What are some comorbid conditions associated with congenital diaphragmatic hernias?
94. How is the diagnosis of a congenital diaphragmatic hernia made?
95. What is the immediate treatment for the neonate with a congenital diaphragmatic hernia? What is the risk of hand ventilation with bag and mask in these neonates?
96. What is the risk of positive pressure ventilation of the lungs of the neonate with a congenital diaphragmatic hernia?
97. What inhaled anesthetics should be avoided in neonates with a congenital diaphragmatic hernia?
98. What clinical circumstance leads to suspicion of a tracheoesophageal fistula in a neonate?
99. What are some other congenital anomalies associated with a tracheoesophageal fistula?
100. How should neonates with a tracheoesophageal fistula be managed?
101. What is pyloric stenosis? What is the incidence of pyloric stenosis per live birth?
102. How does the neonate with pyloric stenosis typically present?

103. What electrolyte imbalances are seen in infants with pyloric stenosis?
104. Is the surgical correction of pyloric stenosis in infants an elective or emergent procedure?
105. How should the induction of anesthesia in infants with pyloric stenosis proceed?
106. What is necrotizing enterocolitis, and which patients are at risk?
107. How is necrotizing enterocolitis treated, and what are some of the anesthetic considerations for this disease?
108. What are gastroschisis and omphalocele? What are the similarities and differences between these conditions?
109. How are gastroschisis and omphalocele treated surgically in the modern era? What are some of the anesthetic considerations for these conditions?
110. What is the significance of a patent ductus arteriosus (PDA) in the premature infant? What are the medical and surgical approaches to treatment?
111. What are some anesthetic considerations and pitfalls for PDA closure in the premature neonate?
112. What is myelomeningocele, and how is it managed surgically? What are some of the anesthetic considerations?

SPECIAL ANESTHETIC CONSIDERATIONS

113. In what remote locations are pediatric anesthetics commonly performed? Are the requirements for preanesthetic evaluation, monitoring, and recovery the same for these anesthetics?
114. What is the ex utero intrapartum therapy (EXIT) procedure, and what are the indications for its use? What are some of the anesthetic considerations?
115. What are some indications for fetal surgery, and what are some anesthetic considerations?
116. What anesthetic and sedative agents have been implicated in developmental neurotoxicity in animal models? Is there clinical evidence to change the practice of pediatric anesthesia?
117. What is a major consideration for former premature infants who present for surgery? How should these infants be managed postoperatively?

ANSWERS*

DEVELOPMENTAL PHYSIOLOGY

1. The oxygen consumption of a neonate is about twice that of an adult. In neonates the oxygen consumption increases from 5 mL/kg per minute at birth to about 7 mL/kg per minute at 10 days of life and 8 mL/kg per minute at 4 weeks of life. Oxygen consumption gradually declines over the subsequent months. (548, Table 34-1)

2. The cardiac output of a neonate is 30% to 60% higher than that of adults. This helps to meet the increase in oxygen demand neonates have as compared with adults. (549)

3. Changes in the cardiac output of a neonate or infant are dependent on changes in the heart rate, because stroke volume is relatively fixed by the lack of distensibility of the left ventricle in this age group. The neonate's myocardium depends heavily on the concentration of ionized calcium, such that hypocalcemia can significantly depress myocardial function. (549)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

4. In neonates, the oxyhemoglobin dissociation curve is shifted to the left. This reflects a P_{50} lower than 26 mm Hg, meaning that less of a Pao_2 is required for a 50% saturation of hemoglobin. Conversely, the oxygen is more tightly bound to hemoglobin in neonates, necessitating a lower Pao_2 for release of oxygen to the tissues. This occurs as a result of fetal hemoglobin. The position of the oxyhemoglobin dissociation curve becomes equal to that of adults by 4 to 6 months of age. (550)

5. The hemoglobin level of a neonate is approximately 17 g/dL. This, along with the increase in cardiac output, helps to offset the increase in oxygen requirements characteristic of neonates. At 2 to 3 months of age the hemoglobin of infants decreases to about 11 g/dL during the time period when fetal hemoglobin is being replaced by adult hemoglobin. This is termed the *physiologic anemia of infancy*, which may persist for a few months. During the remainder of the first year of life the hemoglobin level gradually increases and continues to do so until puberty, when hemoglobin levels approach adult hemoglobin levels. (550)

6. A hemoglobin level of 13 g/dL or less is worrisome in the newborn. In infants older than 6 months of age, a hemoglobin level less than 10 g/dL is worrisome. (550)

7. The foramen ovale closes between 3 and 12 months of age. Twenty to thirty percent of adults have a probe patent foramen ovale. (549)

8. Because of the decreased ability of neonates to vasoconstrict in response to hypovolemia, neonates are less able to tolerate hemorrhage with vasoconstrictive responses. (549)

9. Alveolar ventilation in neonates is 4 to 5 times higher than that of adults. (547, Table 34-1)

10. Tidal volume per weight in neonates is similar to that of adults. (547, Table 34-1)

11. The respiratory rate in neonates is three to four times higher than that of adults. (547, Table 34-1)

12. Carbon dioxide production in neonates is higher than that of adults. The $Paco_2$ in neonates is similar to that of adults, despite the increase in production. This is due to the increase in alveolar ventilation in neonates when compared with adults. (547, Table 34-1)

13. The Pao_2 in the first few days after birth increases rapidly. The initially low Pao_2 is due to a decrease in the functional residual capacity and to the perfusion of alveoli filled with fluid. The functional residual capacity of neonates increases over the first few days of life until it reaches adult levels at about 4 days of age. (547, Table 34-1)

14. The neonate's response to hypoxia is somewhat unpredictable, owing to the immaturity of the central nervous system's regulatory centers for ventilation in this age group. Neonates have decreased ventilatory responses to hypoxemia and hypercarbia. (547)

15. Extracellular fluid volume accounts for approximately 40% of the body weight of the neonate at birth. This compares with approximately 20% of body weight in adults being accounted for by extracellular fluid volume. The proportion of extracellular fluid volume to body weight in neonates approaches the adult proportion by 18 to 24 months of age. (552)

16. Some ways in which infants and children maintain normal body temperature include the metabolism of brown fat, crying, and vigorous movements. The metabolism of brown fat is stimulated by circulating norepinephrine. Children and infants, unlike adults, do not shiver to maintain their body temperature. Maintenance of normal body temperature is more difficult in neonates and infants than in adults because of their larger body surface area-to-volume ratio, as well as the relative lack of fat for insulation. (556)

17. Kidney function at birth is immature. There is a decreased glomerular filtration rate, decreased sodium excretion, and decreased concentrating ability relative to that of an adult. Kidney function progressively matures over the first 2 years of life. Initially, in the first 3 months of life, kidney function increases rapidly to double or triple the glomerular filtration rate possible at birth. Kidney function then matures more slowly from 3 months to 24 months, when adult levels of kidney function are reached. (550)

18. After fluid restriction, the term neonate at birth can only concentrate urine to a maximum osmolarity of about 525 mOsm/kg. After 15 to 30 days of age, neonates are able to concentrate their urine to a maximum osmolarity of about 950 mOsm/kg. Adult levels of urine concentrating ability are achieved by 6 to 12 months of age. (550)

PHARMACOLOGIC DIFFERENCES

19. Some physiologic characteristics of neonates that explain the pharmacologic differences between pediatric and adult responses to drugs include an increased extracellular fluid volume, increased metabolic rate, decreased renal function, and decreased receptor maturity. (550, 551)

20. The uptake and distribution of inhaled anesthetics is more rapid in neonates than in adults. This is most likely due to a smaller functional residual capacity per body weight in neonates, as well as to greater tissue blood flow to the vessel-rich group. The vessel-rich group of tissues includes the brain, heart, kidneys, and liver. This group comprises approximately 22% of total body volume in neonates, as compared with the 10% of total body volume in adults. (551)

21. The minimum alveolar concentration (MAC) of inhaled anesthetics changes from birth to puberty. Preterm neonates have a lower MAC than term neonates, whose MAC is approximately 0.87% that of adults. The MAC of inhaled anesthetic agents is highest in infants 1 to 6 months old. The MAC is 30% less in full-term neonates for isoflurane and desflurane. Sevoflurane MAC at term is the same as at age 1 month. (551)

22. Patients with right-to-left intracardiac shunting have a slower inhaled induction of anesthesia, due to the volume of blood bypassing the lungs and not increasing its anesthetic level. This results in a slower rise in the arterial level of the anesthetic and a slower induction. This effect is most pronounced with less-soluble agents, such as desflurane and sevoflurane, and less pronounced with more-soluble agents, such as halothane and isoflurane. Left-to-right intracardiac shunts have little or no effect on the rapidity of induction. (551)

23. Physiologic factors that make neonates more sensitive to the effects of intravenous anesthetics include an immature blood-brain barrier and a decreased ability to metabolize drugs. They are more sensitive to highly protein-bound drugs because of the lower serum albumin and protein concentrations in neonates. In many cases the increased extracellular fluid volume and volume of distribution present in neonates offsets the increased sensitivity to intravenous drugs when compared with adults, thereby approximately equalizing the dose of initial intravenous injection of drug to achieve a given result. (550-551)

24. The dose of thiopental required to produce loss of lid reflex is similar in neonates, children, and adults. (551)

25. The rate of plasma clearance of opioids is decreased in neonates when compared with adults. (551)

26. Neonates are more sensitive than adults to nondepolarizing neuromuscular blocking drugs. This means that a lower plasma concentration of drug is required to produce similar pharmacologic results. Because of an increased extracellular fluid volume and increased volume of distribution in neonates when

compared with adults, the initial dose of nondepolarizing neuromuscular blocking drug in these two age groups is similar. This is true despite the increased sensitivity to the drug for neonates. (551)

27. The duration of action of nondepolarizing neuromuscular blocking drugs in neonates may be prolonged while the mechanisms for clearance are still immature in the neonate. For example, the clearance of *d*-tubocurarine parallels the glomerular filtration rate at various ages. There exists a great deal of variability among pediatric patients with regard to the duration of effect of nondepolarizing neuromuscular blocking drugs. Monitoring of the neuromuscular junction with a peripheral nerve stimulator is recommended when nondepolarizing neuromuscular blocking drugs are administered to this population. (551)

28. The dose of neostigmine necessary to antagonize neuromuscular blocking drugs in the neonate is less than that of adults, although clinically the same dose may be used. (551)

29. The dose of succinylcholine per body weight necessary to produce neuromuscular blockade in the neonate and infant is increased from the adult dose. This is presumed to be due to the increase in extracellular fluid volume and increase in volume of distribution in neonates and infants. (551)

FLUIDS AND ELECTROLYTES

30. Fluid maintenance and replacement in the pediatric population is based on the patient's age and metabolic rate, underlying disease process, type and extent of surgery, and anticipated fluid translocation. The maintenance rate of pediatric patients is related to their metabolic demand, which in turn is related to the ratio of body surface to weight. Hourly fluid requirements are estimated to be 4 mL/kg for children up to 10 kg, an additional 2 mL/kg for each kilogram of body weight between 10 kg and 20 kg, and an additional 1 mL/kg for each kilogram of body weight above 20 kg. Additional fluid replacement may be required for the patient's initial fluid deficit, third-space losses, or other losses. Fluid replacement can be guided by the patient's systemic blood pressure, tissue perfusion, and urine output. (552, Table 34-3)

31. A goal for urine output when monitoring the intraoperative volume status in the pediatric patient is 0.5 to 1 mL/kg/hr. (552)

32. Glucose administration in the pediatric patient can be considered in patients who are at a high risk for hypoglycemia. Pediatric patients at a high risk for hypoglycemia include newborns of diabetic mothers or neonates whose hyperalimentation has been discontinued. Maintenance fluids of 5% dextrose in 0.45 normal saline can be administered to these patients intraoperatively as a piggy-back infusion by pump with care not to bolus glucose-containing solutions. (552-553)

33. Nonglucose containing isotonic fluids are most appropriate to replace losses. These include lactated Ringer solution and Plasma-lyte A, which both contain physiologic levels of sodium and potassium. Normal saline can be used, but with supraphysiologic levels of sodium and chloride, a hyperchloremic, hypernatremic, metabolic acidosis can occur with the administration of large volumes. (552)

34. Preoperative fluid deficits in the pediatric patient can be estimated by multiplying the number of hours the patient has been NPO by the hourly maintenance fluid requirement based on the 4-2-1 rule. Replace 50% of this deficit in the first hour, and the remaining 50% in the second hour. Minimizing preoperative fluid deficits by allowing clear liquids to be ingested orally up to 2 hours before surgery is an effective strategy to minimize preoperative deficits. (552)

35. For minimally invasive surgery, third-space losses are estimated to be 0 to 2 mL/kg/hr. This includes superficial surgery such as strabismus repair. For mildly invasive surgery such as ureteral reimplantation, these losses are estimated at 2 to 4 mL/kg/hr. For moderately invasive surgery such as elective bowel reanastomosis, fluid losses are estimated at 4 to 8 mL/kg/hr; and for maximally invasive surgery such as bowel resection for necrotizing enterocolitis, fluid losses are estimated to be 8 to 10 mL/kg/hr or greater. To this hourly fluid administration is added the maintenance fluid requirement according to the 4-2-1 rule, the preoperative fluid deficit as noted previously, and replacement for blood loss. The latter is replaced with 3 mL of isotonic crystalloid for each milliliter of estimated blood loss, or 1 mL of colloid such as 5% albumin for each milliliter blood loss, or milliliter for milliliter of blood product such as packed red blood cells. (552-553, Table 34-3)

TRANSFUSION THERAPY

36. A formula that may be used by the anesthesiologist to help guide blood loss replacement is:

$$\text{MABL(mL)} = \text{EBV(mL)} \times (\text{patient Hct} - \text{minimum acceptable Hct})/\text{patient Hct}$$

MABL, maximum allowable blood loss; EBV, estimated blood volume; Hct, hematocrit. The estimated blood volume is between 70 mL/kg at about 5 years of age to 100 mL/kg in the premature newborn. This formula should be applied to the pediatric patient prior to surgery so that when the threshold is reached, it is immediately recognized and the transfusion initiated. (553)

37. The pediatric patient's transfusion threshold varies greatly according to the patient's underlying physiology, age, nature of the surgery, and anticipated ongoing blood loss, and must be individualized. For patients with cyanotic heart disease, a hemoglobin threshold of 12 to 13 g/dL is often used. For otherwise healthy acyanotic patients, a lower threshold of 7 to 8 g/dL is often used; 10-15 mL/kg of PRBC should increase hemoglobin by 2 to 3 g/dL. Leukocyte reduction and irradiation of PRBCs minimizes the risk of cytomegalovirus transmission, graft versus host reaction, and HLA allosensitization. These procedures are used for infants less than 4 months, immunocompromised patients, and transplant or potential transplant recipients. (553)

38. The usual indication for platelet transfusion in a pediatric patient is a platelet count below 50,000 to 100,000/dL, accompanied by surgical bleeding; 5 to 10 mL/kg of platelet concentrate transfusion should increase platelet count by 50,000 to 100,000/dL. (553)

39. Indications for FFP administration in pediatric patients include massive transfusion resulting in markedly reduced levels of coagulation proteins and hemodilution from cardiopulmonary bypass in small infants. Ten to fifteen milliliters per kilogram of FFP will increase most coagulation factors by 15% to 20%, which is often sufficient to improve hemostasis. (553)

40. Indications for cryoprecipitate administration in pediatric patients most often are low fibrinogen concentrations from massive hemorrhage or dilution from cardiopulmonary bypass. One unit of cryoprecipitate administered per 5 kg of patient weight is normally sufficient to restore adequate fibrinogen levels. (553)

41. The lysine analogs ϵ-aminocaproic acid and tranexamic acid reduce fibrinolysis by inhibiting plasmin. Recombinant factor VIIa is used for patients with factor VII deficiency or hemophiliacs with inhibitors to factors VIII and IX. It is also used in cases of massive hemorrhage such as cardiac surgery or trauma, as a life-saving measure to reduce bleeding. This agent causes a "thrombin burst" when exposed to tissue factor, resulting in massive activation of the coagulation cascade. Thrombotic complications have been reported with recombinant factor VIIa. (553)

THE PEDIATRIC AIRWAY

42. Micrognathia is the single most common cause of difficult mask ventilation and tracheal intubation in young pediatric patients. The preoperative airway assessment in children should involve visual inspection for micrognathia, as well as midface hypoplasia or other cranio-facial abnormalities. Pierre-Robin sequence, Goldenhar, and Treacher-Collins syndromes are the most commonly encountered conditions resulting in micrognathia. (554)

43. The approach to the difficult pediatric and adult airway is generally similar: maintain spontaneous respiration; use adjuncts such as the laryngeal mask airway, videolaryngoscope, or fiber-optic bronchoscope to secure the airway; awaken the patient if possible if the airway cannot be secured; avoid neuromuscular blockade until the airway is secured; and have surgical backup for emergency tracheostomy for particularly difficult cases. The major difference between managing the pediatric versus adult airway is that young pediatric patients will not tolerate an "awake" intubation with topical anesthesia of the airway; they must have some level of moderate to deep sedation or general anesthesia. Also, cricothyrotomy is technically difficult in small patients and ventilation via this method ineffective. Thus, this method cannot be used in young pediatric patients. (554)

PREANESTHETIC EVALUATION AND PREPARATION

44. The preoperative history in the pediatric patient often comes from a parent. The history obtained should include such things as congenital anomalies, allergies, bleeding tendencies, and any recent exposure to communicable diseases. A special consideration for the pediatric population is whether the patient has had any recent upper respiratory tract infection, which makes it more likely that the patient will have increased secretions and airway hyperreactivity with anesthesia. Elective surgeries may be delayed in the presence of an upper airway infection. With regard to the airway examination, the presence of loose teeth should be evaluated, and removal of the loose tooth or teeth before airway manipulation should be considered. (555)

45. Laboratory data are typically unnecessary in the routine pediatric patient. Laboratory data should be ordered based on abnormalities in the history and physical examination. Urine pregnancy testing is practiced for menstruating females in many institutions. (555)

46. The recommendations for the preoperative consumption of solids and clear liquids are now standardized. Clear liquids are generally allowed up to 2 hours before induction of anesthesia, breast milk up to 4 hours before induction, and milk or formula allowed up to 6 hours before induction. Solid foods should not be ingested sooner than 6 to 8 hours before anesthesia. These guidelines apply to all ages of pediatric patients. (555-556)

47. Premedication of the pediatric patient should take into consideration the age of the patient, the patient's underlying medical condition, the length of surgery, the mode of induction of anesthesia, and whether the patient will be staying in the hospital after the procedure. Infants younger than 6 months old typically do not require premedication, whereas patients between 9 months and 5 or 6 years old may benefit from premedication before separation from their parents. Premedicants may be administered orally, intravenously, intramuscularly, rectally, sublingually, transmucosally, or intranasally; however, the oral route is strongly preferred. One drug available and commonly used for premedication in the pediatric population is oral midazolam. (556)

INDUCTION AND MAINTENANCE OF ANESTHESIA

48. In the pediatric patient without an intravenous catheter, anesthesia can be induced via inhalation. An inhalation induction can be achieved by initially having the child breathe 70% nitrous oxide and 30% oxygen, followed by incremental increases in the concentration of a volatile anesthetic. The only volatile anesthetic

available for inhalation induction in the United States is sevoflurane, because it is much less pungent than the other volatile anesthetics. Other adjuncts that may be used to decrease patient anxiety and facilitate the induction of anesthesia under these circumstances include having the parents present during the time of induction, flavoring the anesthesia mask with pleasant scents, and maintaining a constant monotone conversation with the patient. A story can be told by the anesthesiologist to distract the patient during induction. (557)

49. An inhaled induction of anesthesia has some inherent risks. First, while the pediatric patient is being induced, the anesthesiologist often increases concentrations of the volatile anesthetic to dangerous inspired concentrations of volatile anesthetic if maintained. Once anesthesia is induced it is important to reduce the inspired concentrations of volatile anesthetic to routine maintenance levels. This is especially true just before intubating the trachea, because connection of the circuit and ventilating the intubated patient with high inspired concentrations of volatile anesthetic while potentially distracted with endotracheal tube positioning is a risk. High inspired concentrations of volatile anesthetic, if continued, can lead to myocardial depression that is difficult to reverse. Another risk of an inhaled induction of anesthesia is that of laryngospasm. Laryngospasm, along with coughing, vomiting, and involuntary movement, can occur in stage 2 (the excitement phase) of induction of anesthesia. Laryngospasm is accompanied by a rocking-boat motion of the chest and abdomen as the patient attempts to inspire against a closed glottis. Laryngospasm should be treated by closing the pop-off valve and creating positive-pressure of about 10 cm H_2O against the glottis. If necessary, positive pressure ventilation can be attempted. In most circumstances these will reverse the laryngospasm and the patient will spontaneously ventilate. Should these two interventions not reverse the laryngospasm, succinylcholine can be administered intravenously or intramuscularly. Succinylcholine is the neuromuscular blocking drug of choice under these circumstances. (557)

50. The placement of an intravenous catheter should be done in every pediatric patient undergoing a surgical procedure other than for very short surgical procedures. (557)

51. The administration of intravenous fluids in pediatric patients can be regulated by the use of a calibrated drip chamber yielding 60 drops/mL, and filled with only 50 to 100 mL of IV fluid, so as to minimize the risk that excessive amounts of fluid are accidentally administered. (552)

52. In the pediatric patient with an intravenous catheter, the induction of anesthesia can be achieved by the intravenous administration of an induction agent such as thiopental or propofol. This is the induction method of choice in patients at risk for the aspiration of gastric contents. (557)

53. Another method of induction in the pediatric patient without an intravenous catheter and in whom an inhalation induction is not possible is by the intramuscular administration of ketamine. This method of induction is used most commonly in developmentally delayed or severely uncooperative children. (557)

54. There are multiple concerns regarding the use of succinylcholine in pediatric patients. First, the administration of succinylcholine can result in cardiac arrhythmias, including bradycardia and, rarely, cardiac sinus arrest. The pretreatment of pediatric patients with atropine may reduce succinylcholine-induced bradycardia. Second, it is believed that in patients who have been administered succinylcholine and have subsequent masseter muscle rigidity, there may be impending malignant hyperthermia. Finally, there have been reports of pediatric patients who were otherwise healthy and went into irreversible cardiac arrest after the administration of succinylcholine. Many of these patients had

hyperkalemia, rhabdomyolysis, and acidosis. It is postulated that these pediatric patients may have had undiagnosed myopathies. Postmortem muscle biopsies have shown many of them to have muscular dystrophy. The group at highest risk of this catastrophic event are males 8 years of age or younger. Because of these concerns, there is now a "black box warning" by the U.S. Food and Drug Administration prohibiting routine use of succinylcholine in pediatric patients. It is only indicated for airway emergencies, such as laryngospasm or rapid sequence induction. Some alternatives that may be used are the nondepolarizing neuromuscular blocking drugs, such as larger doses of vecuronium or rocuronium. (557)

55. Succinylcholine is accepted for use for rapid onset neuromuscular blockade in pediatric patients for the treatment of laryngospasm and in patients at high risk for aspiration of gastric contents in whom rapid sequence induction/intubation is indicated. (557)

56. There are multiple physiologic differences between the pediatric airway and the adult airway. Pediatric patients tend to have a larger tongue relative to the size of their mouths. Particularly true in neonates is that the occiput is larger, so that placing the head in the neutral position naturally places the head in a position favorable for direct laryngoscopy. Extending the head can make direct laryngoscopy difficult. The larynx is more cephalad in pediatric patients, with the cricoid cartilage opposing the C4 vertebra rather than the C6 vertebra as in adults. The larynx is also more anterior. The epiglottis is longer, stiffer, and U shaped and has more of a horizontal lie. The narrowest point of the airway is at the level of the cricoid cartilage in the presence of neuromuscular blockade. These differences between the pediatric airway and the adult airway are present until about the age of 8 years, after which the difference between the pediatric airway and the adult airway is mainly just a difference in size. (554)

57. Because the narrowest point of the pediatric airway is at the level of the cricoid cartilage, it was believed that an endotracheal tube that passes easily through the larynx may cause ischemia or damage to the trachea distally. However, recent imaging studies challenge this notion, and the difference in diameter between the larynx and subglottis in younger children is minimal. Historically, uncuffed tubes were the standard of care in children younger than 8 years of age owing to concerns about subglottic stenosis and postextubation stridor. However, with the introduction of tubes with high volume–low pressure cuffs, recent studies suggest that there is no increased risk of airway edema with cuffed endotracheal tubes and that the use of cuffed endotracheal tubes may decrease the number of laryngoscopies and intubations due to inappropriate tube size. The risk of postintubation tracheal edema is greatest in children between 1 and 4 years of age, whether a cuffed or uncuffed ETT is used. Postintubation tracheal edema/croup can be treated with humidified gases and aerosolized racemic epinephrine. Dexamethasone has also been administered intravenously for the treatment of postintubation tracheal edema. (554)

58. Because of their larger surface area to weight ratio, infants tend lose body heat much more rapidly than adults. This is particularly true in a cold operating room environment. The administration of heated and humidified gases or use of a condenser humidifier in children undergoing prolonged operations is useful in decreasing intraoperative heat loss and in avoiding decreases in body temperature. Warming the operating room, the use of radiant warmers, and warmed intravenous fluids are other methods of maintaining normothermia. (554)

59. Signs for the adequacy of depth of anesthesia for surgery are the same for neonates, infants, and children as they are in adults. Those signs include blood pressure, heart rate, and skeletal muscle movement. Processed electroencephalographic technologies may be used as in the adult population, but are less reliable in younger children. (556)

60. Hypotension in the neonate that accompanies the administration of volatile anesthetics is likely to be indicative of hypovolemia. (552)

61. Intraoperative monitoring in the pediatric population is not any different from intraoperative monitoring in the adult population undergoing comparable surgical procedures. Routine monitors should include blood pressure, heart rate, electrocardiogram, peripheral oxygen saturation, capnography, anesthetic gas concentration, and temperature monitoring. (556)

62. The monitoring of end-tidal carbon dioxide concentrations in small children, infants, and neonates may be complicated by large dead space introduced between the CO_2 sampling line and the trachea by endotracheal tube connectors, condenser humidifiers, and elbow connectors at the end of the Y-piece of the anesthesia circuit. The small tidal volumes of these patients exacerbate the problem and can result in falsely low end-tidal CO_2 readings. In addition, congenital heart disease patients with right-to-left shunting will have a falsely low end-tidal CO_2 due to the blood bypassing the lungs. (556)

63. An appropriately sized blood pressure cuff is one that is greater than one third of the circumference of the limb. A blood pressure cuff that is too small will result in artificially high blood pressures. The opposite is also true, that a blood pressure cuff that is too large will result in artificially low blood pressures. (556)

64. Central venous pressure can be monitored in the neonate via an umbilical vein catheter. The internal jugular vein, femoral vein, or subclavian vein can be used for central venous pressure monitoring in neonates, infants, and children. (549)

65. There are several procedures in which regional anesthetic techniques can be considered in the pediatric population. For circumcision or hypospadias repair, a penile block may be used. For inguinal hernia repair an ilioinguinal and iliohypogastric block may be used. For femur surgery, a fascia iliaca compartment block may be used. For arm and wrist surgery a brachial plexus block may be used. Intravenous regional anesthesia may also be used in the pediatric patient for tendon laceration repairs or extremity fractures. Caudal anesthesia is a common form of anesthesia and is used for postoperative pain relief in the pediatric population in whom the surgical site is below the level of the diaphragm. Conversely, a lumbar epidural anesthetic may also be used in the pediatric patient. (557, 558)

66. For caudal epidural anesthesia, the local anesthetic most commonly used is bupivacaine at a concentration of 0.125% to 0.25%, and ropivacaine at 0.1% to 0.2%. The volume is 0.5 to 1 mL/kg, up to a maximum of 20 mL. The duration of pain relief provided by this dose of local anesthetic in the caudal epidural space is 4 to 6 hours, therefore possibly providing some postoperative pain relief. The dural sac extends more caudad in children than in adults, making inadvertent intrathecal injection a possibility. The risks of caudal epidural anesthesia are minimal. (557)

THE POSTANESTHESIA CARE UNIT

67. It is common practice in pediatric anesthesia to extubate the trachea of the patient during deep anesthesia. The advantage of extubating the trachea during deep extubation is that emergence from anesthesia without a tracheal tube in place avoids coughing and straining on surgical suture lines, as removal of the endotracheal tube is prior to the return of airway reactivity. The decision of when to extubate the trachea is made on a case-by-case basis, however. In some cases airway reflexes are preferred to have returned prior to tracheal extubation, as in patients at risk for the aspiration of gastric contents or with blood and secretions in the airway. (557)

68. Emergence delirium refers to a dissociated state of consciousness that occurs while waking from anesthesia. It occurs more frequently in the pediatric population after anesthesia with sevoflurane or desflurane. During this time the pediatric patient is inconsolable, irritable, incoherent, and/or uncooperative.

The patient may be crying, moaning, kicking, and restless. During this time there may be accidental removal of intravenous catheters, surgical bandages, and drains. During emergence delirium, children usually do not recognize or identify familiar and known objects or people. Emergence delirium is generally self-limiting, and typically lasts only about 5 to 15 minutes. (558)

69. The assessment of pain in postoperative pediatric patients can be particularly difficult as these patients may be nonverbal. There are several scales for assessing pain, including scales that monitor for facial expressions, movement, crying, and consolability. (558)

70. Risk factors for postoperative nausea and vomiting in the pediatric patient population include age 3 years or older, strabismus surgery, duration of surgery, and previous history of postoperative nausea and vomiting in the patient or in a parent or sibling. (558)

MEDICAL AND SURGICAL DISEASES THAT AFFECT PEDIATRIC PATIENTS

71. Respiratory distress syndrome, also referred to as hyaline membrane disease, is a syndrome affecting preterm neonates who at birth have a deficiency of surfactant. Surfactant is necessary to maintain alveolar stability, so that without it alveoli collapse. Surfactant is a surface active phospholipid in the alveoli that can now be administered into the lungs of neonates for the treatment or prevention of respiratory distress syndrome. The compliance of the lung and arterial oxygenation often improve rapidly after its administration. The administration of surfactant has decreased the morbidity and mortality resulting from this syndrome. (563-565)

72. With the alveolar collapse associated with respiratory distress syndrome, there is resultant right-to-left intrapulmonary shunting, arterial hypoxemia, and metabolic acidosis. (563-565)

73. Neonates with respiratory distress syndrome should have their arterial oxygenation closely monitored intraoperatively. The Pao_2 the anesthesiologist should try to maintain in these patients is the Pao_2 level the patient had before surgery. This may require high inspired concentrations of oxygen and positive end-expiratory pressure. The Pao_2 should ideally be monitored from a preductal artery. If the surgical procedure is short and intraarterial monitoring is not feasible, oxygenation may be monitored by pulse oximetry. These neonates are at an increased risk for pneumothorax with positive-pressure ventilation. Neonates with respiratory distress syndrome should be well hydrated. It may be prudent to maintain the hematocrit near 40% to optimize the delivery of oxygen to the tissues. (564)

74. Bronchopulmonary dysplasia is a chronic pulmonary disorder in infants and children who had prolonged respiratory disease at birth, defined as the need for supplemental oxygen beyond 30 days of life after a diagnosis of respiratory distress syndrome. It is thought to result from the required high inspired concentrations of oxygen and mechanical ventilation with high peak airway pressures for a prolonged period of time as treatment for the respiratory disease. Some characteristic findings in patients with bronchopulmonary dysplasia are increased airway resistance, increased airway reactivity, decreased arterial oxygenation due to ventilation-to-perfusion mismatch, and recurrent pulmonary infections. A chest radiograph in these patients may show large lung volumes, fibrosis, and atelectasis. These patients may have chronic hypercarbia as well. The incidence of bronchopulmonary dysplasia has decreased since the advent of surfactant therapy in neonates at risk. (565)

75. Retinopathy of prematurity, also referred to as retrolental fibroplasia, is a condition in which the retinal vasculature becomes neovascularized and scarred. Permanent visual impairment can result. (564)

76. A risk factor for retinopathy of prematurity is a Pa_{O_2} greater than 80 mm Hg or an oxygen saturation greater than 94% in the presence of prematurity. Retinopathy of prematurity has occurred in neonates whose Pa_{O_2} was maintained at about 150 mm Hg for 2 to 4 hours. Neonates whose birth weights are lower than 1500 g are especially at risk. The risk of retinopathy of prematurity becomes negligible 44 weeks after conception. (564)

77. A Pa_{O_2} between 50 and 70 mm Hg or an oxygen saturation between 88% and 93% should be maintained during anesthesia in the premature neonate to minimize the risk of retinopathy of prematurity. (564)

78. Apnea spells that result in the cessation of breathing for 20 seconds or longer can lead to cyanosis and bradycardia. Especially at risk are preterm infants younger than 50 weeks postconception. It is estimated that 20% to 30% of preterm infants have apnea spells during their first month of life. Apnea spells may be increased in the neonate in the postoperative period secondary to the residual effects of inhaled and injected anesthetics that affect the control of breathing. The recommendation for these patients is that apnea and bradycardia monitors be used after surgery that will sound an alarm if apnea or bradycardia is detected in the patient. These patients are not candidates for outpatient surgery because of the risk of apnea occurring at home where health care providers are not available to respond. An alternative is to postpone nonessential surgery until infants are older than 50 weeks postconception. Treating anemia and administering a single dose of IV caffeine citrate will reduce the incidence and severity of postanesthetic apnea in this population. (565)

79. Neonates are at risk of developing hypoglycemia, particularly neonates of diabetic mothers. Hypoglycemia is defined by a plasma glucose concentration less than 40 mg/dL in the preterm neonate, less than 50 mg/dL for the term neonate younger than 3 days old, and less than 60 mg/dL in the term neonate older than 3 days of age. Neonates are at risk of hypoglycemia secondary to their poorly developed system for the maintenance of adequate plasma glucose concentrations. In addition, patients receiving total parenteral nutrition with high dextrose concentrations are at risk for hypoglycemia if the infusion is interrupted. Also, patients with poor nutritional status or liver disease often have inadequate hepatic glycogen stores and are also at risk. (552-553)

80. Manifestations of hypoglycemia in neonates include irritability, seizures, bradycardia, hypotension, and apnea. These clinical manifestations may be masked by general anesthesia, making perioperative vigilance very important; frequent analysis of blood glucose is important in patients at risk. The immediate treatment of hypoglycemia in neonates is the intravenous administration of 0.5 to 1 g/kg of glucose. (552-553)

81. Preterm neonates are at risk of developing hypocalcemia. Hypocalcemia in the neonate is defined by a plasma ionized calcium concentration less than about 1.1 mEq/dL. Fetuses develop their calcium stores during the third trimester, so that the preterm neonate has inadequate calcium stores at birth. (549)

82. Hypocalcemia might occur intraoperatively as a result of citrated blood transfusions or during an exchange transfusion. The rapid infusion of citrate that occurs with citrated blood or fresh frozen plasma transfusions can result in hypotension secondary to hypocalcemia. The hypotension can be minimized by the administration of calcium gluconate, 1 to 2 mg intravenously for every 1 mL of blood transfused. (553)

83. The incidence of malignant hyperthermia in the pediatric population has been reported to be as high as 1 in 12,000 pediatric anesthetics. However, with the virtual disappearance of the use of two of the most potent triggering agents, halothane and succinylcholine, in the pediatric population, this incidence is

now believed to be significantly lower. The incidence of malignant hyperthermia in the adult population is approximately 1 in 40,000 adult anesthetics. (555)

84. The calcium channel is important in the pathophysiology of malignant hyperthermia. There is a defect in the calcium release channel in the sarcoplasmic reticulum of the skeletal muscle, specifically the ryanodine receptor (RYR1 gene mutation is the leading cause). This defect allows for higher concentrations of calcium to be sustained in the myoplasm, resulting in persistent skeletal muscle contractions when a patient at risk for developing malignant hyperthermia is exposed to inciting anesthetic agents or drugs. The genetic coding site for malignant hyperthermia is the ryanodine receptor. (555)

85. Anesthetic triggering drugs for malignant hyperthermia include succinylcholine and volatile anesthetics, halothane being by far the most potent agent. (555)

86. Clinical signs of malignant hyperthermia are related to some of the consequences of sustained skeletal muscle contraction. These include tachycardia, arterial hypoxemia, metabolic acidosis, respiratory acidosis, and increases in body temperature. Early signs of malignant hyperthermia include tachycardia and an increase in the exhaled concentration of carbon dioxide that are otherwise unexplained. A late sign of malignant hyperthermia is the increase in body temperature. (555)

87. The primary treatment for malignant hyperthermia is dantrolene. Dantrolene inhibits the release of calcium from the sarcoplasmic reticulum. The dose of dantrolene to be administered is 2 to 3 mg/kg intravenously and repeated every 5 to 10 minutes until the symptoms are controlled. Other treatment interventions for malignant hyperthermia are directed toward supportive management. First, the inhaled anesthetic being administered should be immediately discontinued. The lungs should be hyperventilated with oxygen. For the hyperthermia, active cooling should be initiated. Active cooling may include cold saline, 15 mL/kg intravenously every 10 minutes. Gastric lavage with cold saline and surface cooling may also be used. For the severely acidotic patient, sodium bicarbonate may be administered at a dose of 1 to 2 mEq/kg intravenously, and guided by arterial pH. Diuresis of the patient should also be considered, either by hydration, mannitol, or furosemide. (555)

88. The patient at risk for malignant hyperthermia may be identified preoperatively by a detailed preoperative medical history and by a family history that especially notes any problems with anesthesia. Preoperative testing of the level of creatinine kinase is not always useful, because only about 70% of patients who are susceptible to malignant hyperthermia have increased resting levels of creatinine kinase. The definitive diagnosis of a patient's susceptibility to malignant hyperthermia requires a skeletal muscle biopsy. The skeletal muscle is then tested in vitro for isometric contracture in response to exposure to caffeine or halothane or both. This test has the highest sensitivity and specificity for MH. Recently, genetic testing for the ryanodine receptor abnormality (RYR1 mutation) has become available. This test is not as sensitive as the contracture test but is highly specific. (555)

89. No anesthetic regimen is known to be reliably safe for administration to patients who are susceptible to malignant hyperthermia. Some drugs that are used in anesthesia that have not been shown to trigger malignant hyperthermia include barbiturates, opioids, benzodiazepines, propofol, etomidate, nitrous oxide, local anesthetics, and nondepolarizing neuromuscular blocking drugs. (555)

90. It is now the consensus of many that preoperative dantrolene is not necessary in susceptible patients because general anesthesia with nontriggering agents has proven to be mostly uneventful. There are multiple preparations for the operating room before anesthetizing a patient at risk for malignant hyperthermia. The vaporizers may be removed or sealed. The soda lime should be changed, and the fresh gas outlet hose may be changed. High fresh gas flows should be maintained for

at least 20 minutes prior to the induction of anesthesia, and an expired gas analyzer should be used to confirm that traces of anesthetic gases have been purged. (555)

91. Regional anesthesia is considered safe for patients at risk for malignant hyperthermia. (555)

92. A congenital diaphragmatic hernia is a congenital defect in the diaphragm that results in the herniation of abdominal viscera into the chest. Almost all the abdominal viscera can be in the chest, including the liver and spleen. It results from the incomplete closure of the diaphragm in an embryologic stage of development of the fetus. The defect in the diaphragm is usually on the left through the foramen of Bochdalek. In the presence of a congenital diaphragmatic hernia, there is an associated hypoplasia of the lung on the ipsilateral side. The degree of hypoplasia depends on the gestational age at which the herniation occurred. Manifestations at birth include a scaphoid abdomen, respiratory distress, acidosis, and profound arterial hypoxemia. The incidence of congenital diaphragmatic hernia is about 1 in every 5000 live births. (562-563)

93. Some comorbid conditions associated with congenital diaphragmatic hernia include polyhydramnios, congenital heart disease, and pulmonary hypertension. (562-563)

94. The diagnosis of a congenital diaphragmatic hernia can be made in utero during ultrasonography of the fetus. The diagnosis at birth is confirmed by the clinical manifestations of the anomaly, by auscultation of intestines and decreased breath sounds over the affected lung area, and by chest radiograph. On the chest radiograph, loops of intestine are seen in the affected thorax, as well as a shift of the mediastinum to the opposite side. (562-563)

95. The immediate treatment of a congenital diaphragmatic hernia in a neonate involves decompression of the stomach with a nasogastric tube, endotracheal intubation minimizing hand ventilation of the lungs, and the administration of oxygen. Positive pressure when ventilating by hand with bag and mask can increase the volume of the gastrointestinal tract with air, further compromising pulmonary function by direct mechanical compression. This can lead to hypotension as well as worsening hypoxemia. The lungs should be ventilated with small tidal volumes at a rate of 60 to 150 breaths/min. Hyperventilation of the lungs with oxygen can improve pulmonary blood flow by reversing the hypoxia and acidosis. High frequency oscillatory ventilation and inhaled nitric oxide are frequently used to improve gas exchange and reduce pulmonary artery pressures. The neonate with a congenital diaphragmatic hernia in whom arterial oxygenation is difficult may require extracorporeal membrane oxygenation (ECMO) for stabilization before surgical intervention. ECMO support of these neonates has led to a decrease in the mortality of neonates with congenital diaphragmatic hernia. Surgery is often delayed in the critically ill neonate with a congenital diaphragmatic hernia while the pulmonary vascular resistance decreases. Surgery may be accomplished while on ECMO or on high-frequency oscillatory ventilation. (562-563)

96. Positive-pressure ventilation of the lungs of a neonate with a congenital diaphragmatic hernia can result in a pneumothorax on the contralateral side of the affected lung if peak airway pressures exceed 25 to 30 cm H_2O. Expansion of the hypoplastic lung after surgical correction of the congenital diaphragmatic hernia should not be attempted because of the risk of pneumothorax or other damage to the normal lung. (562-563)

97. The anesthetic management of neonates with a congenital diaphragmatic hernia undergoing a surgical procedure should include monitoring of arterial oxygenation and the avoidance of nitrous oxide. Nitrous oxide should be avoided because it can diffuse into the loops of intestine in the chest and expand the intestines further, leading to more pulmonary compromise. (562-563)

98. A tracheoesophageal fistula should be suspected when soon after birth a neonate develops cyanosis and coughing during oral feedings. The clinician should also suspect the presence of a tracheoesophageal fistula when an oral catheter cannot be passed into the stomach. The severity of illness in these patients can range from mild to severe. (561)

99. Thirty to forty percent of neonates with a tracheoesophageal fistula have associated congenital heart disease, including ventricular septal defect, tetralogy of Fallot, and coarctation of the aorta. Tracheoesophageal fistula is also a component of the VACTERL association (V for vertebral defects; A for imperforate anus, C for cardiac defects, TE for TE fistula, R for renal anomalies, and L for limb anomalies). Prematurity accompanies tracheoesophageal fistulas about 40% of the time. (561)

100. Neonates with a tracheoesophageal fistula are at risk for pulmonary aspiration, gastric distention, and difficulty with ventilation. These neonates should have a catheter placed in the esophagus to drain secretions and prevent the accumulation of fluids in the esophageal pouch. Manual positive-pressure ventilation of the lungs with a mask should be kept at a minimum to lessen the risk of gastric distention and pulmonary aspiration. When intubating the trachea of an infant with a tracheoesophageal fistula, the anesthesiologist must be careful to place the endotracheal tube distal to the level of the fistula. This can be confirmed through the auscultation of decreased breath sounds over the stomach. Some surgeons or anesthesiologists will perform a rigid or flexible bronchoscopy to diagnose the location of the fistula to aid in endotracheal tube placement. Care should be taken to avoid endobronchial intubation as well. Attention to breath sounds, chest movement with ventilation, peak inspiratory pressures, and oxygen saturation should continue throughout the surgical procedure because small movements in the endotracheal tube can lead to its malposition. (562)

101. Pyloric stenosis occurs as a result of hypertrophy of the pyloric smooth muscle. This muscle hypertrophy, in combination with edema of the pyloric mucosa, results in progressive obstruction of the pylorus. The incidence of pyloric stenosis is 1 in every 500 live births. (564)

102. The usual clinical scenario of an infant with pyloric stenosis is one of persistent vomiting in a male infant at 2 to 8 weeks of age. (564)

103. The electrolyte imbalances that are commonly seen in infants with pyloric stenosis occur as a result of the loss of hydrogen ions that is associated with persistent vomiting. These electrolyte imbalances include hyponatremia, hypokalemia, hypochloremia, and metabolic alkalosis. There is often a compensatory respiratory acidosis. (564)

104. Concerns for the anesthesiologist caring for the patient with pyloric stenosis include the metabolic abnormalities, severe dehydration, and full stomach, often with barium after a radiologic study. These all place the infant at an increased risk for morbidity perioperatively. Although pyloric stenosis is a medical emergency, surgical correction of pyloric stenosis is an elective procedure. The corrective procedure for these infants can be done after 24 to 48 hours of intravenous fluid rehydration, the correction of their electrolyte abnormalities, and suctioning on a catheter placed in the stomach. (565)

105. The induction of anesthesia in infants with pyloric stenosis should be preceded by the emptying of stomach contents with a catheter to minimize the risk of the pulmonary aspiration of gastric contents. Induction should then be done in a rapid sequence fashion with cricoid pressure. Alternatively, an awake intubation may be performed, although this is rarely practiced in the modern era. Extubation of the trachea after the procedure should only be performed when the infant is awake and vigorous because postoperative depression of ventilation is frequently seen in these infants. This may be partially due to an increase

cerebrospinal fluid pH which decreases the respiratory drive. In fact, these patients should be monitored for 12 to 24 hours postoperatively for apnea. (565)

106. Necrotizing enterocolitis is a common surgical emergency in the neonate, primarily in premature newborns. It is an intestinal mucosal ischemic injury sometimes resulting in bowel necrosis. It is seen in premature infants, with incidence inversely proportional to gestational age. Reduced mesenteric blood flow from a patent ductus arteriosus, bacterial infection, and the institution of enteral feeding all have a role in the etiology of necrotizing enterocolitis. (559)

107. Medical treatment of necrotizing enterocolitis includes bowel rest, antibiotics, and serial abdominal examinations and radiographs. Surgical treatment may be emergent, laparotomy, with drainage, bowel resection, and reanastomosis or creation of ostomies. Patients are often unstable and critically ill with sepsis, acidosis, coagulopathy, and pulmonary morbidity. Availability of colloids and blood products, invasive monitoring, inotropic agents, and frequent measurement of blood gases, electrolytes, ionized calcium, glucose, lactate, and hemoglobin are important anesthetic considerations in managing patients with necrotizing enterocolitis. (559-560)

108. Gastroschisis and omphalocele are both abdominal wall defects usually diagnosed in utero by ultrasound, requiring treatment in the neonatal period. Gastroschisis is a defect where the intestines usually protrude to the right of the umbilicus and do not have a covering peritoneal sac. Infants with gastroschisis usually do not have additional associated anomalies. Omphalocele is a midline defect covered by the peritoneal sac with the umbilical cord incorporated into the defect. Patients with omphalocele often have other associated anomalies. (560)

109. Large or giant defects are now managed with a staged approach, whereby the intestines are partially reduced into the peritoneal cavity, and the edges of the defect are sutured to a synthetic "silo." The intestines are then reduced into the peritoneal cavity in several steps over days to weeks. This is followed by final surgical closure of the defect. The former approach of one stage repair has been abandoned because of the high incidence of intestinal ischemia and respiratory morbidity associated with this strategy. Anesthetic considerations include awareness of associated defects with omphalocele patients, especially congenital heart disease. Covering the defect with moist gauze, administering adequate intravenous fluid to account for very large third-space losses with exposed viscera, providing appropriate muscle relaxation, and careful attention to ventilator status as the intestines are reduced are important anesthetic considerations. (560)

110. A patent ductus arteriosus (PDA) is most often seen in premature infants, and can result in pulmonary edema, which complicates respiratory distress syndrome and prevents weaning from mechanical ventilator support. It also may "steal" systemic blood flow resulting in mesenteric ischemia and increasing the risk for necrotizing enterocolitis, hypotension, and cardiac failure from the large left-to-right shunt. Indomethacin treatment is often attempted, but this may result in platelet and renal dysfunction. (563)

111. PDA ligation is often performed at the bedside in the neonatal intensive care unit, and full monitoring including capnography must be provided. Transport to a distant operating room has a significant risk for cardiopulmonary instability. Anesthesia is usually provided with fentanyl, 25 to 50 μg/kg, with an intravenous amnestic agent or low-dose volatile anesthetic. Because the PDA is so large, it can be mistaken for the descending thoracic aorta, and the aorta may be inadvertently ligated. The anesthesiologist must monitor lower extremity perfusion, most commonly via pulse oximeter on the foot, to detect this problem. (563)

112. Myelomeningocele is a defect in the development of the neural tube, resulting in an open neural placode covered only by a thin membrane and cerebrospinal fluid. It is diagnosed in utero with ultrasound, and ranges from small lumbosacral defects with minimal neurologic sequelae, to large thoracolumbar defects with high

paraplegia. After birth, the infant is managed prone so as not to rupture the sac. Anesthesia induction involves either intubation in the lateral decubitus position or brief supine positioning on a padded gel doughnut to protect the sac. A nonlatex environment, including surgical gloves, is crucial to avoid latex sensitization. Muscle relaxants are avoided so the surgeon can evaluate motor function during the repair. The patient is managed prone during the initial days after surgery. (564)

SPECIAL ANESTHETIC CONSIDERATIONS

113. Anesthesia and sedation are delivered in the cardiac catheterization laboratories, magnetic resonance imaging and computed tomography scanners, gastrointestinal and pulmonary procedure suites, interventional radiology, radiation therapy, dental clinics, and many other locations. Magnetic resonance image (MRI) scanning in particular has undergone explosive growth and greatly increased the need for remote sedation and anesthesia services. Requirements for preanesthetic evaluation, monitoring, and recovery are identical to those for operating room surgical anesthesia. MRI-compatible anesthesia machines and monitors are available and full monitoring must be used. In particular, capnography for nonintubated, sedated patients via divided nasal cannula should be used for all sedation cases. (565)

114. The ex utero intrapartum therapy (EXIT) procedure involves partial delivery of the head, chest, and arms of the fetus to manage a severe airway or pulmonary anomaly. The fetus remains connected to the placental circulation to provide oxygenation and carbon dioxide removal during the procedure to secure the airway or manage the airway or lung mass. Indications include large airway, neck, or chest masses such as cystic hygroma, teratoma, and congenital adenomatoid malformation. Two anesthesiologists are required, one for the mother and one for the fetus. The mother requires deep inhalational general anesthesia to reduce uterine tone during the fetal procedure to prevent placental separation. The fetus receives intravenous or intramuscular fentanyl or morphine for analgesia. Resection of the mass or securing the airway by rigid bronchoscopy or tracheostomy is the primary goal. Then, the fetus is delivered. (565-566)

115. Multiple trials of open fetal surgery have been attempted, including congenital diaphragmatic hernia, posterior urethral valves, lung masses, and myelomeningocele. In open fetal surgery mother and fetus are anesthetized, a hysterotomy is done, the fetus exteriorized, the surgery done, and then the fetus returned to the uterus to be delivered as close to term as possible. Two anesthesiologists are required, one for the mother and one for the fetus. Most trials of fetal surgery have not resulted in improved outcomes. However, meningomyelocele repair in utero results in better overall functional outcomes, and so is likely to be increasingly performed. (566)

116. In animal models, agents that bind to γ-aminobutyric acid (GABA) receptors as agonists and to *N*-methyl-D-aspartate (NMDA) receptors as antagonists, have been implicated in neuronal cell death caused by apoptosis. GABA agonists include volatile anesthetics, propofol, and benzodiazepines. NMDA antagonists include ketamine. Most experts agree that there are not sufficient clinical data as of this writing to change clinical practice. (566)

117. Former premature infants who present for surgery are at an increased risk for postanesthetic apnea. This risk increases with increased prematurity at birth and younger age at the time of the anesthetic. The current recommendation is that former premature infants should have their elective surgery delayed until 50 weeks postconceptual age or greater to minimize this risk. Prior to this, and in a case-by-case basis, infants may need to be admitted postoperatively for 24 hours of apnea monitoring. (565)

Chapter

32 ELDERLY PATIENTS

Sheila R. Barnett

WHY GERIATRIC ANESTHESIOLOGY IS IMPORTANT

1. What are some of the challenges encountered when taking care of elderly patients?
2. Is advanced chronologic age a risk factor?

Morbidity and Mortality Rates

3. What are some of the factors influencing mortality rates in the geriatric patient population?
4. How does a postoperative complication impact outcome in very old patients?

Medications to Avoid in the Geriatric Population

5. What are some medications that should be avoided in elderly patients?

Age-Related Physiologic Changes

6. How is organ function affected by aging? How might this affect the elderly patient in the perioperative period?
7. What age-related changes in systolic blood pressure, heart rate, cardiac output, stroke volume, and cardiac conduction occur in the elderly?
8. Why are elderly patients more susceptible to congestive heart failure when subjected to fluid overload than younger counterparts?
9. How do drug-induced heart rate changes in the elderly compare with the heart rate response seen in younger patients administered the same drugs?
10. How do reflex-mediated heart rate increases in response to hypotension differ between elderly and younger patients?
11. What age-related changes in gas exchange, the alveolar-to-arterial oxygen gradient, and the ventilation-to-perfusion ratio occur in the elderly?
12. What age-related changes in vital capacity, forced exhaled volume in 1 second, residual volume, and functional residual capacity occur in the elderly?
13. How do ventilatory responses to hypoxia and hypercapnia change with age? Why is this particularly important to the anesthesiologist?
14. Why does pneumonia occur at an increased frequency in elderly patients?
15. What age-related changes in renal blood flow, glomerular filtration rate, and urine-concentrating ability occur in the elderly? What clinical implications do these have?
16. How do plasma concentrations of creatinine change with age?
17. What age-related change in hepatic blood flow occurs in the elderly? What clinical implication does this have?

18. How does the production of albumin change with age? What clinical implication does this have?
19. What age-related changes in esophageal and intestinal motility and gastroesophageal sphincter tone occur in the elderly? What clinical implications do these have?
20. What clinical relevance do the age-related loss of collagen and decreases in skin elasticity have for the anesthesiologist caring for the elderly patient?
21. What clinical relevance do osteoporosis, osteoarthritis, and rheumatoid arthritis have for the anesthesiologist caring for the elderly patient?
22. What age-related changes in the central and peripheral nervous systems occur in the elderly? How does this affect the minimum alveolar concentration (MAC) of anesthesia in the elderly patient?
23. What physiologic changes occur with aging that predispose the elderly patient to hypothermia?

PERIOPERATIVE CARE IN THE ELDERLY

24. Why is it important to inquire about functional status in the elderly patient?
25. What are some elements of the preoperative evaluation that are of particular relevance to elderly patients?
26. What are some examples of activities of daily living (ADL) and instrumental ADLs (IADL)?
27. Should preoperative testing include a routine electrocardiogram (ECG) based on an age cutoff in elderly patients?
28. What are some of the challenges when obtaining a preoperative assessment in an institutionalized patient?
29. Why should certain antihypertensive medications be held on the morning of surgery?
30. What are some of the physiologic consequences that might be observed in elderly patients taking diuretic medications?
31. How are pharmacodynamic changes in the elderly reflected with regard to inhaled anesthetics and opioids?
32. How are pharmacodynamic changes in the elderly reflected with regard to nondepolarizing neuromuscular blocking drugs?
33. What pharmacokinetic changes in the elderly make them susceptible to cumulative drug effects and adverse drug reactions?
34. What age-related changes in the elderly result in a decreased clearance of drugs? Give some examples of drugs whose elimination times may be affected.
35. What age-related changes in the elderly result in changes in the volume of distribution? Give some examples of drugs whose pharmacokinetic properties may be altered.

CHOICE OF ANESTHESIA

36. What is an advantage that regional anesthesia may have over general anesthesia for hip surgery in elderly patients?
37. In an awake, elderly patient, what is the significance of orthostatic hypotension without an associated increase in heart rate?
38. What is the potential significance of mental status changes that occur with extension and rotation of the head?
39. Why should preoperative anxiolytics be used sparingly in the elderly population? What can be used as a substitute?
40. Why might hand ventilation by bag and mask be difficult in the edentulous patient?
41. Why might endotracheal intubation be difficult in a patient with poor dentition or cervical arthritis?
42. How should the induction dose of anesthetic be altered in the elderly patient?
43. Are there any unique risks to the elderly with the reversal of nondepolarizing neuromuscular blocking drugs with anticholinesterase drugs?

44. What are some postoperative risks that elderly patients are more prone to than younger patients?
45. What types of procedures that elderly patients are likely to undergo might warrant regional anesthesia as an alternative to general anesthesia?
46. What is the advantage to maintaining consciousness in the elderly patient during a regional anesthetic for a surgical procedure?
47. What are some reasons why elderly patients may be more sensitive to regional anesthesia than younger patients?
48. How might the hypotensive effects of a sympathectomy resulting from regional anesthesia be attenuated?
49. What advantage does epidural anesthesia have over spinal anesthesia that can be of particular benefit in the elderly population?

POSTOPERATIVE CARE

50. What are some of the consequences of untreated postoperative pain in the elderly patient?
51. What are some examples of adjuvant nonopioid medication that can be used to treat pain in the elderly patient?
52. What are some of the advantages of postoperative epidural analgesia in elderly patients?
53. How should a regional technique be altered in an elderly patient?
54. What are the most common postoperative neurologic events in elderly patients?
55. When is postoperative delirium in the elderly patient most likely to present?
56. What are some possible clinical manifestations of postoperative delirium in the elderly patient?
57. What are some causes of postoperative delirium in elderly patients?
58. What are some of the consequences of delirium in elderly patients?
59. How is postoperative cognitive dysfunction different from delirium?

ANSWERS*

WHY GERIATRIC ANESTHESIOLOGY IS IMPORTANT

1. The elderly population represents a heterogeneous group of individuals with widely varying functional and reserve capacity. In some patients there may be a wide disparity between the chronologic and physiologic age. In all individuals, aging is associated with a gradual deterioration of organ function. Even though the rate may vary between individuals, some age-related changes are inevitable. Elderly patients may also exhibit atypical symptoms leading to delays in diagnosis and more advanced disease at presentation. Other challenges include polypharmacy, the high prevalence of dementia and cognitive dysfunction in the very elderly, and the difficulty in estimating functional reserve in patients with limited mobility and multiple comorbid conditions. (568, Table 35-1)

2. Advanced age is a risk factor for surgical morbidity and mortality. Elderly patients who require surgery are also at a greater risk of perioperative complications than their younger counterparts. This is due to a combination of the effects of chronic disease and generalized age-related decreases in organ function. Some examples of common age-related changes include a generalized decrease in maximal breathing capacity, vital capacity, glomerular filtration rate, and basal metabolic rate. In addition, decreases in the elderly patient's level of activity may lead to deconditioning and a subsequent inability of the cardiovascular

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

system to respond to perioperative stressors. Overall the comorbid conditions found in elderly patients are the most significant contributors to the development of perioperative complications or perioperative death, rather than the age of the patient itself. (568, Figure 35-1)

Morbidity and Mortality Rates

3. The need for emergency surgery is one of the most important predictors for mortality following surgery in older patients. The circumstances of the emergency itself may be compromising the patient's physiologic status, such as with hemorrhage or dehydration. In these circumstances the older patient with poor baseline function and organ reserve may not be able to respond rapidly to this acute alteration in physiologic state. In addition, emergency cases preclude the preoperative time necessary to control coexisting diseases and maximize organ function. The lack of optimization impacts the ability to withstand the stress imposed by surgery. Other important factors influencing the outcomes in elderly patients include delayed presentation of a condition, high ASA physical status, partial or complete immobility, intracavitary surgery, and congestive heart failure. Older patients tend to present later with more advanced disease and thus be more compromised physiologically at presentation. (569)

4. Complications may be poorly tolerated in very old patients. Patients over 80 years old who developed a postsurgical complication had a fourfold increase in mortality. Complications are also associated with an increase in length of hospital stay and morbidity. The most significant complications include cardiac arrest, renal failure, and myocardial infarction. Avoiding even minor complications is one of the cornerstones of management of geriatric patients undergoing anesthesia and surgery. (569)

Medications to Avoid in the Geriatric Population

5. Aging is associated with decreased central cholinergic reserve, and in elderly patients with dementia this may be significant. Scopolamine is a tertiary quaternary amine and as such crosses the blood-brain barrier. The central anticholinergic effects of scopolamine may lead to significant delirium in elderly patients. Other medications that can similarly cause delirium through central anticholinergic effects include atropine, chlorpheniramine, diphenhydramine, and promethazine. (570)

Age-Related Physiologic Changes

6. Organ function, in general, declines with age. The decline in organ function associated with aging in the elderly has been characterized as a decline in the ability of the elderly patient's organs to adapt, or compensate, in response to acute stressors. The perioperative period is associated with stressors on numerous organs, leaving elderly patients vulnerable to develop worsening organ dysfunction in the perioperative period. Age-related declines in organ function may be difficult to measure preoperatively and the stress associated with surgery may expose previously underappreciated deficiencies. For example, the presence of mild renal insufficiency with normal laboratory testing may predispose the elderly patient to perioperative renal failure, or previously asymptomatic diastolic dysfunction may predispose the elderly patient to postoperative congestive heart failure. (570, Table 35-2)

7. Age-related changes in the cardiovascular system of elderly people include an increase in stiffness of the vasculature and an increase in the presence of diastolic dysfunction. In the absence of cardiac disease per se, the cardiac output and stroke volume are largely preserved. Alterations in the conduction system are common

and older patients are predisposed to developing arrhythmias and heart block. Systemic blood pressure steadily increases with age as a result of the decrease in compliance of arterial walls. Alterations in the cardiac sympathetic nervous system result in a diminished ability to increase heart rate in response to stress. In elderly patients a sedentary lifestyle and deconditioning may lead to diminished cardiac output and reserve capacity. The decrease in cardiac output does not appear to occur in elderly patients who have maintained physical fitness. (571)

8. Aging is associated with increased ventricular stiffening that contributes to delayed left ventricular relaxation during diastole. This is referred to as diastolic dysfunction and leads to a decrease in diastolic filling. Approximately one third of older individuals with normal left ventricular function have diastolic dysfunction. Diastolic dysfunction limits a patient's capacity to handle excess intravascular fluid, and thus excess fluid loading can lead to the rapid development of congestive heart failure. (571, Figure 35-2)

9. The plasma concentration of adrenergic agents required to produce a specific cardiovascular response is increased in the elderly. When adrenergic drugs such as isoproterenol are administered to elderly patients, the change in heart rate is less prominent than the changes in heart rate seen when isoproterenol is administered to younger patients. This is believed to be due to a decrease in the elderly patient's responsiveness at the β-adrenergic receptor. The decrease in responsiveness may occur secondary to a reduced affinity of β-adrenergic agents for the receptor and/or the impairment of adenylate cyclase activation. This same effect of decreased cardiovascular response has also been noted with the administration of atropine and α-adrenergic agonists. The reduction in parasympathetic tone is also reflected in the reduction in beat to beat variability. The levels of circulating norepinephrine rise steadily with aging, supporting a reduction in the sensitivity of the receptor. (571)

10. When hypotension occurs in younger patients, there is a baroreflex-mediated increase in heart rate that occurs to help offset the physiologic effects of the hypotension. In the elderly patient, the reflex-mediated increase in heart rate in response to hypotension is much less pronounced and as a result elderly patients are prone to develop orthostatic hypotension. The decline in baroreceptor sensitivity and cardiac autonomic function has been termed the dysautonomia of aging. It appears to be due to a combination of a decrease in sensitivity of the baroreflexes themselves and a decrease in the ability of the adrenergic receptors to respond, limiting the reflex increase in heart rate. (571)

11. There is an age-related decrease in gas exchange in the elderly patient. The most significant age-related change in the lung of the elderly patient is a deterioration of lung elastin. As a result of the degenerative changes in the lungs, there is a breakdown of alveolar septa. This is accompanied by an increase in both anatomic and alveolar dead space and an increase in ventilation-to-perfusion mismatch. These are reflected by an increase in the alveolar oxygen pressure and a decrease in the Pa_{O_2} by about 0.5 mm Hg per year after 20 years of age. There are no age-related changes in the Pa_{CO_2}. (571)

12. Age-related changes in the pulmonary system of elderly people include a decrease in vital capacity, a decrease in the forced exhaled volume in 1 second, an increase in residual volume, and an increase in functional residual capacity. These occur as a result of the decreased elasticity of the lungs and increased stiffness of the thorax. (571)

13. Elderly patients have a decreased ventilatory response to hypercapnia and hypoxia. When compared with younger patients, this response can be decreased by about one half. It is important that the anesthesiologist be cognizant of this, because this response is further decreased by the administration of opioids and inhaled anesthetics. (571-572)

14. Elderly patients have decreases in pulmonary reserves; a decreased level of laryngeal, pharyngeal, and airway cough reflexes; and an increased propensity to aspirate pharyngeal secretions. Elderly patients also have depressed immune function, probably due to involution of the thymus gland and altered function of T lymphocytes. Together these may explain the increased risk of pulmonary aspiration and an increased incidence of pneumonia in elderly patients when compared with younger patients. (571)

15. Decreases in renal blood flow, glomerular filtration rates, and urine-concentrating abilities accompany aging. These changes are due to alterations in the renal vasculature and may be at least partially due to the age-related decrease in cardiac output. There are also progressive decreases in the total number of nephrons and glomeruli units with age. Clinically, this has some implications for the anesthesiologist caring for the elderly patient. First, elderly patients may be more sensitive to, and less able to adapt to, fluid deprivation or fluid overload. Second, the elderly may be at an increased risk for renal ischemia in the perioperative period. Third, elderly patients have limited ability to concentrate urine and are therefore predisposed to hyponatremia. Finally, drugs that are cleared renally may have a prolonged duration of effect, thereby decreasing the dose requirements of these drugs in the elderly patient. (571)

16. Although renal function decreases with age, in the absence of concomitant renal disease, plasma creatinine concentrations do not change with age. This is because the increase in creatinine that would be expected to accompany the age-related decline observed in the glomerular filtration rate (GFR) is offset by the decrease in muscle mass. There is a decreased production of creatinine secondary to this decrease in muscle mass. (572)

17. Decreases in hepatic blood flow are seen in the elderly as a direct result of decreases in hepatic tissue mass and decreases in cardiac output. Clinically, a delayed clearance of hepatically cleared drugs may result from the decrease in hepatic blood flow in elderly patients. Drugs that may be affected include opiates, barbiturates, benzodiazepines, propofol, etomidate, and most nondepolarizing neuromuscular blocking drugs. (572)

18. The production of albumin is decreased in the elderly, and this may be exacerbated by poor nutrition. Clinically, the reduced albumin may result in a decrease in the binding of drugs administered to elderly patients, and an increase in the free, active portion of the drug. A low preoperative albumin level has been associated with increased mortality after surgery. (572)

19. Esophageal and intestinal motility decrease with age, as does gastroesophageal sphincter tone. Clinically, these age-related changes in gastrointestinal function may lead to an increased risk of pulmonary aspiration in elderly patients undergoing general anesthesia. (572)

20. A loss of collagen and decreases in the elasticity of the skin of elderly people put them at an increased risk of sustaining injury to their skin during surgical procedures, particularly during prolonged procedures. Elderly patients are vulnerable to sustaining decubitus ulcers and injury during the removal of adhesive electrocardiogram pads or tape.

21. Osteoporosis, osteoarthritis, and rheumatoid arthritis occur most frequently in elderly people. These diseases must be considered while positioning the patient for a surgical procedure, as well as while positioning the head and neck for intubation of the trachea. Intubation of the trachea may be more difficult as a result of these diseases.

22. Age-related changes occur in both the central and peripheral nervous systems of elderly people. In the central nervous system there is a progressive decline in central nervous system activity and a loss of neurons. This is especially marked in the

cerebral cortex and is reflected as a reduction of brain size in radiographic studies. Cerebral blood flow decreases in proportion to decreases in cerebral mass. The autoregulation of cerebral blood flow remains intact. In the peripheral nervous system, there is a decrease in the conduction velocity of peripheral nerves and possibly a decrease in the number of fibers in the spinal cord tracts as well. This is reflected in the increase in the thresholds for the perception of stimuli from virtually all the senses, including pain. These physiologic changes in the central and peripheral nervous systems of elderly people result in a decrease in the MAC by as much as 30% from young adult values. This corresponds to a decreased dose of volatile anesthetic required to achieve a given physiologic central nervous system response in elderly patients. (572)

23. There are several factors which together predispose the elderly to hypothermia in the perioperative period. The reduction in metabolic rate that occurs with aging results in a reduction in heat production. Peripheral vasoconstriction is also less efficient in the elderly person, leading to a diminished ability to conserve heat through redistribution. Shivering is also diminished, and when it occurs it may lead to increased oxygen consumption that may not be tolerated in patients with significant cardiac disease. (572)

PERIOPERATIVE CARE IN THE ELDERLY

24. Establishing baseline functional status is one of the most important aspects of the preoperative evaluation of elderly patients. Elderly patients with an excellent functional capacity have a reduced risk of postoperative complications. (572)

25. The preoperative evaluation of the elderly patient scheduled to undergo a surgical procedure should include the routine preoperative elements for any other patients. An additional goal of the preoperative evaluation of elderly patients is to stratify and minimize risk. The preoperative evaluation should include some key elements that are more relevant to patients in this age group in order to achieve this goal. The patient's functional capacity is one of the most important aspects of the elderly patient's preoperative assessment. This includes an evaluation of the patient's physical fitness, as well as their ability to perform their activities of daily living. In addition, a brief assessment of cognition can be used to identify if a patient is at increased risk for developing postoperative cognitive problems such as delirium. A careful inventory of all medications, including over-the-counter drugs, should be documented. For patients on multiple medications it can be helpful to have the patient bring the vials to the hospital on the day of surgery or admission. Polypharmacy is common in the older population and can lead to negative drug interactions perioperatively. Drug and alcohol dependence must also be considered in the elderly patient scheduled for surgery. Finally, the preoperative visit provides an opportunity to begin a discussion on advanced health care directives. (573)

26. Activities of daily living describe common behaviors that allow an assessment of an elderly person's function within their living situations. The basic five ADLs are bathing, dressing, toileting, transferring, and eating. Instrumental activities of daily living (IADLS) describe more advanced activities that would be expected in persons living independently. These include the ability to use the telephone and public transport, do shopping, prepare a meal, do basic housekeeping and budgeting, and the ability to manage one's own medications. (573, Table 35-3)

27. Routine preoperative testing based on age cutoffs leads to unnecessary testing and the risk of false positive and unchecked results. Although it has been popular in the past to use an age cutoff for preoperative ECGs, this approach is not recommended. The preoperative ECG should be ordered when the patient's history or symptoms suggest significant cardiac disease. Since cardiovascular disease is common in older patients, ECGs will still probably remain one of the most commonly ordered preoperative tests. Elderly patients frequently have abnormal

baseline ECGs and part of the preoperative evaluation will need to include comparisons to prior ECGs to establish if the observed changes are new findings. (573)

28. Chronically institutionalized patients can present a unique challenge with regard to their preoperative assessment. These patients frequently have complex medical and medication histories, and in addition may have limited ability to communicate. It may not be practical to request a separate visit to a preoperative clinic for these patients. In these cases a thorough review of the medical record may be performed before the surgery. In all cases, it is important to establish who will be providing consent for the surgery and anesthesia prior to the surgery date. (573)

29. Although most antihypertensive medications are recommended to be taken on the morning of surgery, persistent and difficult to treat postinduction hypotension has been observed in patients treated with ACE inhibitors. For that reason it is recommended that ACE inhibitors be withheld the morning of surgery or for 10 to 12 hours preoperatively. Other antihypertensive medications should generally be continued on the day of surgery. (573)

30. Diuretic medications, in combination with decreases in organ function, may result in electrolyte abnormalities in elderly patients. Common abnormalities include hypokalemia, mild hyponatremia, and contraction alkalosis. These abnormalities can be detected in preoperative laboratory tests. (573)

31. Pharmacodynamic changes in the elderly lead to an increase in sensitivity to certain medications and necessitate a decrease in recommended doses in these patients. The plasma concentration of inhaled anesthetics, opioids, and the benzodiazepine midazolam that is required to produce a specific effect in an elderly person is decreased compared to younger counterparts. For example, the dose of fentanyl and alfentanil required to achieve a given effect in an elderly patient may be decreased by as much as 50% compared to a young adult. The increased sensitivity to anesthetics seen in elderly patients parallels the decrease in cerebral cortex tissue mass and cerebral metabolic rate. This is subsequently reflected as a decrease in the MAC of anesthesia in elderly patients. (574-575, Table 35-5)

32. The plasma concentration of nondepolarizing neuromuscular blocking drugs required to produce a specific twitch response effect is similar in both elderly and younger people. This implies that the sensitivity of elderly patients to nondepolarizing neuromuscular blocking drugs does not change with age. (575)

33. Pharmacokinetics, the absorption, distribution, metabolism, clearance, and excretion of a drug, accounts for the concentration of a drug at the end-organ site or receptor level. Pharmacokinetic changes in the elderly include decreases in drug clearance and changes in the volume of distribution, making the elderly more susceptible to cumulative drug effects and adverse drug reactions. The plasma concentrations of thiopental, propofol, and etomidate required to produce a specific response are similar in both elderly people and younger people. However, age-related pharmacokinetic changes, especially with respect to distribution, may necessitate a reduction in the initial dose of these medications. (574)

34. A decreased clearance of drugs in the elderly can be attributed to decreases in renal blood flow, decreases in the glomerular filtration rate, decreases in hepatic blood flow, and decreases in hepatic microsomal enzyme activity. Decreases in renal blood flow and decreases in the glomerular filtration rate together may result in the prolongation of the effects of pancuronium, digoxin, and several antibiotics in elderly patients. Likewise, decreases in hepatic blood flow and decreases in hepatic microsomal enzyme activity together may result in the prolongation of the effects of vecuronium, lidocaine, propofol, and propranolol in elderly patients. (574)

35. The volume of distribution can be divided into the central volume of distribution and the peripheral volume of distribution. The central volume of distribution refers to the volume of the heart and great vessels, and the venous volume. A decreased central volume of distribution in the elderly produces an increased initial concentration of drug in the plasma after a bolus injection. The decrease in the central volume of distribution has been thought to be due to decreases in total body water in elderly patients. More recently, this theory has come under scrutiny. Nevertheless, higher initial plasma concentrations of drug after the initial bolus of conventional doses of the drug are seen in elderly patients.

Drugs that are affected in this manner include thiopental, propofol, and etomidate when administered for the induction of anesthesia, as well as the initial bolus of opioids. In fact, it has been estimated that elderly patients require about 15% less of a drug dose of thiopental or propofol as a bolus for the induction of anesthesia. The peripheral volume of distribution includes additional volumes of distribution attached to the central volume. The peripheral volume of distribution in elderly patients is increased due to a relative increase in body fat and a decrease in the amount of drug bound by protein. The increased peripheral volume of distribution may also be reflected as a delay in the rate of elimination of lipid-soluble drugs that are stored in fat, such as opioids and the volatile anesthetics. (574)

CHOICE OF ANESTHESIA

36. Regional anesthesia may be advantageous over general anesthesia for hip surgery in elderly patients. Regional anesthesia may be associated with decreases in perioperative blood loss and decreases in the incidence of deep venous thrombosis. There is no evidence, however, that one method of anesthesia is safer than the other. (576)

37. In an awake, elderly patient being evaluated for orthostatic hypotension, the lack of an increase in heart rate upon assuming the upright position in the presence of hypotension may reflect autonomic dysfunction. Other signs of autonomic dysfunction include a lack of beat-to-beat heart rate variability or an absence of sinus arrhythmia with respiration. Autonomic dysfunction may occur secondary to aging and vascular stiffening, coexisting diseases such as diabetes or renal failure, or drug effects. (571)

38. The elderly patient who experiences changes in mental status with extension and rotation of the head may have vertebrobasilar insufficiency or cervical osteoarthritis. In the case of vertebrobasilar insufficiency, cerebral ischemia may result. It is therefore useful to evaluate the elderly patient for symptoms with extension and rotation of the head should this position be necessary for the surgical procedure. (574)

39. Preoperative anxiolytics should be used sparingly in the elderly population because they can cause undesirable levels of sedation and confusion in these patients. In addition, the residual effects of these medicines may persist even after the surgical case has been completed. In lieu of the preoperative anxiolytic medicines, a detailed explanation of the events that will occur before and after the surgical procedure may be a useful anxiolytic substitute. (575)

40. Hand ventilation by bag and mask may be difficult in the edentulous patient secondary to a poor mask-to-face fit. It is often easier to hand ventilate by bag and mask when the edentulous patient's dentures are left in place or an oral airway is used. (574)

41. Endotracheal intubation may be difficult in a patient with poor dentition or cervical arthritis. Difficulty in patients with poor dentition arises because of the need to avoid loose teeth during direct laryngoscopy to avoid dislodgment of the teeth. Patients with cervical arthritis may be difficult to endotracheally intubate because of the decreased range of motion, especially extension, of the neck. (574)

42. The induction dose of an anesthetic should be reduced for an older patient compared to a younger patient. The reduction appears to be mostly due to pharmacokinetic changes. Aging leads to a reduction in the central volume of distribution and clearance of an induction agent such as propofol. The net result is that the drug administered for induction exerts its pharmacologic effects in the circulation for a longer amount of time and the receptors are exposed to a larger initial concentration. The induction dose of anesthetic in the elderly patient is not decreased for pharmacodynamic reasons, because the plasma concentration of induction drug required to produce a desired effect is equal in elderly and younger patients. (574-575)

43. The reversal of nondepolarizing neuromuscular blocking drugs in the elderly patient does not warrant any special considerations for the anesthesiologist, because there are not any unique risks of this in the elderly patient population. The incidence of cardiac dysrhythmias after the administration of glycopyrrolate or neostigmine may be increased in elderly patients who have cardiovascular disease. (575)

44. Several postoperative complications are more common in older patients compared to younger patients. These include cardiovascular events such as myocardial infarction and congestive heart failure, especially from diastolic dysfunction. This is most likely related to the frequency of cardiovascular disease in the elderly population and underlying age-related changes. Central nervous system complications are the next most commonly encountered postoperative complication in the elderly patient. Although cerebral vascular accidents are more common in older patients than in younger patients, they are still uncommon and usually occur in a patient with preexisting cardiac or vascular disease. More common central nervous system events are postoperative delirium and postoperative cognitive dysfunction. These are especially common in older patients with preexisting dementia, depression, and cognitive impairment, for example patients who have had a cerebral vascular accident in the past. Pulmonary complications include postoperative hypoxia and pneumonia. It is possible that early ambulation may minimize some of the pulmonary risks. (576-577)

45. Regional anesthesia is an alternative to general anesthesia for elderly patients undergoing surgical procedures such as transurethral resection of the prostate, gynecologic procedures, inguinal hernia repair, or the treatment of hip fractures. Regional techniques such as peripheral nerve blocks are becoming increasingly popular and may be a valuable adjuvant to general anesthesia in elderly patients. They may reduce the amount of anesthesia needed and improve postoperative pain control. (576)

46. An advantage to maintaining consciousness in the elderly patient during a regional anesthetic for a surgical procedure is that the anesthesiologist is able to communicate with the patient during the procedure. Changes in mental status can herald the onset of a developing adverse event. For example, confusion during a transurethral resection of the prostate may be an early warning sign of the development of hyponatremia or fluid overload. Similarly, a patient may complain of chest pain or shortness of breath signaling the presence of myocardial ischemia. Additionally, there may be decreased immediate postoperative confusion in elderly patients after having received a regional anesthetic as compared with a general anesthetic. (576)

47. Elderly patients may be more sensitive than younger patients to regional anesthesia, especially spinal anesthesia. Possible reasons why this may be true include decreased vascular absorption from the spinal space, decreases in vertebral column length, and a decreased reflex compensatory sympathetic nervous system response. Together, these may manifest as a prolonged duration of action, increased anesthesia level, and exaggerated decreases in blood pressure following a spinal anesthetic. (576)

48. Attenuation of the hypotensive effects of a regional anesthetic may be achieved by the prophylactic administration of an intramuscular dose of ephedrine before administering the spinal anesthetic. Adequate hydration minimizes the effects of a sympathectomy on blood pressure, but does not consistently eliminate the hypotensive effects of spinal anesthesia in elderly patients. (576)

49. Epidural anesthesia is advantageous over spinal anesthesia in that it may be administered more slowly than a spinal anesthetic, with the onset of the resulting sympathectomy being more gradual. This may result in a more gradual decrease in the elderly patient's blood pressure than that seen with a spinal anesthetic. (576)

POSTOPERATIVE CARE

50. Untreated postoperative pain in elderly patients is associated with serious consequences in elderly patients. These include increased length of hospital stay, morbidity, pulmonary complications, and delirium. (576)

51. Acetaminophen can be used to reduce opioid requirements in elderly patients. NSAIDs can also lead to lower narcotic requirements, but the dose must be adjusted to reduce the risk of renal insufficiency or gastrointestinal side effects such as bleeding. Gabapentin is another medication that can be used in the perioperative period to reduce opioid use. It is renally excreted and the dose should be reduced in older patients. (576)

52. Postoperative epidural analgesia in elderly patients has been associated with improved pulmonary function, reduced atelectasis, easier extubation of the trachea, and shorter ICU stays in patients that have had thoracic and upper abdominal surgeries. (576)

53. The metabolism and excretion of local anesthetic drugs is reduced in the elderly. When administering a regional anesthetic in elderly patients, the overall dose should be reduced. (576)

54. The most commonly encountered neurologic events in elderly patients are delirium and postoperative cognitive dysfunction. Postoperative delirium has been estimated to occur in at least 10% to 15% of elderly patients undergoing surgical procedures. It may occur in as many as 40% to 60% of patients undergoing acute repair of a hip fracture. (576-577)

55. Postoperative delirium is most likely to present one or more days after surgery in elderly patients. This type of delirium is termed interval delirium. This is in contrast to emergence delirium commonly seen in pediatric patients that occurs within minutes after the emergence from anesthesia. (576-577)

56. Clinical manifestations of postoperative delirium in elderly patients may include alterations in attention, cognition, and sleep-wake cycles; a reduced level of consciousness; and increases or decreases in psychomotor behavior. These patients are often disoriented to time, place, and person. Close monitoring of these patients is essential to prevent patients from harming themselves by attempting to get out of bed or by pulling out catheters. (577)

57. Causes of postoperative delirium in the elderly patient include drug toxicity, fluid and electrolyte imbalances, and underlying medical problems, such as myocardial ischemia, congestive heart failure, infection, pain, or depression. Antiparkinsonian drugs, antihypertensives, and anticholinergic and psychotropic medications tend to increase the risk of drug interactions with anesthetics and postoperative analgesics to produce postoperative delirium. A deficiency of neurotransmitters such as acetylcholine and dopamine is hypothesized to be the underlying physiologic cause of postoperative delirium. (577)

58. Delirium in elderly patients has been associated with increased mortality, length of hospital stay, and loss of independence evidenced by an increased risk of transfer

to an assisted living and nursing home. Delirium can persist for weeks or even months in elderly hospitalized patients. (576)

59. Postoperative cognitive decline is a subtle alteration in cognitive function and mental ability. Unlike delirium, postoperative cognitive dysfunction is not associated with acute confusion or agitation. Neuropsychological testing is required for its diagnosis. (577)

Chapter

33 ORGAN TRANSPLANTATION

Randolph H. Steadman, Victor W. Xia

1. What are the most commonly transplanted organs?
2. How does donation after brain death differ from donation after cardiac death?
3. What conditions preclude transplantation?
4. What is the most common cause of death in organ transplant recipients?
5. Most transplant candidates are screened for comorbidities prior to being waitlisted. What additional beneficial preoperative measures can be undertaken once a donor is identified?

KIDNEY TRANSPLANTATION

6. Who is a candidate for renal transplantation?
7. What is the major cause of death in dialysis patients?
8. What differs between an extended criteria donor kidney and a standard criteria donor graft?
9. Where is the donor kidney transplanted in the recipient patient? From where does it derive its vascular supply? Where is the ureter anastomosed?
10. What are the preoperative considerations for the patient scheduled to undergo renal transplantation?
11. How is preoperative ischemic heart disease ruled out prior to transplant listing?
12. What is the usual general anesthetic regimen administered for renal transplantation?
13. What consideration must be made when selecting a neuromuscular blocking drug for patients undergoing renal transplantation?
14. Why is optimal hydration important during renal transplantation? What type of crystalloid solution should be used for hydration? What monitoring method may be used to help guide hydration intraoperatively for renal transplantation?
15. Is dopamine of benefit during renal transplant procedures?
16. Why is mannitol administered intraoperatively during renal transplant procedures?
17. Cardiac arrest after completion of the renal artery anastomosis is thought to be secondary to what?

LIVER TRANSPLANTATION

18. Who is a candidate for liver transplantation?
19. How are liver transplant recipients prioritized for organ allocation?
20. What is the 1-month mortality for a waitlisted candidate with a high model for end-stage liver disease (MELD) score (score >30)?

21. What physiologic disturbances are often present in patients before liver transplantation?
22. What is the best screening test for portopulmonary hypertension?
23. What is hepatopulmonary syndrome? Why is it significant?
24. What types of monitoring may be used intraoperatively during liver transplantation?
25. What types of intravenous access are typically established preoperatively for liver transplant procedures? Why should placement be supradiaphragmatic?
26. Why are cell-saver devices used intraoperatively for liver transplantation?
27. Why is calcium administration often required during liver transplantation?
28. What are the three stages of liver transplant procedures?
29. What are the characteristic physiologic derangements of the preanhepatic stage of liver transplant procedures?
30. What are the characteristic physiologic derangements of the anhepatic stage of liver transplant procedures?
31. What is the "piggy-back" technique and why is it used in some patients?
32. What are the characteristic physiologic derangements that occur with reperfusion of the donor graft during liver transplant procedures?
33. Which coagulopathies can occur during liver transplantation?
34. Why is nitrous oxide avoided for maintenance anesthesia during liver transplantation?
35. Why do some anesthesiologists prefer cisatracurium as the nondepolarizing neuromuscular blocking drug for liver transplantation?
36. What signs of donor graft function can be assessed intraoperatively after graft reperfusion?
37. When is extubation of the trachea after liver transplant surgery performed?

HEART TRANSPLANTATION

38. Who is a candidate for heart transplantation? What ejection fraction is commonly seen in patients undergoing heart transplantation?
39. What are the goals for the induction and maintenance of anesthesia for heart transplant patients?
40. What vessels are transected and anastomosed during heart transplant surgery? What does this mean with regard to a central venous or pulmonary artery catheter?
41. What is the indication for isoproterenol during heart transplantation?
42. Does the transplanted heart react better to catecholamines that are direct or indirect acting?
43. Name the physiologic conditions that should be optimized prior to weaning from cardiopulmonary bypass.
44. Name three conditions that may worsen pulmonary hypertension.

LUNG TRANSPLANTATION

45. What type of endotracheal tube is used in lung transplant procedures?
46. What are some intraoperative problems the anesthesiologist may encounter during lung transplant procedures?
47. Why are lung transplant patients predisposed to developing pneumonia in the transplanted lung?

PANCREAS TRANSPLANTATION

48. Who is a candidate for pancreas transplantation?
49. What other organ is often transplanted simultaneously along with the pancreas?

ANSWERS*

1. Organs that may be transplanted in humans include the heart, kidneys, liver, lungs, pancreas, and intestines. The bone marrow may also be transplanted for certain forms of cancer. (580)

2. The diagnosis of brain death is based on the loss of cerebral cortical and brainstem function. The loss of cerebral cortical function is implied from unconsciousness, the lack of spontaneous movement, and unresponsiveness to external stimuli. The loss of brainstem function is implied from apnea and absent cranial nerve reflexes. Clinical studies that may be performed to provide supporting evidence include an electroencephalogram or cerebral blood flow studies. Irreversibility of the diagnosis of brain death should also be established. This is usually achieved by the lack of any improvement in 12 to 24 hours after the diagnosis. Other derangements that must be excluded include central drug effects, postictal states, cardiovascular or metabolic instability, or hypothermia. The diagnosis of brain death is always made before a donor procedure and never in the operating room. However, in the absence of brain death, but in the presence of a devastating and irreversible brain injury, the patient's family may elect to withdraw life support. In the event the family consents to organ donation, withdrawal of support is typically done in the operating room. If the patient succumbs as a result of the withdrawal of life support—experiences cardiac death—organs may be harvested. Under these conditions, the organs undergo a period of ischemia at normal body temperature (termed "warm ischemia"), a condition which necessitates rapid cooling, preservative administration, and procurement to minimize ischemic injury. (580)

3. Untreated systemic infection, incurable malignancy, untreated substance abuse, and lack of sufficient social support to comply with post-transplant care are contraindications to transplantation. (580)

4. The most common cause of death in transplant recipients is infections due to chronic immunosuppression. All physicians, including anesthesiologists, caring for the transplant patient should adhere to strict aseptic technique. (587)

5. Because of the long wait times between listing and transplantation (not infrequently a year or more), preoperative screening tests may need to be repeated particularly when prior results are equivocal. Most important are tests for ischemic heart disease (postoperative cardiovascular mortality is second in frequency to infection), assessment of laboratory results such as electrolytes and hemoglobin, and, if needed, preoperative dialysis. (580)

KIDNEY TRANSPLANTATION

6. Kidneys are the most commonly transplanted major organ. Patients who have end-stage renal disease and are being considered for (or are currently receiving) dialysis are candidates for renal transplantation. Transplantation has led to lower overall morbidity and mortality than dialysis and to improved survival. The most common cause of end-stage renal disease leading to chronic dialysis dependence is diabetes mellitus, followed by hypertension. (581)

7. Cardiovascular disease is responsible for over 50% of deaths in patients receiving dialysis. (581)

8. Extended criteria donors are older donors, donors with diabetes, and grafts with prolonged preservation times (acceptable times vary by organ; for the kidney $>$ 24 to

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

36 hours of cold ischemia is considered prolonged, for the liver > 8 to 12 hours). Organs donated after cardiac death incur additional warm ischemia and are considered as a subcategory of extended criteria grafts. (581)

9. The kidney is transplanted on one side of the recipient's iliac fossa. The vascular supply for the transplanted kidney is derived from the iliac vessels. The ureter of the transplanted kidney is anastomosed directly to the recipient's bladder. (581)

10. Preoperative considerations for the patient scheduled to undergo a renal transplant are similar to any other surgical procedure in which the patient has chronic renal failure. This includes scheduling of hemodialysis prior to surgery to optimize the patient's volume status, electrolytes (particularly potassium), and acid-base balance. The serum glucose levels of the patient with diabetes mellitus should also be evaluated before and during surgery. (581)

11. Preoperative ischemic heart disease should be ruled out preoperatively. Stress echocardiography is probably better than thallium imaging in predicting postoperative cardiac events. Coronary angiography should be considered in high-risk patients. (581)

12. The usual general anesthetic regimen for renal transplant procedures is balanced anesthesia: a combination of volatile anesthetic and short-acting opioid. Nitrous oxide is avoided because it causes bowel distention. (582)

13. When selecting a neuromuscular blocking (NMB) drug, consideration should be given to the method of clearance. A NMB that does not rely primarily on renal clearance should be selected. Cisatracurium is particularly attractive because its metabolism is independent of both the kidney and liver. (582)

14. Optimal hydration is important to improve the early function of the transplanted kidney. The crystalloid solution used for hydration intraoperatively should not contain potassium (e.g., normal saline). Monitoring the patient's central venous pressure may be a useful guide to the patient's state of hydration. (582)

15. Dopamine is often administered intraoperatively during renal transplant in an effort to increase renal blood flow and kidney perfusion. However, no studies support this practice. Other methods of ensuring adequate renal perfusion are the maintenance of systemic blood pressure near normal and the provision of adequate hydration. (582)

16. Mannitol is often administered intraoperatively during renal transplant procedures to facilitate an osmotic diuresis. However, controlled studies supporting an improved outcome are lacking. (582)

17. Reperfusion of the newly transplanted graft can lead to hyperkalemia; however, this life-threatening complication is less frequently seen during kidney transplantation than with liver graft reperfusion. A potassium-containing solution is used to preserve the kidney before transplantation. The washout of this solution and accumulated acid metabolites is believed to be the cause of the hyperkalemia. (584)

LIVER TRANSPLANTATION

18. Patients with acute hepatic failure, chronic end-stage liver disease, tumors (in the absence of extrahepatic spread), and metabolic abnormalities affecting their liver are candidates for liver transplantation. (582)

19. Patient acuity, as determined by the MELD score, is used to allocate organs. The MELD score predicts 90-day mortality in the absence of transplantation. (582)

20. A patient with a MELD score greater than 30 has a 30% probability of dying or becoming too ill for transplant within a 30-day period. (582)

21. Physiologic disturbances in patients with end-stage liver disease affect virtually every organ system. The patient may have encephalopathy, ranging from mild confusion to coma; hyperdynamic circulation due to decreased systemic vascular resistance and an increased cardiac output; decreased plasma volume; and ascites. Arterial hypoxemia may be due to pulmonary effusions, atelectasis, or hepatopulmonary syndrome. Renal dysfunction and oliguria may be present. Patients may have anemia, thrombocytopenia, and coagulopathy. Electrolyte abnormalities that may be present include hypokalemia, hypocalcemia, and hyponatremia. Finally, these patients may have glucose intolerance or frank diabetes. As the age of patients undergoing liver transplantation increases, the proportion with coronary artery disease has increased. (583)

22. Portopulmonary hypertension is defined as pulmonary hypertension (mean pulmonary artery pressure >25 mm Hg) in the presence of portal hypertension. Resting echocardiography is a useful screening test because it identifies nearly all patients with the condition. In patients with an estimated right ventricular systolic pressure greater than 50 mm Hg on echo, right heart catheterization is used to confirm or rule out the diagnosis. There is significant perioperative mortality associated with mean preoperative PA pressure greater than 35 mm Hg. (583)

23. Hepatopulmonary syndrome (HPS) consists of arterial hypoxemia ($Pa0_2 < 70$ mm Hg on room air) in the presence of an intrapulmonary shunt. Liver transplantation cures HPS, albeit over a variable time course. There is, however, an increased risk of perioperative mortality in patients with significant HPS ($Pa0_2 < 50$ mm Hg on room air). (583)

24. Monitors that facilitate the anesthetic management of patients undergoing liver transplant procedures include invasive arterial blood pressure monitoring and monitoring of cardiac filling pressures using a pulmonary artery catheter. These monitors are useful because major shifts in the intravascular volume and hemodynamic instability almost always occur. Arterial blood pressure is best monitored from an artery above the level of the diaphragm because the aorta may be cross-clamped during the portion of the procedure in which anastomosis of the hepatic artery takes place. Transesophageal echocardiograms are useful to monitor the volume status and cardiac function, and to detect emboli. A Foley catheter is used to measure urine output. (583)

25. Peripheral intravenous access should be established preoperatively using several large-bore catheters to allow for the ability to transfuse blood products rapidly. Intravenous catheters should be placed above the level of the diaphragm because the inferior vena cava is typically cross-clamped during the procedure. (584)

26. Cell-saver devices are often used intraoperatively during liver transplant procedures because of the massive amounts of blood loss and massive fluid requirements during the procedure. (584)

27. Calcium administration is often required during liver transplantation because of the frequency of citrate toxicity, caused when the citrate in banked blood binds with ionized calcium, which can cause myocardial depression. This condition is more frequent during liver transplantation, particularly the anhepatic stage, as the liver is unavailable to metabolize citrate. (584)

28. The preanhepatic, anhepatic, and neohepatic stage comprise the stages of the surgical procedure. The preanhepatic stage involves the dissection of the portal venous structures and mobilization of the native liver. The anhepatic stage begins when the native liver's blood supply is interrupted by clamping of the suprahepatic and infrahepatic inferior vena cava and the portal vein. The neohepatic stage begins with the return of vascular supply to the graft, usually via the inferior vena cava and portal vein. (584)

29. The preanhepatic stage of liver transplant procedures is characterized by cardiovascular instability due to sudden decreases in the intraabdominal pressure, and the exacerbation of chronic hypovolemia due to loss of ascites and hemorrhage. Metabolic and electrolyte abnormalities can occur during this stage, including metabolic acidosis and hypocalcemia. Hemorrhage, often requiring the rapid infusion of fluids and blood products, is related to the degree of portal hypertension and adhesions from prior abdominal surgery. (584)

30. The anhepatic stage of liver transplant procedures is characterized by precipitous decreases in venous return and cardiac output. For this reason, cardiac inotropic drugs and sympathomimetic drugs are often administered during this portion of the liver transplant procedure to maintain cardiac output. Hypocalcemia and metabolic acidosis commonly occur during this stage. (584)

31. The piggy-back technique involves the anastomosis of the donor hepatic veins to the recipient vena cava, followed by portal anastomosis. The piggy-back technique is preferred by some centers because it avoids transection of the inferior vena cava, which may preserve venous return. An alternative to the piggy-back technique is the use of venovenous bypass, which involves rerouting blood from the inferior vena cava to the superior vena cava, which can augment venous return. It is not universally used as it prolongs surgery and has unique complications, including air embolism.

32. The neohepatic stage of liver transplant procedures is characterized by the potential for precipitous hyperkalemia, acidosis, and hypothermia due to the cold ischemic effluent from the graft entering the central circulation. The systemic vascular resistance drops, and emboli of blood or air can occur. Hyperkalemia is exacerbated by the washout of the potassium-containing solution used to preserve the liver, in addition to unclamping of the inferior vena cava and portal vein. Hypotension, arrhythmias, and cardiac arrest may potentially occur during this time. (584, Table 36-5)

33. Coagulopathies that can occur during a liver transplant procedure include thrombocytopenia, decreased levels of multiple coagulation factors (due to decreased synthesis and dilution), and fibrinolysis. (584)

34. Nitrous oxide is often avoided for maintenance anesthesia during liver transplantation because it may cause bowel distention. Additionally, nitrous oxide may increase the size of embolized air, and it may increase pulmonary vascular resistance in a population prone to pulmonary hypertension. (583)

35. Cisatracurium is often selected as the nondepolarizing neuromuscular blocking drug, because its elimination is by spontaneous Hofmann elimination and ester hydrolysis, which are independent of liver function. (583)

36. Signs of graft function include improvement in metabolic acidosis (due to metabolism of citrate to bicarbonate), a reduced calcium requirement (again, due to the liver's ability to metabolize citrate), and a rising body temperature (due to exothermic reactions in the liver). Hepatorenal syndrome may occur, as noted, by increasing urine output.

37. The trachea generally remains intubated at the conclusion of the transplant until the patient is hemodynamically stable, bleeding is controlled, and the graft appears to be functioning well. (584)

HEART TRANSPLANTATION

38. Patients with end-stage heart disease are candidates for heart transplantation. Patients with pulmonary hypertension and end-stage heart disease are candidates for heart-lung transplant procedures. Patients undergoing a heart transplant procedure usually have heart disease secondary to coronary artery disease or a cardiomyopathy. The ejection fraction generally seen in these patients is less than 20%. (585)

39. The induction of anesthesia for cardiac transplantation may include a benzodiazepine and an opioid. The maintenance of anesthesia may be opioid based as well. The goal of the anesthetic induction and maintenance is to provide good endotracheal intubating conditions while preserving cardiac function. The potential risk of volatile anesthetics during a heart transplant procedure is myocardial depression, vasodilation, or both. (585)

40. Vessels that are transected and anastomosed during heart transplant procedures include the aorta, pulmonary artery, and left and right atria. These are done during cardiopulmonary bypass. A central venous or pulmonary artery catheter that is in place at the onset of surgery must be pulled back into the internal jugular vein when the patient's heart is excised. (585)

41. Isoproterenol is indicated for the maintenance of myocardial contractility and heart rate in the denervated donor heart during and after weaning from cardiopulmonary bypass. Isoproterenol also decreases pulmonary vasculature resistance. (585)

42. The transplanted heart reacts better to direct-acting catecholamines. Indirect acting drugs including atropine, which work via the autonomic nervous system, are ineffective due to denervation of the graft. (585)

43. Prior to weaning from cardiopulmonary bypass, patients should be normothermic, and free from acid-base and electrolyte disturbances. The lungs are ventilated and the cardiac chambers free from air.

44. Pulmonary hypertension is exacerbated by hypoxemia, hypercarbia, and elevated cardiac output, pulmonary vessel spasm, and emboli. (585)

LUNG TRANSPLANTATION

45. Double-lumen endotracheal tubes are used for intubation of the trachea for lung transplant surgery. This allows isolated ventilation of either the left or right lung, so that one lung may be ventilated while the other is being transplanted. (586)

46. Intraoperative problems during lung transplant procedures may include arterial hypoxemia and pulmonary hypertension. Arterial hypoxemia may occur during one-lung ventilation. Pulmonary hypertension may occur secondary to pulmonary artery clamping, particularly in patients with preexisting elevation of pulmonary pressure. (586)

47. Lung transplant patients are predisposed to pneumonia due to disruption of lymphatic drainage, poor mucociliary function, obstruction of bronchi from clots in the bronchial suture lines, and loss of the cough reflex. Immunosuppression exacerbates the risk of infection. (586)

PANCREAS TRANSPLANTATION

48. Patients with diabetes mellitus are candidates for pancreas transplantation. (586)

49. Most (65%) pancreas transplants are performed simultaneously with kidney transplants because of the advanced nature of the diabetes, which is associated with renal failure. Simultaneous pancreas-kidney transplant recipients experience the best graft survival rates. The success of a pancreas transplant is measured by monitoring blood glucose levels after surgery; blood glucose concentrations may return to normal within hours. (587)

Chapter

34 OUTPATIENT ANESTHESIA

Douglas G. Merrill

HISTORY OF OUTPATIENT SURGERY AND KEYS TO SUCCESS

1. Who created the first outpatient surgery center? When, where, and why?
2. What are the four most important areas to focus on to ensure success in outpatient anesthesia and surgery?
3. What are the primary determinants of predictability of duration and quality of surgical procedures in the ambulatory surgery center?
4. In comparison to hospital practice, is patient safety training usually less of a concern in an outpatient surgery setting, since patients are healthier and procedures are less invasive?
5. Is there value in monitoring of outcomes and the use of that data to support standard care practice (algorithms) and have these techniques been useful in creating higher quality care and improved patient safety?

PREOPERATIVE CONSIDERATIONS

6. What factors should determine the choice of preoperative laboratory and other testing prior to elective ambulatory surgery?
7. Is a patient who had a myocardial infarction within the past 3 months a candidate for surgery in a freestanding surgery center?

TECHNIQUES OF ANESTHESIA FOR OUTPATIENT SURGERY

8. Monitored anesthesia care (MAC) may provide just as much risk as general anesthesia. What risk may be greater for MAC than general?
9. Use of regional anesthesia can result in what process improvements in the outpatient surgery suite?
10. Does neuraxial anesthesia delay discharge of outpatients, particularly elderly males?
11. Should neuraxial anesthesia be avoided because it has a high incidence of postoperative urinary retention?
12. The use of general anesthesia, when compared to regional anesthesia or MAC, increases the likelihood of which four negative outcomes in outpatient anesthesia and surgery?
13. Avoidance of what three anesthetic techniques will increase patient satisfaction, and decrease the likelihood of postoperative nausea and vomiting and postoperative cognitive dysfunction?

TOPICS OF IMPORTANCE IN OUTPATIENT ANESTHESIA

14. What preoperative Hb A_{1c} level indicates that it is "safe" for outpatient surgery to proceed?
15. What is the "rule of 1800" for dosing insulin and how is it useful on the day of surgery?
16. Is the use of dexamethasone appropriate to decrease the risk of postoperative nausea and vomiting in the patient with diabetes?
17. Is it true that treated hypertension is not a predictor of perioperative morbidity?
18. What are the considerations for deciding to provide anesthesia for a patient with a known or suspected personal history of malignant hyperthermia in a freestanding ambulatory surgical center?
19. Which risks are associated with obstructive sleep apnea (OSA)?
20. Of what value is preoperative evaluation and treatment of OSA?
21. What factors would lead to a patient with OSA being cared for in a hospital setting rather than a freestanding ambulatory surgery center?
22. What is the most common cause of perioperative injury associated with remote-site (e.g., office-based) surgery?
23. What factors increase the risk of perioperative trouble in the office setting?
24. What are the advantages of using multimodal analgesia in the outpatient surgery setting?
25. What postoperative plan should cause the team to reconsider the outpatient venue for a case?
26. How soon does tonsillectomy relieve moderate or severe obstructive sleep apnea in pediatric patients and what implication does that have for when and where this procedure should be performed in this patient population?
27. What postoperative complication do outpatient surgery patients rank the prevention of as high as they do the prevention and treatment of pain?
28. Use of the Apfel score to predict postoperative nausea and vomiting has proven valid only for which time period after surgery?
29. What regimen of prophylaxis can virtually eliminate both early and late postoperative and postdischarge nausea and vomiting (PONV/PDNV) in even the highest risk patients?
30. If PONV occurs after the use of ondansetron in the operating room, what should be used to treat it?
31. When should the presence of an upper respiratory infection lead to cancellation of an elective surgical procedure?
32. How should the availability of 23-hour stay facilities affect patient selection for outpatient surgery?
33. Should all patients remain at least 2 hours on site in a free-standing surgery center once in the recovery room (postanesthesia care unit [PACU])?

ANSWERS*

HISTORY OF OUTPATIENT SURGERY AND KEYS TO SUCCESS

1. In 1917, after 100 years of hospital-based surgery made that venue the norm, Dr. Ralph Waters opened the first modern ambulatory surgery center in downtown Sioux City, Iowa. The name of his center (and the article he published describing it) emphasized the value of its practice to both patients and surgeons: "The Downtown Anesthesia Clinic." His motivation was convenience and cost savings for patients, their families, and surgeons. (589)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

2. The four most important areas to focus on to ensure success in outpatient anesthesia and surgery are:
   a. Selection criteria for cases and patients that create a predictable environment
   b. Attention to safety that exceeds that applied in the hospital setting, in which there are many more redundant support systems
   c. Careful monitoring of patient outcomes and the literature to discover the "best practices" to consistently leave postoperative patients clear-headed and as free of nausea and pain as possible
   d. Codification of those best practices into "standard work," which consists of algorithms that direct care so as to increase the predictability of successful outcomes. (589)
3. The careful selection of patients and procedures, as well as the team that works in an operating suite is a primary determinant of the predictability of procedures in the outpatient surgery setting. (589)
4. Since there are fewer redundant systems in an outpatient center than in a hospital, it is more important that practitioners in the outpatient center are more highly trained and practiced in a wider variety of skill sets than would be true in the hospital. (589-590)
5. Evidence exists that the decrease in variation in care based on outcome measurement has provided improved quality of health care. (590)

PREOPERATIVE CONSIDERATIONS

6. Laboratory and other testing should be used only if there is an aspect of a particular patient's medical history that indicates such a need. For instance, the only patients who should have an ECG performed prior to outpatient surgery are those who are older than 65 years or who have a history of congestive heart failure, previous myocardial infarction, angina, high cholesterol, significant valvular disease, or a family history of sudden death. (591)
7. A myocardial infarction sustained within the past 3 months may not preclude a patient from having elective surgery in a freestanding surgery center, unless:
   a. The patient continues to have ongoing pain or evidence of at-risk myocardium
   b. The patient has unstable dysrhythmias
   c. The patient had a drug-eluting coronary stent placed within the last year or a bare-metal stent within the past month, or
   d. The patient also has evidence of *three or more* of the following conditions: a history of congestive heart failure, insulin-dependent diabetes, chronic renal insufficiency (creatinine >2 mg/dL), a transient ischemic attack, or cerebrovascular accident (stroke). (591)

TECHNIQUES OF ANESTHESIA FOR OUTPATIENT SURGERY

8. MAC frequently involves the use of "blow by" oxygen and the close proximity of electrocautery or laser used by the surgeon, which increases the likelihood for fire. If a patient requires obtundation such that augmented inspiratory oxygen is required, and if electrocautery or laser will be in proximity to the airway, then the use of general anesthesia with a closed airway device (laryngeal mask airway or endotracheal tube) may well be safer than MAC. (592)
9. Regional anesthesia can decrease overall anesthesia time and do so without increasing turnover time duration. PACU time can also be decreased. (592)
10. Neuraxial anesthesia, particularly with the use of a low-dose or short-acting agent (such as 2-chloroprocaine), does not delay discharge when compared to general anesthesia. (592)
11. Postoperative urinary retention (POUR) is associated less with anesthesia technique since both neuraxial and general anesthesia impact the autonomic system. Assuming reasonable choices of drugs and doses are made with each, POUR is

associated more with the nature of the patient (age, preexisting benign prostatic hyperplasia, neurologic disease) and procedure (duration, rectal, urinary, or inguinal procedures). An algorithm for the management of POUR should be created and include the use of ultrasound evaluation of the bladder volume. (612)

12. The use of general anesthesia for outpatient surgery increases the risk of PONV/PDNV, postoperative cognitive dysfunction, and delayed discharge when compared to MAC or regional anesthesia. (592)

13. PONV and postoperative cognitive dysfunction can be diminished by avoiding (1) preoperative and intraoperative opioid in lieu of multimodal analgesia, (2) general anesthesia instead of or in addition to regional anesthesia, and (3) inhaled anesthetics in lieu of total intravenous anesthesia. (593)

TOPICS OF IMPORTANCE IN OUTPATIENT ANESTHESIA

14. There is no evidence that a specific Hb A_{1c} level indicates any guarantee of safety, but a level of 7 or lower is an indication that a patient with diabetes has it in good control. A higher level, combined with other indications of comorbidity, should be a concern to the anesthesiologist consultant that risk is higher. The highest value of the lab test is to provide guidance to the patient's primary physician to adjust medication doses to improve control, far enough in advance to potentially improve the level of risk incurred by the patient in the perioperative period. (593)

15. The rule of 1800 is a good approach to dosing insulin on the day of surgery. In this paradigm, the number 1800 is divided by the patient's normal daily insulin dose (i.e., the total daily dose of all forms of insulin, including basal and boluses, or long and shorter acting, taken in a typical 24-hour period). The result determines the probable change in glucose level (mg/dL) that would be anticipated by the use of a single unit of regular insulin. (593)

16. One must alert the patient to the likelihood of blood sugar elevations after any surgical procedure, with or without the use of dexamethasone. It is unusual that antiemetic doses of dexamethasone would elevate the blood glucose to a degree notable apart from the elevation induced by the surgical procedure itself. (594)

17. Hypertension, treated or untreated, is an independent variable that correlates positively with perioperative morbidity. (594)

18. Prior to deciding that a freestanding facility is the appropriate venue to provide anesthesia for a patient with a known or suspected personal history of malignant hyperthermia, the requirement should be that the center can replicate exactly the standard of care for treatment of a malignant hyperthermia episode. This would include more than 36 vials of dantrolene (more than 36 are needed in view of the increased incidence of obesity), blood gas capability, and ready availability of intensivists, respiratory therapists, and ventilators such that early stabilization and transfer to the hospital will be of equivalent safety to the care that would be provided in the hospital (595)

19. Patients with OSA are at increased risk for cerebrovascular events, myocardial infarction, bleeding, and perioperative respiratory events (e.g., difficult intubation). (595)

20. The value of preoperative evaluation and delineation of OSA severity is that patients with OSA can be treated with continuous positive airway pressure (CPAP) for a few weeks and thereby decrease their risk. CPAP therapy can induce decreases in blood pressure readings, tongue and hypopharyngeal muscle size, and result in less bleeding in the postoperative period. (595)

21. Recognition of moderate or severe OSA combined with a need for general anesthesia and a likely need for moderate doses of opioid should lead to a decision to

provide overnight or hospital care in view of the high risk for respiratory impairment due to the unobserved use of opioids. (596)

22. Inadequate monitoring is the most frequent cause of injury associated with anesthesia provided at off-site locations. (596)

23. Factors associated with increased risk of perioperative mishap in the office setting include the use of unqualified providers for either surgery or anesthesia and a lack of appropriate equipment and training for resuscitation and other emergencies, as well as inadequate access (delayed transfer) to hospitals. (596)

24. The various therapies used for multimodal analgesia provide high patient satisfaction and opportunities for fast-tracking. They decrease acute and chronic postoperative pain and therefore the need for postoperative opioids. They also decrease PONV, time to discharge, and reduce immune suppression and tumor metastasis. (596)

25. Anticipation of a requirement for significant opioid doses for postoperative analgesia is a good reason to redirect the case to the inpatient setting. (596)

26. Pediatric tonsillectomy performed for moderate or severe obstructive airway disease actually results in increased obstruction, not relief, in the first 24 hours after surgery. This is the reason that both ENT and anesthesiology professional society guidelines recommend against performance of tonsillectomy in children 36 months or younger as outpatients (597)

27. PONV is a postoperative complication that patients rank as high as they rank postoperative pain. (597)

28. The Apfel score is predictive for the incidence of onsite PONV but not for PDNV. (597)

29. A regimen of both IV dexamethasone 8 mg and ondansetron 4 mg intraoperatively, followed by oral tablets of 8 mg ondansetron at discharge and on postoperative days 1 and 2, can virtually eliminate early and late PONV/PDNV in even the highest risk patients. (597)

30. If nausea or vomiting occurs in the PACU despite use of IV ondansetron intraoperatively, it is more effective to use small doses (6.25 mg) of intravenous promethazine rather than repeat the use of ondansetron. (597)

31. The presence of an upper respiratory infection should lead to cancellation of an elective outpatient surgical case if the planned surgical procedure requires endotracheal intubation, the patient has underlying cardiac or pulmonary comorbidities, or the procedure will directly impact the airway. Irrespective of comorbidities or the type of procedure to be done, the presence of systemic symptoms (fever, malaise), wheezing, or dyspnea should also lead to postponement. (598)

32. The presence of 23-hour overnight stay facilities onsite should potentially increase the variety of surgical procedures that can be done, but not affect the patient health criteria for admission to an outpatient surgery center. Whereas such facilities can provide the option to manage surgical-related issues (e.g., drains, IV PCAs) they do not change the safety equation regarding patients with unstable cardiovascular conditions or obstructive sleep apnea, for example. (606)

33. Use of the postanesthetic discharge scoring system (PADSS) allows patients to be discharged safely without a minimum time requirement in the recovery room. (612)

Chapter

35 PROCEDURES PERFORMED OUTSIDE THE OPERATING ROOM

Lawrence Litt

CHARACTERISTICS OF REMOTE LOCATIONS

1. What are some fundamental capabilities available in the operating room that must also be available for the delivery of anesthesia in remote locations?
2. What are some special challenges facing the anesthesiologist when delivering anesthesia and at the conclusion of anesthesia in remote locations?
3. What are some safety concerns facing the anesthesiologist delivering anesthesia in remote locations?

RADIATION SAFETY

4. Why might patients require anesthesia for diagnostic and therapeutic radiologic procedures?
5. How might the anesthesiologist limit his or her exposure to radiation during diagnostic and therapeutic radiologic procedures?

ALLERGIC REACTIONS

6. What are some side effects associated with intravenously administered contrast agent? What prophylaxis may be administered to patients at risk of a serious adverse reaction to intravenously administered contrast agent?

NONINVASIVE X-RAY PROCEDURES

7. What is magnetic resonance imaging (MRI)? For what evaluations is it useful?
8. What are some contraindications to undergoing MRI?
9. What are some features of MRI that make it difficult for the patient to tolerate?
10. How should the patient be monitored when undergoing an anesthetic for MRI?
11. How must anesthetic equipment and monitors in the MRI center be altered for MRI compatibility? What are the risks of using standard operating room monitors?
12. How must accidental extubation of the trachea during MRI be managed?
13. Why is there an increased risk of hypothermia for patients in the MR imager?
14. What is computed tomography?
15. How does the management of anesthesia for patients undergoing computed tomography compare with the management of anesthesia for patients undergoing MRI?

INVASIVE X-RAY PROCEDURES

16. Why more so in interventional radiology procedures than in diagnostic radiology procedures can there be a need for the anesthesiologist to suddenly change to the management of blood coagulation parameters by giving medications or taking new actions?
17. What drug should be immediately available for injection, and at what dose, in invasive radiology procedures where there has been administration of a full anticoagulation dose of heparin?

18. Patients taking antiplatelet drugs are often asked to stop taking those drugs several days before a surgical procedure to allow the body to generate new platelets unaffected by the drugs. However, interventional radiology procedures must sometimes be done in such patients before the effects of antiplatelet drugs have completely worn off. What action must the anesthesiologist take if serious bleeding occurs before antiplatelet agents have worn off, and the international normalized ratio, prothrombin time, partial prothrombin time, and fibrinogen are all normal?

RADIATION THERAPY

19. Why might patients require anesthesia for radiation therapy?
20. Why must remote monitoring devices be used for patients undergoing radiation therapy under anesthesia?

ELECTROCONVULSIVE THERAPY

21. What patients are candidates for electroconvulsive therapy (ECT)? How is ECT accomplished?
22. What are some cardiopulmonary effects of ECT? In what sequence might these effects occur?
23. What are the most common causes of mortality after ECT?
24. How is cerebral blood flow affected by ECT?
25. How is intragastric pressure affected by ECT?
26. What are some contraindications and relative contraindications to ECT?
27. What are some post-ECT manifestations in the patient?
28. What is the recommendation for the ingestion of solids and liquids before the performance of ECT?
29. Why is preoperative medication not recommended for the patient who is to undergo ECT?
30. What agents might be used for the induction of anesthesia in a patient undergoing ECT?
31. After unconsciousness results from the induction of anesthesia, why might succinylcholine be administered to the patient? Before this is done, why might a tourniquet be applied to an extremity of the patient?
32. How can the airway of the patient undergoing ECT be managed? What equipment should be available to the anesthesiologist?
33. What monitors should be used during the administration of an anesthetic for ECT?

CARDIAC CATHETERIZATION

34. Why might patients require anesthesia for cardiac catheterization? What adverse effects might the anesthetic have on cardiac function during these procedures?
35. What $Paco_2$ should be maintained during anesthesia for cardiac catheterization?
36. What complications can occur as a result of cardiac catheterization procedures?
37. How might anxiety be allayed during cardiac catheterization procedures?
38. Why might the onset of action of inhaled or injected anesthetics be altered in patients undergoing cardiac catheterization procedures?

CARDIOVERSION

39. Why does a patient undergoing elective cardioversion require sedation and amnesia? How might this be accomplished?
40. How can the patient's airway be maintained during anesthesia for cardioversion?
41. What monitors should be used during anesthesia for a patient undergoing cardioversion?

EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY

42. What is extracorporeal shock wave lithotripsy (ESWL)?
43. What are the shock waves timed with during ESWL to avoid cardiac dysrhythmias?
44. Why is anesthesia required for patients undergoing ESWL?
45. What are some advantages of general anesthesia for patients undergoing ESWL?
46. What sensory level of regional anesthesia is recommended for patients undergoing ESWL with this anesthetic technique?

47. Why is intravenous fluid administration important during ESWL?
48. What are some contraindications to ESWL?

DENTAL SURGERY

49. What patients might require anesthesia for a dental procedure?
50. Why might an anticholinergic be administered to a patient before a dental procedure?
51. What agents can be used for the induction of anesthesia in patients requiring anesthesia for a dental procedure? What agent can be used in uncooperative patients when there is no intravenous access before the induction of anesthesia?
52. How is tracheal intubation usually accomplished to facilitate the dentist's ability to perform dental procedures in patients requiring general anesthesia for the procedure?
53. What are some special concerns for the patient during emergence and in the recovery period after having undergone a dental procedure under general anesthesia?

ANSWERS*

CHARACTERISTICS OF REMOTE LOCATIONS

1. Fundamental capabilities for monitoring, the delivery of supplemental oxygen, mechanical ventilation of the lungs, the delivery and scavenging of inhaled anesthetics, anesthesia equipment, and the availability of suction must all be available for the delivery of anesthesia in remote locations. (618)
2. Special challenges facing the anesthesiologist when delivering anesthesia in remote locations include limited access to the patient's airway, poor availability of accessory help, and the potential difficulty in quickly obtaining emergency equipment. Special challenges facing the anesthesiologist at the conclusion of anesthesia in remote locations are based on the greater amount of distance the anesthesiologist must transport the patient before reaching the postanesthesia care unit. These may include a greater need for a supplemental oxygen supply and continuous monitoring. (618-619)
3. Some safety concerns that may face the anesthesiologist delivering anesthesia in remote locations include the possibility of exposure to increased radiation and the scavenging of waste anesthetic gases. (618-619)

RADIATION SAFETY

4. Patients, usually children, who cannot remain still or who cannot cooperate with instructions are most likely to require general anesthesia or sedation for diagnostic and therapeutic radiologic procedures. Adults may also require sedation or general anesthesia for radiologic procedures, especially patients who are developmentally delayed or have sustained trauma. (620)
5. The anesthesiologist should attempt to limit his or her exposure to radiation by wearing a lead apron and thyroid shield, through the use of movable lead glass screens, and by remaining as far away as possible from the radiation source, preferably at least 1 to 2 m. (619)

ALLERGIC REACTIONS

6. Common side effects associated with the administration of intravenous contrast agents are nausea and vomiting, a perception of warmth, headache, and mild urticaria. Severe reactions may include vomiting, rigors, feeling faint,

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

bronchospasm, chest pain, arrhythmias, and renal failure. Life-threatening reactions include severe bronchospasm, glottic edema, pulmonary edema, arrhythmias, seizures, and cardiac arrest. The newer nonionic contrast dyes of lower osmolarity tend to be associated with fewer incidences of allergic reactions. Even so, patients at risk for an adverse reaction to a contrast agent should be pretreated with medicines to minimize the reaction to the contrast agent. Prednisolone can be administered at a dose of 50 to 100 mg intravenously both the night before and the morning of the procedure. Diphenhydramine, 50 mg, should also be given intravenously just before the procedure. Adequate hydration is necessary in these patients to maintain their intravascular volume because the intravenous contrast medium also acts as an osmotic load for the patient, inducing diuresis. (619-620)

NONINVASIVE X-RAY PROCEDURES

7. MRI is a radiologic technology that provides digitalized tomographic images of the body by exposing the body to a very high-strength constant magnetic field and high-frequency alternating electric and magnetic fields. MRI does not produce any ionizing radiation. These studies are useful for the evaluation of neurologic and soft tissues, because they can distinguish between fat, vessels, and tumor. (620)
8. MRI is contraindicated in patients who have any implanted metals that are attracted or repelled by a magnetic field, or easily heated by alternating electromagnetic fields. Examples of metallic items include artificial cardiac pacemakers, aneurysm clips, some intravascular clips, and some biologic pumps. Contraindicated items with metals that can be dangerously heated and cause injury are standard pulse oximeter probes, standard electrocardiogram electrodes, temperature probes, pulmonary artery catheters containing wires, and epidural catheters containing wires. (621)
9. MRI is difficult for the patient to tolerate based on the positioning of the patient during the study. The patient must lie on a long thin table and then be moved into a long thin tube that has walls close to the face of the patient. Patients during MRI may become claustrophobic. In addition, the MR imager makes loud booming noises that may augment a patient's discomfort. (621)
10. The patient undergoing an anesthetic during MRI should have his or her blood pressure, pulse oximeter oxygen saturation, and cardiac rhythm continually monitored with special MRI-compatible equipment. Capnograph monitors may also be used to detect end-tidal carbon dioxide, especially when monitoring from a distance. Extensions must be placed on all monitoring equipment because the patient moves into the MR imager during the study. (621)
11. Standard operating room monitors and anesthetic equipment must not be used. Special MRI-compatible monitoring equipment, such as a fiber-optic pulse oximeter, must be available for use in the MRI center. No ferromagnetic components are allowed for use near the scanner, because any ferromagnetic material will be forcefully attracted by the magnet and may cause injury to individuals in or near the scanner. Plastic, nonmagnetic steel, and aluminum components replace metal ones within special anesthetic machines, monitoring and intravenous infusion equipment, and ventilators specially made for compatibility with the MR imager. Aluminum gas cylinders must be used instead of standard iron gas cylinders. Again, traditional pulse oximeters must not be used in the MR imager, because they can cause very serious burns to the patient. (621)
12. Accidental extubation of the patient's trachea during MRI must be managed by immediate discontinuation of imaging, removing the patient from the imager, and rapidly controlling the patient's airway. In the event that resuscitative equipment is necessary in an emergency, the patient must be moved far enough away from the MR imager to prevent metal components of the resuscitative equipment from becoming attracted to the magnet. (621)

13. The airflow through the MR imager increases the amount of heat loss from the patient, placing the patient at an increased risk of hypothermia. This risk is of particular concern for pediatric patients undergoing MRI. (621-622)

14. Computed tomography (CT) is a radiologic imaging study that produces a two-dimensional image from data obtained by rotating an x-ray beam around the subject. Thus CT scanners emit ionizing radiation. (620)

15. Anesthesia for CT scanning is similar to that for MRI. That is, access to the patient is limited and monitoring is remote. Unlike with the MR imager, the avoidance of ferromagnetic equipment is not necessary. (620-621)

INVASIVE X-RAY PROCEDURES

16. Interventional radiology cases can require sudden management changes in coagulation parameters because unforeseen bleeding in an anticoagulated patient can occur suddenly as a complication. If this occurs, the anticoagulation may need to be immediately reversed. If the bleeding is intracerebral, reversal of the coagulation can be essential for saving the patient's life. (622-623)

17. When interventional radiology patients are heparinized during a procedure, the anesthesiologist must have protamine immediately available, preferably already drawn up and at a port where it can be injected safely and followed by a flush injection. (622-623)

18. If adequate platelet function prevents the cessation of bleeding in patients medicated with long-acting antiplatelet medications, then platelet transfusions are needed. There are no drugs available for suddenly reversing the effects of long-acting antiplatelet drugs. (622-623)

RADIATION THERAPY

19. Patients undergoing radiation therapy may require anesthesia for immobilization during the procedure. Immobilization during radiation therapy is important because large doses of radiation are focused on specific target sites, and movement during the procedure can result in tissue damage to areas inadvertently radiated. The duration of the procedure is very brief, requiring that the patient must remain immobile for only a brief amount of time. (620)

20. Remote monitoring devices must be used for patients being sedated or anesthetized while undergoing radiation therapy because high doses of radiation require that all individuals must leave the area during the treatment period. (623)

ELECTROCONVULSIVE THERAPY

21. Patients who have severe clinical depression that is refractory to medicines, patients who have become acutely suicidal, patients who are acutely psychotic or schizophrenic, and patients with acute mania are all candidates for electroconvulsive therapy (ECT). ECT is accomplished by administering an electric stimulus to the patient that is sufficient to induce a grand mal seizure. The mechanism for the short-term benefit derived from ECT is unknown, but is thought to be due to either the release or reestablishment of neurotransmitter levels. Controversy remains regarding the long-term benefit of ECT. (624)

22. Cardiopulmonary effects of ECT are reflected as stimulation of the parasympathetic nervous system followed by stimulation of the sympathetic nervous system. Initially, the anesthesiologist may see bradycardia and hypotension, followed by an increase in heart rate, an increase in blood pressure, and cardiac dysrhythmias. Apnea may also be seen during ECT. (624-625)

23. The most common causes of mortality after ECT are myocardial infarction and cardiac dysrhythmias. (625-626)

24. Dramatic increases in cerebral blood flow occur during ECT. (625-626)

25. Intragastric pressure is increased during ECT. (625)

26. Contraindications and relative contraindications to ECT include pheochromocytoma, increased intracranial pressure, recent cerebrovascular accident, cardiovascular conduction defects, high-risk intrauterine pregnancy, and aortic or cerebral aneurysms. (624-626)

27. After ECT, and the resultant grand mal seizure, the patient is likely to be postictal. Headache, confusion, agitation, cognitive impairment, and apnea may all be present after the procedure. (625-626)

28. Before the performance of ECT the patient must have fasted from solids and liquids just as a patient would before general anesthesia. This is to minimize the risk of the pulmonary aspiration of gastric contents, because protective airway reflexes will be lost with the induction of anesthesia and potentially during the seizure activity. (625)

29. Preoperative medication is not recommended before an ECT procedure because the duration of the preoperative medicine would likely be longer than the duration of the procedure itself. This may cause a delay in the awakening of the patient and a delay in the recovery of the patient from the procedure. An intravenous anticholinergic drug may be administered to a patient undergoing ECT before the administration of anesthesia to prevent the parasympathetic nervous system–mediated bradycardia that is frequently seen early in ECT. The anticholinergic drug would therefore have to be given 1 to 2 minutes before the induction of anesthesia. The routine administration of an anticholinergic is not recommended, however, because the duration of the bradycardia is typically brief. (625)

30. Most induction agents for general anesthesia may be used to induce anesthesia in patients undergoing ECT. These include propofol (1 to 1.5 mg/kg intravenously [IV]), thiopental (1.5 to 3 mg/kg IV), and methohexital (0.5 to 1 mg/kg IV). Careful hemodynamic monitoring must accompany the induction of anesthesia for ECT and continue throughout the entire procedure. (625)

31. After the induction of anesthesia and the onset of unconsciousness, succinylcholine is often administered in subclinical doses (0.3 to 1.0 mg/kg IV) to the patient undergoing ECT. The goal of succinylcholine administration is to attenuate the effects of seizure activity on skeletal muscle, mainly the tonic-clonic muscular contractions that may cause some harm to the patient. Because the administration of succinylcholine before ECT may mask the seizure activity that results from ECT, isolation of an extremity with a tourniquet is often done before succinylcholine administration. Physiologically, this prevents the administered succinylcholine from reaching the neuromuscular junctions in the isolated extremity distal to the tourniquet. Clinically, this allows for the physician to confirm that seizure activity has resulted from the ECT by observing the muscular contractions in the isolated extremity. (625)

32. The airway of the patient undergoing ECT can be managed by hand with a mask provided the patient is not at risk for the aspiration of gastric contents. Before the induction of anesthesia the patient must be well preoxygenated. The anesthesiologist must be prepared to ventilate by hand with bag and mask using supplemental oxygen before the onset of seizure activity and also in the postseizure period, given that apnea may follow seizure activity even after the termination of the effects of succinylcholine. The anesthesiologist must have all equipment needed to intubate the trachea of the patient should it become necessary. Suction must also be available in the event that the regurgitation of gastric contents or excessive oral secretions should occur. (625-626)

33. Routine monitors must be used during an ECT procedure, including pulse oximetry, blood pressure monitoring, and a continuous electrocardiogram. In addition to these, a peripheral nerve stimulator may be useful to confirm neuromuscular

blockade and the recovery of skeletal muscle from neuromuscular blockade. An electroencephalogram may also be used to confirm grand mal seizure activity during ECT. (625)

CARDIAC CATHETERIZATION

34. Adults may undergo cardiac catheterization for a variety of procedures, including percutaneous valve procedures, pacemaker and/or implanted cardiac defibrillators (ICD), and angioplasty with or without stent placement. Anesthesia for these cases can be very challenging given that cardiac function may be severely compromised. In addition, the cardiologist may induce fibrillation during a procedure for ICD implant to test the new device. Children undergoing cardiac catheterization for the diagnosis of congenital cardiac lesions might require anesthesia for the procedure. The anesthetic employed must not have any significant effect on existing cardiac shunts so as not to interfere with the results of the study. The administration of anesthesia may cause myocardial depression or a decrease in preload by decreasing venous return, so care must be taken by the anesthesiologist to minimize these cardiovascular changes. (626)

35. The $Paco_2$ that should be maintained during anesthesia for patients undergoing cardiac catheterization should be equal to the patient's resting $Paco_2$ so as not to influence myocardial activity or pulmonary pressure. (626)

36. Complications that can occur as a result of cardiac catheterization include bleeding at the vascular access site, perforation of the heart wall or great vessels, embolism, cardiac dysrhythmias, and heart block. In addition, thrombosis may occur in patients with a high hematocrit. (626)

37. Anxiety during cardiac catheterization procedures may be allayed by the administration of a benzodiazepine, possibly in combination with a short-acting opioid. This may be important in patients with coexisting cardiopulmonary problems because of the potential for the exacerbation of their underlying disease by the anxiety. (626)

38. The onset of action of inhaled or injected anesthetics may be altered in patients undergoing cardiac catheterization secondary to the influence of left-to-right or right-to-left shunts that may be present in this patient population. A left-to-right shunt causes the arterial partial pressure of an inhaled anesthetic to be higher than it otherwise would be because the blood that has passed ventilated alveoli does not pass through tissues before returning to the heart. Although the clinical effect of a left-to-right shunt is negligible, a right-to-left shunt can be serious because it has the opposite effect. A right-to-left shunt causes the arterial partial pressure of an inhaled anesthetic to be lower than it otherwise would be secondary to the dilutional effect of the blood that enters the systemic circulation without passing by ventilated alveoli after returning from the tissues. The rate of induction, and subsequent onset of action, of inhaled anesthetics may therefore be slowed in the presence of a right-to-left shunt. (626)

CARDIOVERSION

39. Elective cardioversion can be painful during the electric shock, requiring the patient to have sedation and amnesia for a brief period during the administration of the shock. This can be accomplished by the intravenous injection of a short-acting induction drug such as etomidate or propofol after preoxygenation and just before the administration of the electric shock. (626-627)

40. The patient's airway can be maintained during anesthesia before and after the cardioversion by hand with a mask provided the patient has fasted before the procedure. Equipment that should be available to the anesthesiologist providing anesthesia for cardioversion include a bag and mask for the support of ventilation, a supplemental oxygen source, suction, and the appropriate equipment for emergent intubation of the trachea. (626-627)

41. Monitoring of blood pressure, pulse oximetry, and the electrocardiogram should be the standard during anesthesia for cardioversion. (626-627)

EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY

42. Extracorporeal shock wave lithotripsy (ESWL) is a noninvasive method using shock waves for the disintegration of renal stones. All lithotripters have an energy source, a system to focus the shock wave, and a system to visualize and localize the renal stone. The first lithotripters required that patients be immersed in a water bath supported in a seated position. The immersion itself altered the patient's physiology. For example, the central venous pressure often increased and the patient often became hypotensive after being immersed in warm water. Newer lithotripters do not require a water bath, are on multifunctional tables where cystoscopy and ureteral stent placement may also take place, and provide more focused shock waves to minimize pain at the entry site. (627)

43. Shock waves in ESWL are timed with the patient's heart rate and are triggered by the R wave on the patient's electrocardiogram. The shock waves are subsequently delivered during the refractory period of the heart muscle, thus minimizing the risk of cardiac dysrhythmias. Despite this, atrial and ventricular premature complexes, atrial fibrillation, and supraventricular tachycardia have all been reported. (627)

44. Anesthesia is required for patients undergoing ESWL for two reasons. First, the impact of the shock waves on the patient can be painful, especially in the immersion bath model of shock wave lithotripters. Second, immobilization of the patient is important for the success of the procedure. The shock waves are focused on the renal stones, and any movement of the patient can displace the focus of the shock wave so that it is no longer effectively targeting the renal stones. (627)

45. Advantages of general anesthesia for patients undergoing ESWL include rapid onset, better patient immobilization, and the control of ventilatory parameters to minimize stone movement with respiration. (627)

46. For a patient undergoing ESWL with a regional anesthetic, a T6 sensory level is necessary to ensure patient comfort during the procedure. Unfortunately this high level of anesthesia and sympathetic nervous system blockade may be associated with hypotension. This may be exacerbated by the sitting position necessary for some lithotripters. (627)

47. Intravenous fluid administration is important during ESWL for the maintenance of an adequate urine output. This helps facilitate the passage of stones that have been disintegrated by the shock waves. (627)

48. Contraindications to ESWL include pregnancy, coagulopathy, morbid obesity, and aortic aneurysms. Patients with pacemakers may undergo ESWL provided the pacemaker is placed above the diaphragm and not in the abdomen. (627)

DENTAL SURGERY

49. Anesthesia for a dental procedure is usually required for patients who are very young or developmentally delayed and unable to tolerate the procedure. (628)

50. An anticholinergic may be administered to a patient before a dental procedure for its antisialagogue effect. (628)

51. Any of the induction agents used to induce general anesthesia may be used for patients undergoing dental procedures, including methohexital, thiopental, propofol, and etomidate. When there is no intravenous access available, and the patient is uncooperative, the anesthesiologist may use intramuscular ketamine for the induction of anesthesia. (628)

52. Tracheal intubation is usually accomplished nasally to facilitate the dentist's ability to perform dental procedures on those patients requiring general anesthesia for the procedure. (628)

53. During the emergence from general anesthesia for dental procedures the anesthesiologist must exercise caution with regard to the patient's airway. The patient must have intact laryngeal reflexes for the safe extubation of the trachea. Oral bleeding and secretions that occurred intraoperatively may have led to gastric distention and irritation. Ongoing oozing and secretions may also place the patient at a greater risk for laryngospasm. The removal of oropharyngeal packing must be confirmed. In the recovery area, the patient's airway must be closely observed by personnel with the appropriate equipment for airway management, including suction. (628)

Chapter

36 POSTANESTHESIA RECOVERY

Theodora K. Nicholau

1. What is the postanesthesia care unit (PACU)?
2. What are the requirements for monitoring in the PACU?
3. What are the American Society of Anesthesiologists (ASA) practice guidelines for post anesthesia care?
4. What are some postoperative physiologic disorders that may manifest in the PACU?

AIRWAY OBSTRUCTION

5. What is the usual mechanism of airway obstruction in the post general anesthesia patient? How does it present clinically?
6. What is the initial intervention to deal with airway obstruction?
7. How may residual neuromuscular blockade manifest in an awake patient?
8. How is residual neuromuscular blockade assessed in an awake patient?
9. What are some factors that contribute to prolonged nondepolarizing neuromuscular blockade in the PACU?
10. What are some factors that contribute to prolonged depolarizing neuromuscular blockade in the PACU?
11. What operative factors may result in life-threatening airway edema in the immediate postoperative period?
12. What leak tests can be performed to evaluate airway patency in patients at risk for airway edema prior to extubation of the trachea?
13. What are some special considerations for patients with obstructive sleep apnea for postanesthesia care?

HYPOXEMIA IN THE PACU

14. What are some potential causes of hypoxemia in the PACU? Which of these is most common?
15. What are some potential causes of postoperative hypoventilation?
16. What is the ventilatory response to carbon dioxide?
17. In the PACU, how can hypoxemia secondary to hypercapnia be reversed?
18. What is diffusion hypoxia?
19. Describe the hypoxic pulmonary vasoconstriction (HPV) response and list the conditions and medications that may inhibit it.
20. What is the significance of an increased venous admixture in the PACU?

PULMONARY EDEMA IN THE PACU

21. What are the typical causes of noncardiogenic pulmonary edema in the PACU?
22. What is postobstructive pulmonary edema?
23. What is transfusion-related acute lung injury (TRALI)? When is it likely to present?
24. How is TRALI distinguished from transfusion-associated circulatory overload?

OXYGEN SUPPLEMENTATION

25. What is the F_{IO_2} that can be delivered through simple nasal cannula? What are some other options for oxygen delivery in the PACU?
26. What is a high flow nasal cannula? What is its advantage?
27. Is there a role for continuous positive airway pressure (CPAP) and noninvasive positive-pressure ventilation (NIPPV) in the PACU?

HEMODYNAMIC INSTABILITY

28. What is the significance of hypertension in the PACU?
29. What are some factors associated with significant hypertension in the PACU?
30. What are some causes of hypotension in the PACU?
31. How is myocardial ischemia detected in the PACU?
32. What are some factors which may contribute to cardiac arrhythmias in the PACU?
33. What are some possible causes of sinus tachycardia in the PACU?
34. How should new-onset atrial fibrillation be managed in the PACU?
35. What drugs may contribute to ventricular tachycardia in the PACU?
36. What are some possible causes of bradycardia in the PACU?

DELIRIUM

37. What is the incidence of postoperative delirium in patients older than 50 years of age?
38. What are some risk factors and causes of postoperative delirium?
39. What is emergence excitement?

RENAL DYSFUNCTION

40. What is the differential diagnosis of postoperative renal dysfunction?
41. How is oliguria defined? What are some causes of oliguria in the PACU?
42. What are the risk factors for postoperative urinary retention?
43. What are some specific causes of oliguria presenting in the PACU that require immediate attention to prevent ongoing injury?

BODY TEMPERATURE AND SHIVERING

44. What is the incidence of postoperative shivering? How should it be treated?
45. What are some adverse effects of postoperative hypothermia?

POSTOPERATIVE NAUSEA AND VOMITING

46. What are some factors associated with an increased incidence of postoperative nausea and vomiting (PONV)?
47. What is the simplified risk score for identifying patients at risk for PONV? How can PONV be prevented and/or treated?

DELAYED AWAKENING

48. What are some common causes of delayed awakening in the PACU?

DISCHARGE CRITERIA

49. What are the principles used to determine PACU discharge criteria?
50. What are the components of the Aldrete scoring system?

ANSWERS*

1. The postanesthesia care unit (PACU) is the area equipped and staffed to monitor and care for patients as they emerge from general anesthesia and surgery. Clinical monitoring in the unit is focused on the cardiopulmonary system, with vigilant attention to airway patency and protection, oxygenation, and ventilation, as well as hemodynamic stability. Vital signs are recorded at the minimum every 15 minutes.

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

The unit is located adjacent to the operating room to allow for prompt intervention by anesthesia and surgical staff if needed. (632)

2. Standards and practice parameters for postanesthesia care have been adopted by the ASA. The Standards for Postanesthesia Care is a document that delineates the minimal requirements for monitoring and care in the unit. These are minimal standards that are to be exceeded when deemed appropriate by the judgment of the anesthesia caregiver.

   There are five standards that address each of the following in a general manner: (1) appropriate staffing and equipment of the unit, (2) transportation to the PACU by the anesthesia caregiver, (3) transfer of care from the anesthesia provider to the PACU nurse, (4) evaluation and monitoring of the patient in the unit, and (5) discharge of the patient from the unit. (632, 648)

3. Unlike the general ASA standards, the ASA practice guidelines for postanesthesia care provide specific recommendations for clinical evaluation and therapeutic intervention for physiologic disorders that may present in the PACU. (632)

4. A number of postoperative physiologic disorders may manifest in the PACU. These include nausea and vomiting, oliguria, hypoventilation, bleeding, hypothermia, delirium, pain, and delayed awakening. Not surprisingly, data from the U.S. closed claims database show that the most devastating outcomes are the result of airway, respiratory, or cardiovascular compromise. Hypertension or hypotension, cardiac arrhythmia, airway obstruction, hypoventilation, and hypoxemia require immediate attention and intervention. (632, Table 39-1)

AIRWAY OBSTRUCTION

5. Airway obstruction in the PACU is most often due to the loss of pharyngeal tone resulting from the residual depressant effects of inhaled and intravenous anesthetics and/or the persistent effects of neuromuscular blocking drugs. In awake patients, the pharyngeal muscles contract synchronously with the diaphragm. This activity serves to pull the tongue forward and tent the airway open as the diaphragm creates the negative pressure for inspiration. In the PACU, this pharyngeal muscle activity may be lost and the resultant compliant pharyngeal tissue collapses with negative inspiratory pressure causing obstruction. When this occurs there is a characteristic paradoxic breathing pattern consisting of retraction of the sternal notch and exaggerated abdominal muscle activity. This rocking motion becomes more prominent with increasing airway obstruction. Airway obstruction can be associated with arterial hypoxemia and desaturation on pulse oximetry. (632)

6. Airway obstruction can usually be treated by the jaw thrust maneuver. When this is not sufficient to relieve the obstruction, CPAP can be applied via face mask. If necessary, this can be followed by placement of nasal and oral airways, and in extreme cases laryngeal mask airway or endotracheal tube placement. (632)

7. Residual neuromuscular blockade in the awake patient may manifest as a struggle to breathe. In a patient whose mental status is not clear enough to communicate clearly the patient may appear agitated. (633)

8. Clinical assessment of residual neuromuscular blockade is preferred to the application of the train-of-four ratio and titanic stimulation in awake patients, as both are painful interventions. Clinical evaluation includes grip strength, tongue protrusion, the ability to lift the legs off the bed, and the ability to lift the head off the pillow for a full 5 seconds. Of these, the sustained head lift most directly reflects the ability of the patient to maintain and protect the airway. An extubated patient's ability to oppose and fix the incisor teeth against a tongue depressor is another clinically reliable indicator to pharyngeal tone. This maneuver correlates with an average train-of-four ratio of 0.85. (633)

9. Factors which may contribute to prolonged nondepolarizing neuromuscular blockade include drugs, diseases, and metabolic states. Drugs which prolong neuromuscular blockade include residual inhaled anesthesia, local anesthetics (lidocaine and other sodium channel blockers), cardiac antiarrhythmic drugs (procainamide), antibiotics (aminoglycosides most commonly), calcium channel blockers, furosemide, and corticosteroids. Metabolic states which may prolong neuromuscular blockade include hypothermia, respiratory acidosis, renal or hepatic failure, hypermagnesemia, and hypocalcemia. Of these, hypothermia and respiratory acidosis are easily recognized and reversible. (633, Table 39-2)

10. Factors which may contribute to prolonged depolarizing neuromuscular blockade include excessive doses of succinylcholine, reduced plasma cholinesterase activity, inhibited cholinesterase activity, and atypical plasma cholinesterase which is a genetic variant. Plasma cholinesterase activity may be reduced due to decreased plasma levels, extremes of age, disease states (hepatic failure, malnutrition, uremia), pregnancy, plasmapheresis, glucocorticoids, and contraceptives. Inhibited cholinesterase activity may be reversible (neostigmine, edrophonium) or irreversible (echothiophate). (633, Table 39-2)

11. Operative factors which may result in life-threatening airway edema in the immediate postoperative period include prolonged procedure in the prone or Trendelenburg position; aggressive fluid resuscitation; surgical procedures on tongue, pharynx, and neck (most common examples are thyroidectomy, carotid endarterectomy, and cervical spine procedures); and hematoma at the surgical site (again, common examples include thyroidectomy and carotid endarterectomy). In the case of volume resuscitation and procedures requiring prone or trend positioning, airway edema may be accompanied by facial and/or scleral edema. In cases such as neck dissection, carotid endarterectomy, and thyroidectomy, life-threatening airway edema may be the result of increased pressure from a hematoma that is not evident on external physical examination. (634)

12. Leak tests can be performed to evaluate airway patency in patients at risk for airway edema prior to extubation of the trachea. One leak test evaluates the patient's ability to breathe around an occluded endotracheal tube (ETT) with the cuff deflated. One can also measure the intrathoracic pressure required to produce an audible leak around the ETT with the cuff deflated. Another method is to measure the exhaled tidal volume before and after the ETT cuff is deflated. (634)

13. There are some special considerations for patients with obstructive sleep apnea for postanesthesia care. These patients should not be tracheally extubated until they are fully awake. Because of their increased risk for airway obstruction, one should minimize the use of opioids and avoid benzodiazepines or any drugs that depress respiratory drive or promote sleepiness. To this end, the application of continuous regional anesthetic techniques should be used whenever possible. Patients should have CPAP available postoperatively. The patient's home CPAP or BiPAP (bilevel positive airway pressure) device should be placed on the patient upon admission to the unit. The time in the PACU should be used to evaluate the patient to determine the appropriate degree of monitoring required once discharged from the unit. As a general rule, patients should be monitored with continuous pulse oximetry on the surgical ward. However, because pulse oximetry will not detect carbon dioxide retention in a patient that is receiving supplemental oxygen, many patients with sleep apnea will require intensive care unit level monitoring. (634)

HYPOXEMIA IN THE PACU

14. There are multiple potential causes of hypoxemia in the PACU. These include shunting, V/Q mismatch, congestive heart failure, pulmonary edema, alveolar hypoventilation, diffusion hypoxia, aspiration of gastric contents, pulmonary embolus, pneumothorax, posthyperventilation hypoxia, increased oxygen

consumption (as from shivering), acute lung injury (e.g., sepsis or transfusion related), advanced age, and obesity. Of these, atelectasis (shunt) and alveolar hypoventilation are the most common causes of postoperative hypoxemia in the PACU. (635, Table 39-3)

15. Among the potential causes of postoperative hypoventilation is anesthetic drugs, residual neuromuscular blocking drugs, impaired ventilatory muscle mechanics, increased levels of carbon dioxide production, and coexisting pulmonary disease. Each of these causes of alveolar hypoventilation leads to a corresponding increase in arterial partial pressure of carbon dioxide ($Paco_2$). In a patient breathing room air at sea level, hypoventilation to a $Paco_2$ of 80 will result in hypoxemia, even when the patient has normal lungs without significant A-a gradient. This is demonstrated through the alveolar gas equation. Alveolar oxygen pressure (Pao_2) in this scenario is 50. Supplemental oxygen can mask alveolar hypoventilation by leading to normal saturation of oxygen detected by pulse oximetry. (635, Table 39-4, Figure 39-1)

16. Minute ventilation increases in response to elevated $Paco_2$. Normally minute ventilation increases by approximately 2 L/min for every 1 mm Hg increase in arterial Pco_2. In the PACU, this linear response to Pco_2 may be depressed by residual vapor or intravenous anesthetics in addition to the administration of narcotics and benzodiazepines. (635)

17. Reversal of hypercapnic hypoxemia can be achieved by the addition of or increase in the concentration of supplemental oxygen and/or the normalization of Pco_2. Normalization of Pco_2 can be accomplished by stimulation of the patient to wakefulness, the pharmacologic reversal of the effects of narcotics, benzodiazepines and muscle relaxants, or in some cases control of the airway and initiation of positive-pressure ventilation. (636)

18. Diffusion hypoxia refers to the rapid diffusion of nitrous oxide into the alveoli at the end of a nitrous oxide anesthetic. Nitrous oxide dilutes the alveolar gas producing a transient decrease in alveolar oxygen pressure that can persist for up to 5 to 10 minutes after discontinuation of nitrous oxide. In the absence of supplemental oxygen, arterial hypoxemia may ensue. (636)

19. The hypoxic pulmonary vasoconstriction (HPV) response is the attempt of normal lungs to optimally match ventilation and perfusion by constricting vessels that perfuse poorly ventilated alveoli. This vasoconstrictive response shifts blood flow to well-ventilated regions of the lung. The HPV response is inhibited by agents that produce pulmonary vasodilation: inhaled anesthetics, Nipride, and dobutamine to name a few. Physiologic conditions that inhibit this response include pneumonia and sepsis. (636)

20. Increased venous admixture refers to the contribution of mixed venous blood to arterial hypoxemia. This effect is typically significant only in cases of low cardiac output where blood returns to the heart in a severely desaturated state. In the normal lung only, 2% to 5% of the cardiac output is shunted through the lungs, but conditions that increase shunt fraction may significantly increase the effect of venous admixture to hypoxemia. In the PACU, conditions that may increase pulmonary shunt fraction include atelectasis, pulmonary edema, and the aspiration of gastric contents. (636)

PULMONARY EDEMA IN THE PACU

21. Pulmonary edema in the immediate postoperative period is most often due to cardiogenic causes. Noncardiogenic causes of pulmonary edema in the PACU include pulmonary aspiration, sepsis, and transfusion-related lung injury. (637)

22. Postobstructive pulmonary edema is a transudative edema that results from the exaggerated negative pressure generated by inspiration against an obstructed

airway. This negative intrathoracic pressure further promotes venous return, which additionally contributes to transudation of fluid. Young muscular healthy males are most at risk due to their increased muscle mass and ability to generate significant inspiratory force. The most common cause of postobstructive pulmonary edema is laryngospasm. Objective data include hypoxemia and associated bilateral diffuse infiltrates. The diagnosis depends on clinical suspicion once other causes of pulmonary edema are ruled out. (637)

23. TRALI refers to pulmonary edema associated with fever and systemic hypotension after the transfusion of plasma containing blood products. Although fresh frozen plasma and whole blood are the obvious culprits, packed red blood cells and platelets also contain plasma and can trigger TRALI. Typically the physiologic effects of TRALI are manifest within 1 to 2 hours after transfusion, but can occur up to 6 hours after transfusion. A complete blood count obtained with the onset of symptoms would reveal an acute decrease in the white blood cell count reflecting the sequestration of granulocytes within the lung and exudative fluid. The diagnosis is made by an increased alveolar-to-arterial oxygen difference and bilateral pulmonary infiltrates in a chest radiograph. If TRALI is suspected, the transfused blood container bag should be returned to the blood bank for evaluation. (637)

24. TRALI may be difficult to differentiate from transfusion-associated circulatory overload since both manifest as pulmonary edema after the transfusion of blood products. They can be distinguished by the fever and hypotension associated with TRALI, as well as by the characteristics of the resulting edema fluid; exudative in the case of TRALI and transudative in the case of transfusion-associated circulatory overload. In either case treatment is supportive, including supplemental oxygen and diuresis. (637)

OXYGEN SUPPLEMENTATION

25. As a general rule, each liter per minute of oxygen flow through simple nasal cannula will increase the F_{IO_2} by 0.04. The delivery of oxygen by this method is limited by lack of humidification and temperature correction of the gas. The maximum rate of 6 L/min results in approximately 0.44 F_{IO_2}. Other options for oxygen delivery in the PACU include a face mask, non-rebreather face mask, high flow nebulizers, and high flow nasal cannula. Other than the high flow nasal cannula, each of these oxygen delivery methods are limited in the F_{IO_2} they can provide secondary to the entrainment of room air when the patient inhales. (637)

26. High flow delivery systems, such as the high flow nasal cannula, can deliver oxygen at a rate of 40 L/min. Patients tolerate such high flows because the inspired gas is humidified and warmed to 99.9% relative humidity and 37° C. These devices deliver oxygen directly to the nasopharynx throughout the respiratory cycle, and the high flow may enhance the F_{IO_2} by a CPAP effect. (638)

27. The decision to use noninvasive modes of ventilation in the PACU must be guided by careful consideration of both patient and surgical factors. Hemodynamic instability, refractory hypoxemia, and the inability to protect the airway due to altered mental status are standard contraindications to NIPPV. Additional contraindications to consider in this setting include an increased risk of aspiration due to the surgical procedure (i.e., esophagectomy), inability to properly apply the nasal or facemask delivery apparatus because of facial surgery (sinus surgery), or the need to avoid oropharyngeal and gastric distention by positive-pressure ventilation (esophageal and gastric operations, etc.). With the above considerations in mind, home settings of CPAP are recommended routinely for patients with obstructive sleep apnea in the PACU. In the appropriate patient population, application of CPAP in the PACU has been shown to reduce the incidence of intubation, pneumonia, and sepsis in patients who undergo abdominal surgery. (638)

HEMODYNAMIC INSTABILITY

28. Hypertension and tachycardia in the PACU have been shown to be predictive of unplanned admission to the critical care unit. (638)

29. Patients with essential hypertension are at greatest risk for postoperative hypertension in the immediate postoperative period. Some additional factors to consider include pain, emergence excitement, hypercarbia, gastric distention, drug withdrawal, increased intracranial pressure, and urinary retention. Craniotomy and carotid endarterectomy are surgical procedures that place the patient at increased risk. (638, Table 39-5)

30. A combination of one or more of the following physiologic derangements may account for hypotension in the PACU. These include a decrease in preload, a decrease in afterload, or intrinsic pump failure.

Decreased preload may be due to inadequate volume resuscitation in patients who undergo preoperative bowel preparation and/or whose surgical procedure results in ongoing translocation of fluid (most often major intraabdominal procedures), unrecognized or ongoing blood loss, or loss of sympathetic tone as a result of neuraxial blockade (spinal or epidural).

Intrinsic pump failure often results from exacerbation of preexisting cardiac conditions, such as cardiomyopathy, valvular disease, arrhythmias, or coronary artery disease. Cardiac tamponade, pulmonary embolus, and tension pneumothorax should be ruled out in at-risk patients, such as those who undergo intraoperative central line placement, intrathoracic or mediastinal invasion, or total hip arthroplasty.

Decreased afterload can be attributed to iatrogenic sympathectomy. This may be due to high neuraxial blockade (spinal or epidural), or blunting of sympathetic drive by narcotics and residual intravenous anesthetics (propofol or dexmedetomidine) in patients who rely on sympathetic tone to maintain blood pressure (examples include sepsis and patients with pericardial disease). Other causes include frank sepsis and anaphylaxis.

A high spinal anesthetic is an example of all three, because it results in a sympathectomy that dilates venous and arterial vasculature to produce decreased preload and afterload. It also affects the cardioaccelerator fibers of T4, resulting in intrinsic cardiac failure secondary to bradycardia. (638-639, Table 39-6)

31. It is difficult to reliably detect myocardial ischemia in the PACU, because patients are often unable to identify or communicate symptoms of cardiac ischemia in the immediate postoperative period. Patients with postoperative myocardial infarction complained of chest pain less than 20% of the time. Often PACU patients will attribute cardiac pain to incisional pain or vice versa. Furthermore, interpretation of the postoperative EKG must be done with the patient's cardiac history and risk index in mind. In low-risk patients, ST segment changes do not usually reflect myocardial ischemia. Relatively benign causes of ST segment changes in low-risk patients include anxiety, esophageal reflux, hyperventilation, and hypokalemia.

Routine postoperative 12-lead EKG monitoring is reserved for patients with known or suspected coronary artery disease that undergo intermediate- or high-risk surgery. Intermediate-risk surgeries include intraabdominal and thoracic surgery, carotid endarterectomy, head and neck surgery, orthopedic surgery, and prostate surgery. High-risk surgeries include major emergency surgery, aortic and other major vascular surgery, and unanticipated prolonged procedures with large fluid shifts or blood loss. In contrast to low-risk patients, ST segment and T wave changes in high-risk patients can be significant and must be taken seriously even in the absence of typical signs and symptoms. In high-risk patients, ST changes suggestive of ischemia should prompt further evaluation to rule out myocardial ischemia by monitoring serum troponins. (639)

32. Factors which may contribute to cardiac arrhythmias in the PACU may include hypoxemia, hypercarbia, pain, agitation, electrolyte abnormalities, myocardial ischemia, endogenous or exogenous catecholamines, hypertension, fluid overload, anemia, drug withdrawal, hyperthermia, and hypothermia. (640, Table 39-7)

33. Possible causes of sinus tachycardia in the PACU include pain, agitation, fever, hypercarbia, hypovolemia, anemia, and shivering. Less common and more ominous causes include the onset of cardiogenic or septic shock, pulmonary embolism, thyroid storm, and malignant hyperthermia. (640)

34. New-onset atrial fibrillation which presents in the PACU should be rapidly treated. If the patient is hemodynamically unstable, prompt cardioversion is indicated. Control of the heart rate is a goal of treatment in these patients and can be achieved with β-adrenergic blockers or calcium channel blocking drugs. Diltiazem is the calcium channel blocker of choice in this circumstance. Often rate control is enough to convert the heart rhythm from new-onset atrial fibrillation to sinus rhythm in the PACU. If chemical conversion is indicated, an amiodarone loading dose can be initiated. (640)

35. Premature ventricular contractions and ventricular bigeminy are common in the PACU. They are most often a result of increased sympathetic tone as may accompany pain or hypercarbia. Ventricular tachycardia is rare in the PACU, and is indicative of underlying cardiac abnormality. In the case of torsades de pointes, the administration of drugs that prolong the QT interval, such as amiodarone, procainamide, droperidol, and serotonin uptake inhibitors to name only a few, may contribute to the cardiac abnormality. (640)

36. Bradycardia in the PACU is often iatrogenic. Drug related causes include the administration of β- or calcium channel blockers, anticholinesterase reversal of neuromuscular blockade, narcotic administration, and sedation with dexmedetomidine. Procedure-related and patient-related causes include bowel distention, increased intracranial pressure or intraocular pressure, and high spinal anesthesia that blocks the cardioaccelerator fibers originating from T1 to T4. Underlying conduction abnormalities and myocardial ischemia are indications for emergent intervention. (641)

DELIRIUM

37. The incidence of postoperative delirium in patients older than 50 years old is approximately 10%. The incidence is highest in patients undergoing joint replacement. (641)

38. Postoperative delirium may be patient-related, iatrogenic, or surgery-related. The most significant predictors of postoperative delirium are advanced age, preoperative cognitive impairment, decreased functional status, alcohol abuse, and previous history of delirium. Intraoperative factors that are predictive of postoperative delirium include surgical blood loss, hematocrit less than 30, and the number of intraoperative transfusions. Some additional causative factors include arterial hypoxemia, hypercapnia, pain, sepsis, inadequate hydration, medications, and electrolyte abnormalities. (641)

39. Emergence excitement is a transient confusional state that is associated with the emergence of general anesthesia. It is more common in children than adults, with a peak incidence in children between the ages of 2 and 4 years. More than 30% of children will experience delirium at some period during their PACU stay. It typically resolves quickly and is followed by an uneventful recovery. (641)

RENAL DYSFUNCTION

40. The differential diagnosis of postoperative renal dysfunction includes preoperative, intraoperative, and postoperative causes. Frequently the cause is multifactorial, and a preexisting renal insufficiency may be exacerbated by an intraoperative insult.

For example, preoperative infection, contrast radiologic studies, or hepatic dysfunction may put patients at risk for decompensation of renal function from intravascular volume depletion intraoperatively. In the PACU, diagnostic efforts should focus on the identification and treatment of readily reversible causes of oliguria. (642)

41. Oliguria is defined as a urine output of less than 0.5 mL/kg/hr. Postoperative oliguria may be due to prerenal, renal, or postrenal causes. Prerenal causes include hypovolemia due to bleeding, sepsis, third space fluid loss, inadequate volume resuscitation, hepatorenal syndrome, low cardiac output, renal vascular obstruction, or intraabdominal hypertension. Intrarenal causes include acute tubular necrosis, radiographic contrast dyes, rhabdomyolysis, tumor lysis, and hemolysis. Postrenal causes include urinary retention, surgical injury or obstruction to the ureters, or mechanical obstruction to the urinary catheter. The most common cause of oliguria postoperatively is the depletion of intravascular volume. (642, Table 39-9)

42. Postoperative urinary retention refers to the inability to void despite a bladder volume of more that 500 to 600 mL. Risk factors include age over 50, male gender, intraoperative volume resuscitation, duration of surgery, bladder volume on admission, and type of surgery, in particular anorectal procedures or joint replacement. Other contributors include perioperative medications such as anticholinergics, β-blockers, and narcotics. (642)

43. Three causes of oliguria presenting in the PACU that should be immediately treated to prevent ongoing injury include intraabdominal hypertension, rhabdomyolysis, and contrast nephropathy. Intraabdominal hypertension should be ruled out by measuring the bladder pressure in any oliguric patient with a tense abdomen postoperatively. Persistently elevated intraabdominal pressure impedes renal perfusion and leads to renal ischemia.

    Rhabdomyolysis should be diagnosed and treated in oliguric patients who have suffered a major crush or thermal injury, including intraoperative thermoablation of tumors. Rhabdomyolysis should also be ruled out in morbidly obese patients who undergo prolonged surgical procedures. Volume loading and treatment with mannitol and loop diuretics can be used to flush renal tubules and prevent ongoing renal tubular damage.

    Contrast nephropathy should be considered in patients who have undergone angiography with intravascular stent placement. These patients often have chronic renal insufficiency, and are at increased risk to develop renal failure secondary to an IV contrast load. Perioperative hydration with normal saline and alkalization with sodium bicarbonate have been shown to be effective renal protective measures. Sodium bicarbonate infusions at 1 mL/kg/hr should be continued for 6 hours after contrast exposure. (642-643)

BODY TEMPERATURE AND SHIVERING

44. The incidence of postoperative shivering may be as high as 65% after general anesthesia. Postoperative shivering is not always associated with a decrease in body temperature; shivering in normothermic patients is thought to result from uninhibited spinal reflexes manifested as clonic activity. Postoperative shivering can be treated with opioids and clonidine. Meperidine is the most effective treatment for postoperative shivering. (643)

45. Adverse effects of postoperative hypothermia include shivering, inhibition of platelet function, coagulation factor activity, and drug metabolism. These may result in exacerbation of postoperative bleeding, prolonged neuromuscular blockade, and delayed awakening. Forced air warmers can be used to warm patients with postoperative hypothermia. (643)

POSTOPERATIVE NAUSEA AND VOMITING

46. Patient-related factors associated with an increased incidence of postoperative nausea and vomiting (PONV) include female gender (postpuberty), nonsmoking status, childhood (past infancy), and history of motion sickness or PONV. Anesthetic factors include use of volatile anesthetics or nitrous oxide, administration of large doses of neostigmine, and perioperative opioids. Significant surgical factors include type of procedure, such as eye muscle or middle ear surgery, gastric distention as in swallowed blood, and duration of surgery. (643)

47. There is a simplified risk score for identifying patients at risk for PONV. It is a four point score that allots a single point for each of the following factors: (1) female gender, (2) history of motion sickness or PONV, (3) nonsmoking, (4) use of postoperative opioids. A score of 0, 1, 2, 3, or 4 correlates to an incidence of 10%, 21%, 39%, 61%, and 79%, respectively. Although prophylactic measures to prevent PONV are more effective than rescue drugs administered in the PACU, some patients have PONV despite prophylaxis. There are several drugs available for the treatment of PONV, including scopolamine, hydroxyzine, promethazine, droperidol, metaclopromide, ondansetron, dolasetron, and dexamethasone. Dexamethasone is most effective when given prophylactically at the start of surgery, and ondansetron is most effective when given 30 minutes before the end of anesthesia. (643-644)

DELAYED AWAKENING

48. Residual effects of anesthetic or sedating drugs are the most common cause of delayed awakening in the PACU. If narcotic or benzodiazepines are suspected, then careful titration of the reversal drugs, naloxone and flumazenil, can be used. For example, in adults 20- to 40-μg increments of naloxone are used to avoid abrupt reversal of analgesia and associated hypertension and tachycardia. The use of flumazenil should be done with caution to avoid precipitation of seizures. Both naloxone and flumazenil have short half-lives, so the patient should be carefully observed for resedation. Rarely physostigmine may be used to reverse the CNS effects of anticholinergic drugs. Hypothermia and hypoglycemia should also be considered as potential causes of delayed awakening postoperatively. (644)

DISCHARGE CRITERIA

49. PACU discharge criteria are based on the principles that patients must be observed until they are no longer at risk for respiratory depression and their mental status has returned to baseline. No specific length of stay is required and hemodynamic parameters are based on the patient's baseline measurements. (645)

50. The Aldrete scoring system is an objective measure assigning points, or a score, to a patient to determine readiness for discharge. Components of the Aldrete scoring system include an activity, breathing, circulation, consciousness, and oxygen saturation. The patient must be able to breathe comfortably, clear secretions, and oxygenate adequately. (645)

Chapter

37 PERIOPERATIVE PAIN MANAGEMENT

Meredith C.B. Adams, Robert W. Hurley

1. What factors correlate with the severity of postoperative pain?
2. What are some potential adverse physiologic effects of acute postoperative pain?
3. What are some potential benefits of the effective management of acute postoperative pain?
4. What are the principles of multimodal perioperative analgesia?
5. What are the goals of an acute pain management service?

NEUROPHYSIOLOGY OF PAIN

6. What is nociception?
7. What are nociceptors? How are they stimulated?
8. What is the neurologic pathway of afferent pain impulses?
9. Where along the neurologic pathway of afferent pain impulses can modulation of the painful stimulus occur?
10. How can the modulation of painful stimuli occur in the periphery? What pharmacologic agents may be particularly useful for the modulation of painful stimuli in the periphery?
11. How can the modulation of painful stimuli occur at the level of the spinal cord?
12. How can the modulation of painful stimuli occur above the level of the spinal cord?
13. Name some excitatory and inhibitory neurotransmitters believed to have a role in the modulation of painful stimuli.
14. What is the difference between preemptive analgesia and preventative analgesia?

ANALGESIA DELIVERY SYSTEMS

15. Name some routes for the administration of analgesic drugs.
16. What is the limitation of the oral administration of analgesic agents for the management of acute postoperative pain? When is this route of administration appropriate?
17. What benefit does the intramuscular administration of analgesic agents have over oral administration? What are some problems with this method of administration?
18. Does ketamine have a role in the perioperative period? What are the side effects of low dose ketamine therapy?
19. How is a patient taking oral buprenorphine managed preoperatively, intraoperatively, and postoperatively?
20. What are the advantages and disadvantages of the subcutaneous, transdermal, and transmucosal administration of opioids?
21. Describe patient-controlled analgesia (PCA). What is the lockout interval?
22. What are some of the advantages of patient-controlled analgesia?
23. How do neuraxially administered opioids exert their effect?
24. What are some of the potential benefits of neuraxial opioids for postoperative analgesia?
25. What are some of the potential adverse effects of neuraxial opioids for postoperative analgesia? What different potential adverse effects may be caused by neuraxial infusion of local anesthetics?

26. What is the early depression of ventilation that may be seen with the neuraxial administration of an opioid believed to be due to?
27. What is the delayed depression of ventilation that may be seen with the neuraxial administration of an opioid believed to be due to? Why might this effect be more pronounced with morphine than with fentanyl?
28. Which patients may be most at risk for delayed depression of ventilation from the administration of a neuraxial opioid?
29. What characteristic of an opioid administered into the intrathecal space determines its time of onset and its duration of action?
30. What are the disadvantages of a single-dose administration of opioid in the intrathecal space for the management of acute postoperative pain?
31. What may be the reason for the clinical impression that the incidence of side effects associated with intrathecally administered opioid is higher than the incidence of side effects associated with the epidural administration of opioid for postoperative analgesia?
32. Why does the epidural administration of opioid require more drug than the intrathecal administration of the same opioid? What dose of epidural opioid is equipotent to the same opioid administered in the intrathecal space?
33. Why is it believed that fentanyl produces a more segmental band of anesthesia than morphine when administered in the epidural space?
34. How do the resulting plasma concentrations of fentanyl compare when the same dose of fentanyl is administered intravenously versus epidurally?
35. Why might a local anesthetic be added to the opioid for administration in the epidural space for the management of postoperative pain?
36. What is the concern regarding the concurrent use of neuraxial analgesia and anticoagulants? What are some general concepts regarding this issue covered in the American Society of Regional Anesthesia guidelines?
37. What factors increase the risk of postoperative epidural abscess associated with epidural analgesia?

ALTERNATIVE APPROACHES TO MANAGEMENT OF ACUTE POSTOPERATIVE PAIN

38. What is an advantage and a disadvantage of peripheral nerve blocks for the management of acute postoperative pain?
39. What are the advantages and disadvantages of the intraarticular administration of analgesics?
40. Are there any unique benefits of the paravertebral blockade technique?
41. What are the advantages of perioperative continuous perineural catheters in both upper and lower extremity surgeries?
42. What is the role of clonidine as an adjuvant in peripheral nerve blockade?
43. How is intrapleural regional analgesia achieved? What is an advantage and a disadvantage of this technique for the management of acute postoperative pain?
44. What are the indications for a transverse abdominis plane block? What advantages does this peripheral block offer?

ANSWERS*

1. Factors that positively correlate with severity of postoperative pain include preoperative opioid intake, anxiety, depression, pain level, and the duration of surgery. Factors that are negatively correlated include the patient's age and the level of the surgeon's operative experience. A perioperative plan should be developed that encompasses these factors to lessen the severity of the patient's postoperative pain. (650)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

2. Potential adverse physiologic effects of acute postoperative pain include hypoventilation, atelectasis, ventilation-to-perfusion mismatching in the lungs, hypercapnia, pneumonia, systemic hypertension, tachycardia, cardiac dysrhythmias, myocardial ischemia, deep vein thrombosis, decreased immune function, ileus, nausea and vomiting, urinary retention, hyperglycemia, sodium and water retention, insomnia, fear, and anxiety. Poorly controlled postoperative pain may also be a factor in developing chronic postsurgical pain. (650-651, Table 40-1)
3. Some potential benefits of the effective management of acute postoperative pain include improvement in patient comfort, a decrease in perioperative morbidity, enhanced postoperative rehabilitation, and a possible decrease in chronic postsurgical pain. It may also reduce cost by shortening the time spent in postanesthesia care units, intensive care units, and hospitals. (650)
4. The goals of multimodal analgesia include sufficient diminution of the patient's pain to instill a sense of control over their pain, enable early mobilization, allow early enteral nutrition, and attenuate the perioperative stress response. The secondary goal of this approach is to maximize the benefit (analgesia) while minimizing the risk (side effects of the medication being used). (653-654)
5. The goals of an acute pain management service are to evaluate and treat postoperative pain to minimize the period of recuperation, decrease duration of hospital stay, improve patient satisfaction, and to inhibit the development of chronic (persistent) pain through early intervention. (653-654)

NEUROPHYSIOLOGY OF PAIN

6. Nociception is used to describe the recognition and transmission of painful stimuli. Pain is described as an unpleasant sensory and emotional experience caused by actual or potential tissue damage. (652)
7. Nociceptors are the free nerve endings of afferent myelinated A-delta and unmyelinated C nerve fibers. Nociceptors are stimulated by thermal, mechanical, or chemical tissue damage. (652)
8. Nociceptors, on stimulation, send axonal projections to the dorsal horn of the spinal cord and synapse on second-order neurons there. The axonal projections of the second-order neurons cross to the contralateral half of the spinal cord and ascend the spinothalamic tract to the thalamus in the brain. In the thalamus, these second-order neurons synapse with third-order neurons that send axonal projections to the sensory cortex. Before reaching the thalamus, the second-order neurons divide and also send axonal branches to the reticular formation and periaqueductal gray matter. (652)
9. Modulation of the painful stimulus can occur at almost every level along the afferent neurologic pain pathway. It can occur at the site of stimulation of the nociceptors or at any synapse. In addition, modulation of nociception can even occur by the inhibition of the afferent sensory pathways by descending inhibitory pathways originating at the level of the brainstem. (652)
10. Modulation of painful stimuli can occur in the periphery by decreasing or eliminating the endogenous mediators of inflammation in the vicinity of the nociceptor. Examples of endogenous mediators of inflammation include prostaglandins, histamine, bradykinin, serotonin, acetylcholine, lactic acid, hydrogen ions, and potassium ions. These endogenous inflammatory mediators sensitize and excite nociceptors, leading to the conduction of the painful stimulus. Pharmacologic agents that are particularly useful for the modulation of painful stimuli in the periphery are aspirin and nonsteroidal antiinflammatory agents (NSAIDs). These agents modulate painful stimuli by decreasing the synthesis of prostaglandins. (652, Table 40-2)

11. The modulation of painful stimuli can occur at the level of the spinal cord through the effects of excitatory or inhibitory neurotransmitters in the dorsal horn of the spinal cord. (652)

12. The modulation of painful stimuli can occur above the level of the spinal cord through the effects of a descending inhibitory pathway that originates in the brainstem. The descending inhibitory pathway synapses in the substantia gelatinosa region of the spinal cord. There are at least two types of descending inhibitory pathways, the opioid and α-adrenergic pathways. The opioid descending pathway releases endorphins and enkephalins, whereas the α-adrenergic descending pathway releases norepinephrine. Both these pathways work by hyperpolarizing the nerve fibers of the ascending pain pathway and potentially negate the action potential that would otherwise have resulted from the stimulation of the nerve by the painful stimulus. Neurotransmitters or second messenger effectors (e.g., substance P, protein kinase C-γ) may also play important roles in spinal cord sensitization and chronic pain. (652, Table 40-3)

13. Examples of pain modulating neurotransmitters include glutamate, aspartate, vasoactive intestinal polypeptide, cholecystokinin, gastrin-releasing peptide, angiotensin, and substance P. Examples of inhibitory neurotransmitters that are believed to modulate painful stimuli include enkephalins, endorphins, and somatostatin. (652, Table 40-3)

14. The precise definition of preemptive analgesia is one of the major controversies in perioperative pain medicine, and contributes to the confusion regarding its clinical relevance. The concept is that the development of central or peripheral sensitization of pain transmission after a traumatic injury can result in amplification of the pain response in the postoperative period. Preemptive analgesia can be defined as an analgesic intervention initiated before the noxious stimulus develops in order to block peripheral and central pain transmission. Preventive analgesia can be functionally defined as an attempt to block pain transmission prior to the injury (incision), during the noxious insult (surgery itself), and after the injury and throughout the recovery period. Unfortunately, few trials have examined the concept of preventive analgesia in a rigorous fashion. Confining the definition of preemptive analgesia to only the immediate preoperative or early intraoperative (incisional) period may not be clinically relevant or appropriate because the inflammatory response may last well into the postoperative period and continue to maintain peripheral sensitization. (654)

ANALGESIA DELIVERY SYSTEMS

15. Routes for the administration of analgesic drugs include oral, transmucosal, transdermal, intramuscular, intrapleural, intravenous, subcutaneous, rectal, neuraxial, and by injection to block a peripheral nerve. (654, Table 40-4)

16. The limitation of the oral administration of analgesic agents for the management of acute postoperative pain is the lack of ability to titrate it effectively to pain and the prolonged amount of time it takes to reach its peak effect. Patients are also limited by their perioperative NPO status. The oral route of administration for analgesic agents is appropriate when the pain the patient is experiencing has decreased and there is no longer a need for rapid adjustments in the level of analgesia. (655-656)

17. The intramuscular injection of analgesic agents has a more rapid onset and more rapidly reaches its peak effect than the oral route of administration of analgesic agents. There are some problems with the intramuscular administration of analgesics, however. Following intramuscular administration, the plasma concentration of the drug can vary among patients by three to five times, making dosing of the drug difficult. The use of this route has been replaced primarily by intravenous patient-controlled analgesia dosing, which provides a more standardized dosing interval. (656)

18. Ketamine can be effective in small doses for postoperative analgesia partly due to its NMDA antagonistic properties, which can attenuate central sensitization and opioid tolerance. Low-dose ketamine infusions have a low incidence of hallucinations or cognitive impairment. Ketamine is comparable to opioids with regard to its side effects of dizziness, itching, nausea, or vomiting. The use of ketamine in patients at high risk for the development of chronic postsurgical pain should be considered. (656)

19. Buprenorphine is commonly used for detoxification or maintenance therapy for patients with opioid abuse disorders (addiction). It is now more frequently being prescribed for the treatment of pain in non-addicts as well. It poses additional challenges to the anesthesiologist in the operative setting because of its pharmacodynamics and pharmacokinetics. Buprenorphine is a partial agonist at the μ-opioid receptor, and when used with a full agonist, such as morphine or fentanyl, it acts as an antagonist. Therefore the analgesia the patient experiences is less than what the patient would normally experience for a given dose of morphine or fentanyl. The pharmacokinetics of buprenorphine are somewhat unpredictable, making it hard to predict when its partial agonist properties will have worn off after the last dose of buprenorphine taken prior to surgery. This uncertainty leads to the risk of unexpected respiratory depression from the full opioid agonist as the buprenorphine unbinds from the opioid receptor.

    There are numerous ways in which to handle the perioperative analgesic care of a buprenorphine patient. The simplest is to maintain the buprenorphine therapy throughout the perioperative setting by converting the oral dose to intravenous and continuing to administer it intraoperatively and postoperatively while the patient is NPO. Any additional analgesic needs made necessary by the surgical operation can be addressed with an additional full agonist opioid. In this manner, the complex pharmacokinetic properties of buprenorphine can be avoided. (656)

20. Opioids can be administered through subcutaneous, transdermal, and transmucosal routes. Subcutaneous delivery can be an effective method for patients without intravenous access or who need long-term access at home. Subcutaneous therapy is primarily used for cancer patients. Transdermal fentanyl results in a variable range of serum concentrations and analgesic response across patient populations and requires 24 to 48 hours to reach peak levels. These limitations can lead to adverse outcomes for patients in the perioperative period because of side effects such as respiratory depression. The primary indication for transmucosal opioid therapy is for an adult opioid-tolerant oncology patient for breakthrough pain. (656-657)

21. Patient-controlled analgesia (PCA) is a method of delivering an opioid for analgesia to a patient. In this form of analgesic delivery, the patient controls his or her own administration of the opioid by pressing a button connected to a pump. The pump is programmed to deliver a preset small intravenous dose of opioid when triggered by the patient. The lockout interval is the interval of time that must pass after the last self-administered dose before the patient can deliver another small dose of opioid to himself or herself. (654)

22. There are several advantages of patient-controlled analgesia. These include high patient acceptance and for patients a sense of control, improved titration of drug, and subsequent patient comfort with less total drug administered, less sedation, improved sleep at night, and a more rapid return to physical activity after surgery. (654-655)

23. The analgesic site of action of the neuraxial administration of opioids can be primarily spinal or systemic, depending on their lipid solubility. There are mechanistic differences between continuous epidural infusions of lipophilic (e.g., fentanyl, sufentanil) and hydrophilic (e.g., morphine, hydromorphone) opioids. For continuous epidural infusions of lipophilic opioids the analgesic site of action is not clear, although several randomized clinical trials suggest that it is

systemic. Hydrophilic opioid epidural infusions have a primarily neuraxial mechanism of action. (657)

24. Potential benefits of the neuraxial administration of opioids for postoperative analgesia include superior pain control, improved postoperative pulmonary function, decreases in cardiovascular complications, decreases in infectious complications, and decreases in total hospital costs. (657)

25. Potential adverse effects of the neuraxial administration of opioids for postoperative analgesia include pruritus, urinary retention, nausea and vomiting, sedation, and early and delayed depression of ventilation. Local anesthetic infusions are more likely to cause hypotension and motor block than opioid infusions. (657-658)

26. The early depression of ventilation that is seen with the neuraxial administration of opioids usually occurs in the first 2 hours after the administration of the opioid. Early respiratory depression is believed to occur as a result of vascular uptake and redistribution of the opioid. (657-658)

27. The delayed depression of ventilation that is seen with the neuraxial administration of opioids usually occurs 6 to 24 hours after the administration of the opioid. It is believed to be due to the cephalad spread of the opioid in the cerebrospinal fluid to the medullary centers of the brain. The medullary centers are in the area of the fourth cerebral ventricle. This effect may be more pronounced with the less lipid-soluble opioids, such as morphine, than with the more lipid-soluble drugs, such as fentanyl. The more lipid soluble the opioid is, the more readily it will attach to opioid receptors on the spinal cord. This makes less medication available for diffusion to the brain. The opposite occurs with the less lipid-soluble drug, leaving more drug available for diffusion to the medullary centers. (657-658)

28. Patient characteristics contribute to the risk of depression of ventilation from the administration of neuraxial opioid. Factors that increase the risk for the depression of ventilation include larger dose, geriatric age group, concomitant administration of systemic opioids or sedatives, the possibility of prolonged or extensive surgery, the presence of comorbidities, and thoracic surgery. (657-658)

29. The lipid solubility of intrathecally administered opioids is the primary determinant of its time of onset and duration of action. The onset time is shorter with more lipid-soluble drugs, and the duration of action is shorter. Conversely, less lipid-soluble drugs have a longer onset time and a prolonged duration of action. (657)

30. Typically, the intrathecal administration of opioid is administered as a single dose in conjunction with a local anesthetic block for a surgical procedure. Disadvantages of a single dose intrathecal administration of opioid for the management of acute postoperative pain include the lack of titratability and the need for other analgesic options after the initial intrathecal opioid effect subsides. (657)

31. The clinical impression that intrathecal opioid results in a higher incidence of side effects when compared with the epidural administration of the same opioid probably comes as a result of the administration of excessive doses of opioid in the intrathecal space. The same receptors are being stimulated in both cases, so theoretically equipotent doses at the receptor should result in similar desired and undesired effects. (657)

32. The epidural administration of opioid requires more medication to be administered than if it were administered intrathecally because the drug must diffuse across the dura to reach the spinal cord and exert its effect. In addition, fat, connective tissue, and the epidural veins all take up opioid that is deposited in the epidural space. In contrast, the intrathecal administration of opioid places the opioid directly

at its site of action. The dose of epidurally administered opioid is approximately 10 times the dose of intrathecally administered opioid to produce an equipotent effect. (657)

33. Fentanyl administered in the epidural space is believed to produce a more segmental band of anesthesia than morphine because of its increased lipid solubility. The increased lipid solubility of fentanyl causes it to bind to opioid receptors in the spinal cord adjacent to the area in which it enters the intrathecal space. Morphine, being more hydrophilic, binds less readily and instead diffuses in the intrathecal space. This results in a wider distribution of anesthesia with morphine than with fentanyl when administered in the epidural space. (657)

34. The plasma concentration of fentanyl when administered intravenously is similar to the plasma concentration of fentanyl when the same dose is administered epidurally. This is thought to occur from the systemic absorption of fentanyl from the epidural space by the vasculature in the epidural space. This implies that at least part of the analgesic effect of fentanyl administered epidurally is through its systemic effects. (657)

35. Local anesthetic added to the opioid solution for administration in the epidural space results in a synergistic analgesic effect. This is believed to occur because of the blockade of painful stimuli at two different sites at the spinal cord. The opioid administered acts by binding to opioid receptors. The local anesthetic administered acts at the nerve roots and in the dorsal root ganglia by blocking the transmission of afferent impulses. The synergistic effect of these two classes of drugs allows for a decreased dose of each to be administered to the patient. This has the added benefit of a decreased risk of the potential side effects of both drugs. (657)

36. The concern regarding the concurrent use of neuraxial analgesia and anticoagulants is for the formation of a spinal or epidural hematoma. The incidence of spinal or epidural hematoma related to neuraxial analgesia is rare, but can be catastrophic and requires immediate surgical attention. General concepts for the management of neuraxial analgesia with anticoagulation include: (1) the timing of neuraxial needle or catheter insertion or removal should reflect the pharmacokinetic properties of the specific anticoagulant, (2) frequent neurologic monitoring is essential, (3) concurrent administration of multiple anticoagulants may increase the risk of bleeding, and (4) the analgesic regimen should be tailored to facilitate neurologic monitoring, which may be continued in some cases for 24 hours after epidural catheter removal. (658)

37. Factors that increase the risk of postoperative epidural abscess associated with epidural analgesia include a longer duration of anesthesia and the presence of coexisting immunocompromising or complicating disease such as malignancy or trauma. The overall incidence of postoperative epidural abscess associated with epidural analgesia is extremely rare, however. (658)

ALTERNATIVE APPROACHES TO MANAGEMENT OF ACUTE POSTOPERATIVE PAIN

38. An advantage of peripheral nerve blocks for the management of acute postoperative pain is their ability to provide good management of postoperative pain while not affecting the patient systemically. Thus the patient is not at risk for any of the negative effects of systemic opioids. A disadvantage of peripheral nerve blocks for postoperative pain is their relatively short duration of action. (659)

39. Intraarticular injection of opioids may provide analgesia for up to 24 hours postoperatively and prevent the development of chronic postsurgical pain. However, superiority of this delivery method over systemic administration has not been demonstrated. Continuous intraarticular administration of bupivacaine has been associated with chondrolysis in the glenohumeral joint. (659)

40. Paravertebral blockade has been directly correlated with improved outcomes for patients undergoing breast surgery. This technique has also been found to decrease the development of chronic postsurgical pain, as well as the acute pain associated with the procedure. (659)

41. Continuous perineural catheters for upper extremity procedures have been associated with increased pain relief with minimal opioid supplementation with increased patient satisfaction and sleep quality. Continuous catheters for major foot and ankle surgery are also associated with an earlier discharge. (659-660)

42. Clonidine is beneficial in extending the duration of preoperative blockade, but has less utility with perineural catheters. The mechanism is most likely peripheral α_2-adrenergic receptor-mediated and dose-dependent. Clonidine is a better preemptive analgesic when added to a local anesthetic block than when used as a single drug. Side effects, including hypotension, bradycardia, and sedation, are less likely to occur with lower doses. (659)

43. Intrapleural regional analgesia is most frequently used for the management of acute postoperative pain after a thoracotomy. It is achieved by the injection of a local anesthetic solution through a catheter placed in the intrapleural space. The catheter is often placed intraoperatively by the thoracic surgeon one interspace lower than that of the surgical incision. The local anesthetic diffuses to the intercostal nerves and produces a multilevel, unilateral intercostal nerve block. Unfortunately, this technique provides little analgesia for patients unless it is actually placed in the paravertebral space from the intrathoracic approach. An advantage of this technique for postoperative pain management is the potential for pain relief without hemodynamic changes associated with epidural analgesia. A disadvantage of this technique is that the local anesthetic may be lost through the pleural drainage tubes that are placed after a thoracotomy. Complications associated with this technique include pneumothorax and high plasma concentrations of local anesthetic. The majority of local anesthetic infused into the intrapleural space flows to the dependent aspect of the patient, which is most often the lung bases where analgesia is not needed. The efficacy of this technique for postoperative pain management is therefore highly variable and has mostly been abandoned. This technique is less frequently used than epidural catheters or paravertebral blocks. (Chapter 40, 10)

44. The transverse abdominis plane block has been used for many abdominal procedures, including abdominal hysterectomy, cesarean section, and laparoscopic cholecystectomy. Theoretical advantages of this technique over other modalities include avoidance of both neuraxial involvement and lower extremity blockade, decreased urinary retention, and decreased systemic side effects. Ultrasound guidance has made this a more reliably achieved peripheral blockade. (660)

Chapter

38 CRITICAL CARE MEDICINE

Lundy Campbell, Michael A. Gropper

MECHANICAL VENTILATION

1. List the typical indications for mechanical ventilation in the ICU.
2. What are some common causes of respiratory failure?
3. What are some common causes of ventilatory failure?
4. What are some indications for the need for airway protection?
5. What are some common modes of mechanical ventilation?
6. Describe the key ventilator settings in continuous mandatory ventilation (CMV) mode.
7. How can the inspiratory and expiratory time be adjusted in CMV mode?
8. What effect does a patient's breathing effort have when mechanically ventilated in CMV mode?
9. Describe the key ventilator settings in synchronized intermittent mandatory ventilation (SIMV) mode.
10. What effect does a patient's breathing effort have when mechanically ventilated in SIMV mode?
11. Describe the key ventilator settings in pressure support ventilation (PSV) mode.
12. What is positive end-expiratory pressure (PEEP)?
13. How does PEEP improve oxygenation?
14. What are some possible adverse effects of PEEP?
15. What are some criteria that must be met before a patient can be considered ready for a trial of weaning from mechanical ventilation?
16. What is the preferred method of protocol-driven weaning from mechanical ventilation?

NONINVASIVE POSITIVE-PRESSURE VENTILATION

17. What is noninvasive positive-pressure ventilation (NIPPV)? What are two modes of NIPPV?
18. What is continuous positive airway pressure (CPAP)? What are some benefits of CPAP?
19. What is bilevel positive airway pressure (BiPAP)?
20. What are some advantages of NIPPV?
21. What are some indications for NIPPV?
22. What are three contraindications to noninvasive mechanical ventilation?

ACUTE RESPIRATORY DISTRESS SYNDROME

23. What are the American-European Consensus Conference Definitions for acute lung injury (ALI) and the acute respiratory distress syndrome (ARDS)?
24. List three direct causes and three indirect causes of acute respiratory distress.
25. What are the basic principles for the treatment and the management of mechanical ventilation of patients with ALI or ARDS?

SEDATION AND ANALGESIA IN THE INTENSIVE CARE UNIT

26. What are some indications for patient sedation in the intensive care unit (ICU)?
27. What are the components of the Ramsay sedation scoring system?
28. What are the common side effects of the use of opioids for the sedation of critically ill patients?
29. What are the common side effects of the use of benzodiazepines for the sedation of critically ill patients?
30. What are the common side effects of the use of propofol for the sedation of critically ill patients?
31. List the common clinical findings in propofol infusion syndrome.
32. What are the advantages of ketamine as a sedative in the ICU?
33. What is the mechanism of action of dexmedetomidine? What are its hemodynamic effects?

SHOCK

34. What defines shock?
35. List three major categories of shock. How can they be differentiated using central venous pressure (CVP) and cardiac output (CO) measurements?
36. What are some common causes of hypovolemic shock?
37. What are the common clinical findings of hypovolemic shock?
38. What is the treatment for hypovolemic shock?
39. What are the causes of cardiogenic shock?
40. What are the common clinical findings in cardiogenic shock?
41. What is the treatment for cardiogenic shock?
42. What are some common causes of vasodilatory shock?
43. What are the common clinical findings of vasodilatory shock?
44. What is the treatment for vasodilatory shock?
45. Upon which receptor subtypes does dopamine have agonist activity?
46. Upon which receptor subtypes does epinephrine have agonist activity?
47. What are the advantages of norepinephrine use in septic shock?
48. Upon which receptor does phenylephrine have agonist activity?
49. What are the hemodynamic effects of dobutamine infusion?
50. How does vasopressin differ in its mechanism of action when compared to norepinephrine?

ACUTE RENAL FAILURE

51. What clinical signs may be an indication of acute renal failure (ARF)?
52. How should ARF be evaluated?
53. What are some indications for acute hemodialysis in the setting of ARF?

DELIRIUM

54. How is delirium defined?
55. What is the incidence of delirium in the adult ICU population?
56. How is mortality impacted by the presence of delirium in the critically ill?
57. What are some common causes of delirium in a patient in the ICU?
58. What is the common method of delirium assessment in the ICU?
59. What is the treatment for delirium in a patient in the ICU?

NUTRITIONAL SUPPORT

60. What are some important clinical benefits of providing optimal nutrition to patients in the ICU?
61. What are the advantages and disadvantages of enteral versus parenteral nutrition?

RAPID RESPONSE TEAMS

62. How might rapid response teams improve outcomes?

INTENSIVE INSULIN THERAPY

63. What is the current understanding of the effectiveness of intensive insulin therapy? What are the risks of this intervention?

END-OF-LIFE ISSUES

64. What is the role of the physician intensivist when a patient's family has elected to stop treatment of a critically ill patient?

ANSWERS*

MECHANICAL VENTILATION

1. Mechanical ventilatory support is typically initiated for the treatment of respiratory failure due to impaired oxygenation, impaired carbon dioxide excretion (ventilatory failure), and airway protection. Patients receive mechanical ventilatory support to (1) reduce the work of breathing, (2) reverse progressive respiratory acidosis or hypoxemia, (3) reduce the risk for aspiration, or (4) ensure a patent airway with severe neck and facial swelling or trauma. (666)
2. Common causes of respiratory failure may include trauma, ARDS, sepsis, pneumonia, and cardiogenic and noncardiogenic pulmonary edema. (666)
3. Ventilatory failure may be due to chronic obstructive pulmonary disease (COPD), asthma, and/or drug intoxication. (666)
4. Airway protection indications are usually limited to conditions such as altered mental status, head and neck trauma or swelling, or significant neuromuscular disorders. (666)
5. Common modes of mechanical ventilation include continuous mandatory ventilation, synchronized intermittent mandatory ventilation, pressure support ventilation, and PEEP. (666-667)
6. In CMV mode, the ventilator is programmed to deliver a set tidal volume at a set respiratory rate, thereby resulting in the delivery of a predictable minute ventilation. The ventilator will deliver its preset tidal volume at its preset time. (666)
7. To regulate the amount of time that the ventilator spends cycling in inspiration and expiration, the inspiratory flow rate is set. By increasing inspiratory flow, the set tidal volume is delivered in a shorter time, which allows more time for exhalation. (666)
8. The patient's breathing efforts are unsupported in CMV mode. The ventilator continues to deliver its preset tidal volume at its preset time regardless of patient effort. (666)
9. In SIMV mode, the ventilator is programmed to deliver a set tidal volume and respiratory rate. In SIMV mode, however, the ventilator attempts to synchronize mandatory breaths to the patient's own spontaneous breaths. If the patient does not initiate a breath within a set time, the ventilator delivers the set tidal volume as in CMV mode. Therefore a minimum minute ventilation is maintained in SIMV mode. (666)
10. If a patient initiates a breath during the preset time for a mandatory breath, a preset tidal volume will be delivered. Additional breaths initiated by the patient beyond those set in the SIMV mode are supported by the ventilator with an augmentation of the tidal volume by a preset pressure. It is therefore a pressure-supported breath. (666)
11. In pressure support ventilation, the ventilator does not deliver a preset tidal volume but, instead, relies on the patient's intrinsic respiratory drive. Typically, the

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

amount of pressure support is set between 5 and 20 cm H_2O pressure to ensure adequate tidal volume and minute ventilation. In this mode, tidal volume will vary with patient effort. To use pressure support ventilation, the patient must possess an intact respiratory drive, and no residual skeletal muscle paralysis can be present. (666)

12. PEEP is positive airway pressure that is applied at the end of expiration during mechanical ventilation. The typical PEEP range is between 5 and 20 cm H_2O pressure. (667)

13. PEEP functions to increase mean airway pressure and thereby minimize atelectasis. PEEP increases the functional residual capacity of the lungs and, in patients with a lung injury, results in improved pulmonary compliance. The recruitment of alveoli, or the inflation of previously collapsed alveoli, by PEEP can lead to improved oxygenation in a mechanically ventilated patient. (667)

14. Excessively high levels of PEEP can overdistend and damage alveoli. Excessive PEEP may also cause hemodynamic collapse by reducing preload to both the right and the left ventricles with a resultant fall in cardiac output. Finally, if there is inadequate time allowed for the exhalation of the delivered tidal volume, there can be a buildup of end-expiratory pressure that can lead to hemodynamic collapse. (667)

15. To consider weaning from mechanical ventilation, a patient must have recovered from the process that originally required mechanical ventilatory support, be hemodynamically stable, be able to manage their pulmonary secretions, and be able to protect their airway against the aspiration of gastric contents with an intact mental status and gag reflex. The patient should be maintaining adequate oxygen saturation with an inspired oxygen concentration of 40% or less, be able to initiate breaths, and be strong enough to generate an adequate tidal volume. The patient's respiratory strength is usually considered sufficient for weaning if the patient is able to generate a negative inspiratory force of at least -20 cm H_2O or a vital capacity of at least 10 mL/kg. In normal tidal breathing, a tidal volume of at least 5 mL/kg and a minute ventilation of no more than 10 L/min should be observed to ensure readiness for weaning from mechanical ventilation. In general, higher tidal volumes and lower respiratory rates predict success in weaning from mechanical ventilation. (667)

16. Protocol-driven weaning has been shown to reduce the length of time that patients remain on mechanical ventilatory support when compared to traditional physician weaning methods. Typically, protocol-driven weaning is managed by bedside providers (nurses and respiratory therapists) without the need for continuous physican input. In this method, patients are weaned from mechanical ventilation via a standard protocol, and when a patient meets the criteria for extubation, a physician is notified and the patient is extubated if the physician agrees. From multiple clinical trials, it has been shown that the fastest and most cost-effective weaning method is once-daily CPAP or T-piece weaning trials that are protocol driven by nurses and respiratory therapists. (667-668)

NONINVASIVE POSITIVE-PRESSURE VENTILATION

17. NIPPV is the application of positive pressure to provide support of oxygenation and ventilation without an endotracheal tube. Two modes of NIPPV are (1) CPAP and (2) BiPAP. (668)

18. CPAP is constant positive airway pressure that is applied throughout both the inspiratory and expiratory phases of ventilation. CPAP improves oxygenation and ventilation by recruitment of collapsed alveoli, helps maintain a patent airway in the setting of airway obstruction such as sleep apnea, and increases mean airway pressure in patients with COPD.

19. BiPAP is similar to pressure support with PEEP ventilation because the ventilator cycles between two sets of positive-pressure settings. Positive pressure is delivered throughout the respiratory cycle, with a higher positive pressure being applied during inspiration. With BiPAP, a "backup" ventilator rate may be set. (668)

20. When compared to mechanical ventilation with an endotracheal tube, noninvasive positive-pressure ventilation has a reduced risk of ventilator-associated pneumonia, can be rapidly and easily applied with a properly fitted face mask, and can be used during short periods only, as during sleep. (668)

21. Noninvasive mechanical ventilation, or noninvasive positive-pressure ventilation (NIPPV) is indicated in a patient who has a potentially rapidly reversible pulmonary process that requires ventilatory support. In patients with acute exacerbations of COPD, there is strong evidence that NIPPV is an effective treatment that can reduce the need for subsequent endotracheal intubation and reduce mortality. NIPPV has been used successfully to treat other forms of acute respiratory failure such as pneumonia, congestive heart failure, and postsurgical respiratory failure. NIPPV may be just as effective as conventional ventilation with respect to oxygenation and removal of carbon dioxide in these patients, and it is associated with fewer serious complications and a shorter ICU stay. (668)

22. There are specific contraindications to the use of NIPPV. The most frequently encountered problem is lack of patient compliance. Because NIPPV requires a tight-fitting mask for effective ventilation, many patients find it uncomfortable and it is poorly tolerated by those who are claustrophobic. There is also a subset of patients in whom NIPPV will not be effective in reversing their respiratory and/or ventilatory failure. It has been well-shown in the medical literature that continued use of NIPPV is harmful in this patient subset. In addition, NIPPV provides no airway protection, so it should not be used in patients with altered mental status since they may not be able to protect their own airway against aspiration. The same is also true for any patients who may have other reasons for an inability to protect their own airway, such as neuromuscular weakness or facial trauma or swelling. (668)

23. The American-European Consensus Conference defines ALI and ARDS as follows:

    The lung injury must have an acute onset.
    There must be bilateral infiltrates present on chest radiographs.
    The pulmonary artery occlusion pressure must be 18 mm Hg or less, or there must be clinical absence of left atrial hypertension.
    There must be a defined gas exchange problem as evidenced by arterial to inspired measured oxygen levels ($Pa_{O_2}/F_{I_{O_2}}$ ratio). For ALI this ratio must be less than or equal to 300 ($Pa_{O_2}/F_{I_{O_2}} \leq 300$), and for ARDS this ratio must be less than or equal to 200 ($Pa_{O_2}/F_{I_{O_2}} \leq 200$). (669, Table 41-1)

ACUTE RESPIRATORY DISTRESS SYNDROME

24. Direct causes of acute lung injury include pneumonia, the aspiration of stomach contents, pulmonary contusion, reperfusion pulmonary edema, amniotic fluid embolus, and inhalational injury. Indirect causes of acute lung injury include sepsis, severe trauma, cardiopulmonary bypass, drug overdose, acute pancreatitis, near drowning, and transfusion-related acute lung injury (TRALI). (669, Table 41-2)

25. The treatment of ARDS generally remains supportive. The use of low tidal volume ventilation in patients with ALI or ARDS (6 mL/kg) versus the traditional standard tidal volumes (12 mL/kg) has been shown to decrease mortality. Lower tidal volumes function to "protect" the lung by preventing overdistention of remaining normal lung regions. Patients who are ventilated with lower tidal volumes tend to have lower arterial oxygen tension and higher arterial carbon dioxide tension. This is termed permissive hypercapnia and hypoxemia, in

recognition of the fact that to normalize arterial blood gas, significantly more harmful mechanical ventilation may be required. (669)

SEDATION AND ANALGESIA IN THE INTENSIVE CARE UNIT

26. Indications for patient sedation in the ICU include the provision of analgesia, anxiolysis, or amnesia and to protect the patient from removing intravenous lines, catheters, drains, or tubes. In certain circumstances sedation may be administered to prevent seizures, decrease intracranial pressure, treat for the withdrawal from substances such as ethanol, and to sedate while administering concomitant neuromuscular blocking drugs. (669)

27. The RASS is a widely used tool to help quantify the level of sedation of a patient in the ICU. It is a linear scale from 1 to 6 that describes a patient's ability to respond to stimulation while under sedation. The stimulation provided to the patient is either a verbal command or a light glabellar tap. The response to this stimulation varies from a RASS score of 1: "Anxious and agitated or restless, or both," to a RASS score of 6: "No response to a light glabellar tap." The RASS score of 3: "Responding to commands only" is usually considered to be the optimum sedation level. (669-670, Table 41-3)

28. Opioids may be useful for sedation in the critically ill patient when the patient has pain either as a result of surgery, from indwelling catheters, or for sedation during a painful procedure, such as chest tube placement. The most dangerous side effect of opioids is that of respiratory and central nervous system sedation that can be synergistic when combined with other sedatives, such as benzodiazepines. Other side effects of opioids when used for sedation include constipation, urinary retention, and tolerance. (670-671)

29. Due to their mechanism of action on GABA receptors, benzodiazepines have multiple side effects. These include significant CNS depression (especially when combined with opioids), accumulation of drug or active metabolites when administered over a prolonged period, and life-threatening withdrawl if removed too quickly in patients who have become tolerant of their effects. In addition, when sedation with benzodiazepines is compared to dexmedetomidine, patients receiving benzodiazepines appear to have longer duration of mechanical ventilation, as well as an increased risk of delirium. (671)

30. Despite its ease of use, propofol has many significant side effects which may limit its use in the ICU. Propofol causes hypotension by decreasing myocardial contractility and reducing systemic vascular resistance. In hemodynamically unstable patients with low cardiac output or low afterload (or both), propofol must be used with caution. Propofol is also a profound respiratory depressant. Although most patients who receive propofol in the ICU are intubated and maintained on mechanical ventilation, occasionally propofol may be used in nonintubated patients. In these patients, extreme caution must be exercised to prevent severe respiratory depression with profound respiratory acidosis. Propofol is formulated in a lecithin base and therefore has a high fat content. Patients who are receiving long-term infusions of this drug must be periodically checked for hypertriglyceridemia. There have been many case reports of patients developing severe pancreatitis after prolonged propofol administration. (671)

31. This is a rare syndrome that is associated with the prolonged use of propofol as a sedative agent in the ICU setting. Generally, propofol infusion syndrome is defined as a relatively sudden onset of metabolic acidosis with cardiac dysfunction and at least one of the following findings: rhabdomyolysis, hypertriglyceridemia, and renal failure. Some studies have also used hepatomegaly due to fatty liver infiltration and lipemia as additional criteria. The early cardiac findings include bradycardia and right bundle branch block. If propofol infusion syndrome is suspected, the propofol infusion should be discontinued immediately and another sedative agent should be chosen, as the mortality of this syndrome has been reported to be as high as 80%. (671)

32. Ketamine has proved to be useful in the ICU because of its ability to produce profound analgesia without significant respiratory depression. This makes ketamine an excellent choice for patients with chronic pain who may require excessively large doses of opioids for pain relief, or in patients who are already on large doses of narcotics and in whom a further increase of narcotics will have minimal effects due to tolerance. Ketamine is also useful for patients who need to undergo brief, painful procedures in the ICU. Ketamine also has intrinsic sympathomimetic properties that increase systemic blood pressure and heart rate during its infusion. This may be useful when sedation and analgesia are required for a hemodynamically unstable patient. Ketamine is often combined with propofol in such patients to counteract the reduced blood pressure associated with propofol while providing adjuvant analgesia. Ketamine may not be useful in neurosurgical patients because it increases intracranial pressure, increases cerebral metabolic oxygen requirements, and decreases the seizure threshold. (671-672)

33. Dexmedetomidine acts by binding to α_2 receptors both centrally and peripherally. Central α_2-binding at presynaptic neurons inhibits the release of norepinephrine. The central effects of these drugs produce analgesia, sedation, anxiolysis, and hypotension. At the level of the spinal cord, α_2-activation is thought to modulate pain pathways, and this is the probable site of action for the analgesic effects of this drug. With increasing doses, dexmedetomidine begins to bind peripheral α_1 and α_2 receptors, inducing vasoconstriction and hypertension at very high doses. Overall, in the recommended dosage range, the effect is to decrease systemic blood pressure by means of a decrease in both systemic vascular resistance and heart rate. (672)

SHOCK

34. Shock is a clinical condition in which there is inadequate tissue perfusion and oxygenation to end organs such as the brain, heart, liver, kidneys, and abdominal viscera. Early in its course, shock may be reversible, but ongoing shock results in multiorgan system failure and ultimately death. (673)

35. The major categories of shock include hypovolemic, cardiogenic, and septic (or other forms of vasodilatory shock). In hypovolemic shock, both CO and CVP are reduced due to decreased venous return. In contrast, cardiogenic shock is typified by a decrease in CO due to poor pump function, but CVP is usually increased. Finally, in septic shock, CVP is usually decreased due to profound vasodilation and pooling of blood in the splanchnic beds, but CO is typically increased in early sepsis. However, CO may be normal or even depressed in later more advanced septic shock. (673, Table 41-5)

36. The most common cause of hypovolemic shock is major blood loss, as can occur in trauma, surgery, or with massive gastrointestinal hemorrhage. (673)

37. Hypovolemic shock is caused by inadequate circulating blood volume, and therefore decreased preload and cardiac output. There is usually a baroreceptor-mediated reflex tachycardia and an increase in systemic vascular resistance. Gluconeogenesis is induced, as is sodium reabsorption from the kidneys. In addition to being hypotensive, the patient may appear cool, clammy, and pale with increased plasma glucose levels and decreased urine output. (673)

38. The treatment for hypovolemic shock requires adequate intravenous access and aggressive fluid therapy to restore circulating blood volume. Fluid resuscitation can be guided by the use of a central venous monitor or arterial blood pressure variation, as well as laboratory analysis of metabolic variables. Vasopressor therapy can be used to increase systemic blood pressure, but is generally not effective until circulating blood volume is restored. (673-674)

39. Cardiogenic shock occurs when the heart is not able to pump an adequate cardiac output. The most common cause of cardiogenic shock is myocardial infarction.

Other causes include severe myocarditis, endocarditis, or a tear or rupture of a portion of the heart. (674)

40. If the right ventricle is the initial site of failure, the increased right-sided preload will be noted as increased CVP, detected clinically as distended neck veins, peripheral edema, or hepatic congestion. If the left ventricle fails, the increased preload can be detected as increased pulmonary capillary wedge pressure, which causes cardiogenic pulmonary edema and rales on physical examination. In either scenario, cardiac output is low, and systemic blood pressure is therefore reduced. On physical examination, a patient in cardiogenic shock appears cool and pale secondary to the high systemic vascular resistance and shunting of blood away from the skin and skeletal muscle beds. (674)

41. The goal for treatment of cardiogenic shock is to improve cardiac output and decrease afterload to reduce myocardial demand. Resuscitation should be guided by the use of central venous monitors, direct arterial blood pressure measurements, and echocardiography. Vasodilator therapy can be used to reduce preload and afterload. Dobutamine therapy may also be useful. Treatment with diuretics must be done with extreme caution. In cardiogenic shock refractory to treatment an intraaortic balloon counterpulsation (IABP) or ventricular assist device (VAD) may be indicated. (674)

42. The most common cause of vasodilatory shock is sepsis. Other causes of vasodilatory shock include anaphylaxis, stroke, and spinal shock as from a high spinal cord injury. Vasodilatory shock is also the final common pathway for late-shock stages of cardiogenic and hypovolemic shock. (674)

43. In the initial stages of vasodilatory shock an increase in cardiac output may compensate for the decrease in systemic vascular resistance and the patient may appear warm and vasodilated. With worsening metabolic acidosis myocardial perfusion becomes impaired, and the patient will become increasingly cool and clammy. (674)

44. The treatment for vasodilatory shock involves adequate fluid volume resuscitation in conjunction with possible vasopressor therapy. The underlying cause of the disorder should also be treated. In septic shock early identification of the source of the infection and treatment with broad-spectrum antibiotics is necessary. (674-675)

45. Dopamine has both direct and indirect agonist activity at the dopamine$_1$ (DA_1), β_1, and α_1 receptors. Its pharmacologic action varies with dose and within individuals. At low doses (0 to 5 μg/kg/min), dopamine has predominantly DA_1 receptor agonist activity. This causes dilation of the renal arterioles and promotes diuresis. At moderate doses (5 to 10 μg/kg/min), the β-effects of dopamine begin to dominate. These β_1-effects cause an increase in myocardial contractility, heart rate, and cardiac output. At high doses (10 to 20 μg/kg/min), the α_1-agonist effects predominate and dopamine acts to increase vascular smooth muscle tone, which increases systemic vascular resistance. This causes a decrease in splanchnic and renal blood flow similar to the effects of high-dose phenylephrine. (675)

46. Epinephrine causes direct stimulation of α_1, β_1, and β_2 receptors. At lower doses, epinephrine acts primarily as a β receptor agonist, whereas at higher doses, it has increasing α_1 receptor effects. Increases in heart rate, myocardial activity, and cardiac output reflect β_1 receptor effects. The principal β_2-effects are bronchial and vascular smooth muscle relaxation. At higher doses, the α_1-effects of epinephrine act to increase systemic vascular resistance and reduce splanchnic and renal blood flow while maintaining both cerebral and myocardial perfusion pressure. (675-676)

47. Norepinephrine is a direct-acting adrenergic agonist with activity at both the α_1 and β_1 receptors. As a result, norepinephrine increases blood pressure through its α_1-effects on increasing systemic vascular resistance. The β_1-effects of

norepinephrine also contribute to increased myocardial contractility and cardiac output. There has been renewed interest in norepinephrine specifically for the treatment of septic shock. It is thought that this β_1-activity may help offset the myocardial dysfunction associated with severe sepsis and septic shock. Both preclinical and limited clinical data suggest that norepinephrine is the pressor of choice for patients in septic shock. (676)

48. Phenylephrine is a direct-acting, highly selective α_1 receptor agonist which increases systemic vascular resistance and arterial blood pressure. Phenylephrine can cause a reflex bradycardia, which can decrease cardiac output. Phenylephrine can be used to increase systemic vascular resistance in shock, but in high doses higher than 200 μg/min it has little additional therapeutic effect and may cause splanchnic ischemia. (676)

49. Dobutamine is a mixed β_1 and β_2 receptor agonist. As a result, the primary effect of dobutamine is to increase both heart rate and myocardial contractility. Dobutamine also relaxes vascular smooth muscle via binding at β_2 receptors. This combination acts to increase cardiac output by improving ventricular function (β_1-effect) and decreasing systemic vascular resistance (β_2-effect). Because of its β_2-effects, some patients may become hypotensive, particularly those with decreased intravascular volume. (676)

50. Vasopressin is a potent vasoconstrictor that does not work via the adrenergic receptor system as do most other vasopressors and inotropes. Rather, vasopressin binds to peripheral vasopressin receptors to induce potent vasoconstriction via phosphodiesterase inhibition. In contrast to norepinephrine, vasopressin has no intrinsic inotropic effects. However, vasopressin remains efficacious as a vasoconstrictor even in the setting of severe acidosis. As such vasopressin may provide a useful alternative to catecholamines, which do not function well in the setting of profound acidemia. (676)

ACUTE RENAL FAILURE

51. The definition of ARF varies, but it is often described as an abrupt decrease in renal function, which is defined as urine output less than 0.5 mL/kg/hr or a 50% increase in serum creatinine over a 24-hour period. (676-677)

52. Acute renal failure is normally categorized as prerenal (inadequate renal perfusion pressure), intrarenal (vascular, glomerular, or interstitial dysfunction), or postrenal (usually obstructive). In the management of ARF, it is essential to recognize and treat prerenal failure by ensuring adequate fluid resuscitation and systemic blood pressure, as well as to identify any postrenal obstruction through the use of ultrasound or other imaging techniques. If the ARF has been determined to be intrarenal, it most likely represents acute tubular necrosis. In addition to the history, which may include exposure to nephrotoxic drugs or prolonged hypotension, examination of urinary sediment may show renal tubular epithelial cells or granular casts. (676-677)

53. Indications for acute hemodialysis include excessive intravascular fluid volume, hyperkalemia, acidemia, uremia, toxins, or other electrolyte abnormalities. (677)

DELIRIUM

54. Delirium is defined by the DSM-IV as a disturbance of consciousness with reduced ability to focus or sustain attention that is associated with a change in cognition or perceptual disturbances that are not accounted for by a preexisting dementia. (677)

55. Delirium is widespread in the adult ICU population with estimates of an incidence between 48% and 87%, depending on the acutal population studied. Because there are two forms of delirium, the hyperactive and hypoactive subtypes, the diagnosis is difficult to make and the actual incidence of delirium is frequently underestimated. Hyperactive delirium is usually quite obvious when present,

because patients are typically combative and have profound altered mental status. Hypoactive delirium on the other hand is much more incidious, since patients are typically quiet and may appear calm and content on casual examination. (677)

56. Delirium is not a benign condition. Numerous studies have shown an increased risk of mortality among ICU patients who develop delirium. These risks vary from a greater than threefold increase in 6-month mortality to a 10% increase in the risk of death for every day spent in a state of delirium in the ICU. Delirium is associated with an increased number of days a patient will spend mechanically ventilated, as well as increased days in the ICU and hospital. In addition, delirium is associated with an increased risk of developing dementia in later life. It is unclear whether delirium may actually cause dementia, or if patients who are at greatest risk of dementia or have an early subclinical form of dementia are more likely to have episodes of delirium in the ICU. (677)

57. The causes and conditions assciated with delirium in the ICU setting are numerous. They include preexisting cognitive impairment, advanced age, increasing severity of illness, multiorgan dysfunction, sepsis, immobilization, sleep deprivation, pain, mechanical ventilation, and the use of psychoactive drugs, particularly benzodiazepines. (677)

58. To actively treat delirium, it must be diagnosed first. The most widely used method of monitoring for delirium is the CAM-ICU assessment for delirium. CAM stands for confusion assessment method, and this tool should be used daily to assess for delirium in all ICU patients except those who are deeply sedated or comatose. (677)

59. Delirium in a patient in the ICU setting should be treated by first searching for an underlying cause and correcting the cause. Attempts should be made to actively orient the patient to their surroundings. If delirium still occurs, haloperidol may be helpful in improving orderly thought processes. (677)

NUTRITIONAL SUPPORT

60. Providing optimal nutrition to patients in the ICU is important for wound healing, to maintain skeletal muscle mass and strength, and for the prevention of infection. Optimal nutrition may facilitate weaning from mechanical ventilation and rehabilitation. (677)

61. Patients may be fed either enterally (usually by a nasojejunal feeding tube) or parenterally (intravenously). If possible, it is always preferable to feed enterally. Advantages of enteral feeding include decreased cost, ease of administration, maintenance of normal gastrointestinal physiology, and less risk for infection. Parenteral nutrition formulas are easily infected, which greatly increases the risk for catheter-related blood stream infections. Additionally, without enteral feeding, the normal gastrointestinal tract begins to atrophy. Such atrophy causes loss of mucosal thickness, alteration of pH, and loss of gastrointestinal tract–associated lymphoid tissue. These changes can result in replacement of normal gastrointestinal tract flora with more pathologic organisms and increased translocation of these organisms across the increasingly atrophic gastrointestinal tissue, leading to an increased risk of sepsis. Parenteral nutrition is usually reserved for those patients in whom enteral feeding is not possible. This includes patients with bowel obstruction or ischemia, short gut syndrome, or other malabsorption problems. (678)

RAPID RESPONSE TEAMS

62. Rapid response teams frequently use ICU professionals, including physician intensivists, critical care nurse practitioners, ICU nurses, and respiratory therapists. These teams form a multidisciplinary group to evaluate and treat patients early in the course of a physiologic decline, and make interventions which will hopefully avert an impending cardiopulmonary arrest. (678)

INTENSIVE INSULIN THERAPY

63. Recently, there has been considerable controversy regarding the optimum method of blood glucose control in critically ill patients. Initially, it was thought that intensive insulin therapy to achieve a blood glucose level between 80 to 100 mg/dL would improve survival in ICU patients. This notion has been questioned, and recent studies have shown that intensive insulin therapy to keep very tight glucose control does not improve survival, but increases the risks of significant hypoglycemia and actually increases mortality. This is in part due to increased episodes of hypoglycemia associated with strict control. Currently, the best level at which blood glucose should be maintained in critically ill patients has not been elucidated, but the evidence would support maintaining a blood glucose level in a moderate range between 140 to 180 mg/dL. This level minimizes the risks of severe hypoglycemia (less than 40 mg/dL) and hyperglycemia (greater than 200 mg/dL). (678)

END-OF-LIFE ISSUES

64. The physician intensivist should not regard death as a failure, but rather as a normal course of life. Indeed, the physician may be called upon for his or her professional opinion when the family is making its decision. Once a family has elected to stop treatment of a critically ill patient, the physician should attempt to make the passing of life as dignified as possible. Mechanical ventilatory support can be terminated and either T-piece ventilation or extubation of the trachea should take place. Vasopressor therapy and hemodialysis may be discontinued. In addition, patients should be given adequate sedation for the relief of discomfort, but not to "hasten" death. (678-679)

Chapter

39 TRAUMA, BIOTERRORISM, AND NATURAL DISASTERS

Eric Y. Lin

ACUTE MANAGEMENT OF TRAUMA PATIENTS

1. Trauma is the most common cause of death in what age group?
2. What resources are available at hospitals specializing in trauma (e.g., "level 1" trauma centers)?
3. In reference to traumatic injuries, what is "The Golden Hour"?
4. What are the management priorities when caring for a trauma patient?
5. What is ATLS? What is its relevance to all trauma providers?
6. What are the "ABCDEs" of trauma?
7. A motor vehicle accident victim arrives with an endotracheal tube in situ, a blood pressure of 80/60, heart rate 120, and an obvious right ankle deformity with exposed bone. What is the first step in management of this patient?
8. List the indications for endotracheal intubation after life-threatening trauma.
9. Prior to the arrival of a trauma patient, what should providers do to prepare for possible endotracheal intubation?
10. What intravenous medications are most commonly used to intubate the trachea in severely injured patients?
11. In the context of traumatic brain injury, what is a plateau wave?
12. How should a trauma patient's head be positioned for asleep endotracheal intubation if the stability of the cervical spine is unknown?
13. In the event of airway obstruction and an inability to perform endotracheal intubation, how should the airway be secured?
14. How is shock defined in trauma care? What blood pressure and heart rate values are consistent with shock?
15. What are the most sensitive and specific markers of shock in trauma patients?
16. Into what three anatomic spaces can a trauma patient massively hemorrhage? How would identification of orthopedic injuries limit internal bleeding?
17. What degree of chest tube output requires operative intervention?
18. What does persistent hematuria in a trauma patient indicate?
19. What is the treatment for hypovolemic shock following injury?
20. What is the definition of massive transfusion? What is the significance of blood product ratios in massive transfusion?
21. What is the Glasgow Coma Scale (GCS) and how is it used to evaluate a trauma patient? What GCS score is considered "severe"? Why do patients with severe traumatic brain injury (TBI) require endotracheal intubation, even if protecting their airway?
22. What secondary insults should be avoided in patients with traumatic brain injury?
23. At what intracranial pressure (ICP) is treatment frequently recommended? Name some methods used to treat an increased ICP.
24. What osmotic diuretic is commonly used to decrease an elevated ICP?

25. Why should glucose-containing intravenous solutions be avoided in patients with traumatic brain injury?
26. Should corticosteroids be administered to a patient with traumatic brain injury and signs of an elevated ICP?
27. When should hyperventilation be performed to decrease ICP? What is the danger of excessive hyperventilation?
28. When does a trauma patient require cervical spine stabilization at the time of initial assessment? How do trauma providers "clear" a patient's cervical spine?
29. How is the "E" of the "ABCDEs" addressed in the initial evaluation of a trauma patient?
30. How does the initial evaluation of a burn injury patient differ from other trauma patients?
31. What are some indications for endotracheal intubation in the trauma patient with a burn injury? What is the danger of delaying endotracheal intubation in a patient with suspected inhalational injury?
32. How is the percentage of body surface area burned estimated in an adult?
33. Why should burn patients be initially placed on 100% oxygen, regardless of pulse oximetry reading?
34. Why do burn patients require larger than typical amounts of fluid resuscitation? What volume of intravenous fluid should be initially ordered?
35. What type of fluid should be used to resuscitate burn patients? Why do burn patients often receive a different volume over the first 24 hours than that initially calculated?
36. How should providers evaluate a patient with a suspected closed-head injury?
37. What is a plateau wave in the ICP wave tracing?

EMERGENCY SURGERY FOR TRAUMA

38. How does the time since a patient's last meal affect the initial airway management of a trauma patient?
39. How does the maintenance of general anesthesia differ in emergency trauma surgery compared to elective outpatient surgery?
40. How can movement during surgery be prevented if a trauma patient is too unstable to tolerate high levels of general anesthetic agents?
41. What are the basic principles of intraoperative fluid management for trauma patients needing emergency surgery?
42. What diagnostic tests are used to guide intraoperative fluid therapy?
43. What preparations are needed prior to surgical opening of the peritoneum in an exploratory laparotomy for abdominal injuries?
44. What injuries might result from trauma to the abdomen? How is the diagnosis of intraabdominal hemorrhage made in a trauma patient?
45. What is "damage control" surgery and how does it benefit trauma patients?
46. What is the treatment for a hypotensive motorcycle accident victim with pelvic instability on examination and presumed pelvic bleeding?
47. What is the definition of abdominal compartment syndrome?

MASS CASUALTY DISASTERS

48. What types of mass casualty disasters are possible? What are intentional disasters?
49. How long should hospitals be prepared to manage mass casualty disasters before state and national resources arrive?
50. What roles do anesthesia providers play during mass casualty events?
51. What are the goals of mass casualty triage? How are patients classified? What is an "expectant" mass casualty patient?
52. Where does decontamination of mass casualty patients occur?
53. What are the advantages of ketamine, when compared to other anesthetic agents, in facilitating surgical procedures during mass casualty scenarios?
54. What are the risks of neuraxial blockade in mass casualty patients?

NUCLEAR EXPOSURE

55. How does the initial assessment of a trauma patient differ if the injuries occurred during a nuclear power plant explosion?
56. How are nuclear disaster patients decontaminated?
57. What are the typical findings in acute radiation syndrome and what can be done to prevent it?

CHEMICAL AND BIOLOGIC TERRORISM

58. What are "category A" agents, with respect to bioterrorism?
59. The appearance of five young patients in the emergency department with low-grade fever and myalgias for several days, who all now present with severe substernal chest pain and severe hypoxemia, should raise suspicions of exposure to what bioterrorism agent? What finding on chest radiograph would support this diagnosis? What else should be done for these patients and exposed individuals?
60. How do the cutaneous manifestations of smallpox and varicella zoster differ?
61. How long is aerosolized plague viable if released in weaponized form? How is a patient with pneumonic plague managed?
62. A group of travelers were exposed to an unknown vapor during a terrorist attack. Twelve hours later, several of those exposed experience difficulty breathing and progressive weakness, with decreased salivation and urinary retention. What category A bioterrorism agent is the most likely cause of these symptoms? What treatment is available, and what precautions should a care provider take? How would the presumed agent differ if those exposed had *increased* salivation and urinary *incontinence*?
63. What is a nerve agent?
64. What is the treatment for Sarin-exposed individuals? How does pretreatment with pyridostigmine provide protection from nerve gas exposure?

ANSWERS*

ACUTE MANAGEMENT OF TRAUMA PATIENTS

1. Trauma is the leading cause of death among those younger than 45 years old. An estimated 5 million people worldwide die each year from injuries. (681)
2. Specialized trauma centers maintain the staff, space, and supplies required to provide immediate trauma care. This includes a number of different physician specialties (emergency medicine, trauma surgery, anesthesiology, neurosurgery, diagnostic and interventional radiology, orthopedic surgery), nursing staff, dedicated patient care areas in the emergency department, operating rooms, intensive care unit (ICU), immediate diagnostic resources, and a blood bank. In the United States, a hospital designated as a level 1 trauma center must be able to provide such services on an immediate basis 24 hours a day. (681)
3. "The Golden Hour" refers to the first hour after a patient sustains major injuries. Most trauma-related deaths occur during this first hour, usually as a result of uncontrolled hemorrhage. Early recognition and treatment of shock is therefore a major priority in acute trauma care. (681)
4. The immediate priorities in acute management of trauma patients are to keep the patient alive, identify life-threatening injuries, stop any ongoing bleeding, and provide definitive treatment as early as possible. (681)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

5. ATLS is the acronym for the Advanced Trauma Life Support course that is administered worldwide through the American College of Surgery's Committee on Trauma. ATLS is important to trauma providers because it provides a standardized algorithm that can be universally applied to all trauma patients, regardless of a provider's background or available resources. While trauma providers may vary from the basic ATLS algorithm based on availability of certain resources, knowledge of ATLS is useful to all trauma providers because it establishes a baseline for trauma management and a universal language (e.g., primary survey, secondary survey, ABCDEs) that providers all share. (682)

6. The "ABCDEs" of trauma refers to the appropriate sequence of priorities in trauma management: Airway, Breathing, Circulation, Disability (neurologic status), Exposure/Environment. Providers must immediately assess the ABCDEs, in sequence, when initially evaluating a trauma patient. Compromise at any step should be corrected before moving on to the next. (681-685, Table 42-1)

7. Acute management of any trauma patient must begin with confirmation of a patent airway, therefore the first step in managing this patient is to confirm proper position of the endotracheal tube (ETT). Capnography, auscultation of bilateral breath sounds, pulse oximetry, direct laryngoscopy, arterial blood gases, and fiber-optic bronchoscopy are all commonly used to confirm that an "in situ" ETT is, in fact, in the trachea. (682)

8. Indications for endotracheal intubation after life-threatening trauma include inadequate airway protection, impending loss of airway (e.g., inhalational injury, expanding neck hematoma), laryngeal or tracheal injury, inadequate ventilation or oxygenation, severe head injury, and need for surgery under general anesthesia. (682, Table 42-2)

9. Management of a trauma patient should include prior preparation of functioning *suction*, *oxygen* delivery devices (oxygen source, breathing circuit, ventilator), *airway* equipment (face mask, oral/nasal airways, intubation equipment), *pharmaceuticals* (for intubation of the trachea and management of hemodynamics), *intravenous access* with fluids and tubing, *monitors*, and personal protective equipment. Assistants to help with cervical spine and aspiration precautions should be designated, as well as equipment and personnel needed for a surgical airway if endotracheal intubation cannot be performed. (682-683, Table 42-3)

10. Etomidate or ketamine are most often used as the intravenous induction agent for severely injured patients, given the risk of hypovolemic shock and hemodynamic instability with induction. Propofol can be used for induction of stable patients without signs of shock. Succinylcholine is the most commonly used neuromuscular blocking agent to quickly provide optimal conditions for rapid sequence intubation of the trachea. Succinylcholine can be safely used in trauma and burn patients within the first 24 hours after injury, provided no other contraindications exist. (682-683)

11. A plateau wave is an abrupt and sustained increase in intracranial pressure that can occur in patients with traumatic brain injury, often in response to painful stimulation. This severe intracranial hypertension can last for 20 minutes before resolving, often dropping rapidly to a level lower than the previous baseline. (683, Figure 42-1)

12. If a patient's cervical spine stability is unknown and the airway must be secured, asleep endotracheal intubation should proceed with the patient's head stabilized in the neutral position on a flat, rigid surface. Such manual, in-line stabilization should be performed by an assistant whose goal during intubation is to prevent atlanto-occipital extension during direct laryngoscopy. (683-684, Table 42-3)

13. Inability to mask ventilate or intubate the trachea necessitates immediate invasive intervention such as emergency cricothyrotomy or tracheotomy. (683)

14. Shock is defined as inadequate perfusion to vital organs. Low, normal, and high blood pressure and heart rate can be seen in patients with shock. Compensatory mechanisms and other factors, such as pain and agitation, allow patients with shock to maintain normal or even elevated blood pressure and/or heart rate. Decompensated hypovolemic shock, or late shock, will lead to profound hypotension and tachycardia. Spinal shock is characterized by hypotension and bradycardia. Clinicians should therefore maintain a high level of suspicion for shock in patients with severe injuries, regardless of a normal blood pressure and heart rate. (683)

15. Abnormal base deficit and lactate are the best independent markers of shock after trauma. The degree of base deficit also correlates with the severity of shock, volume deficit, morbidity, and nonsurvival. One or both markers should be checked in all trauma patients with risk of shock. (683)

16. Massive hemorrhage can occur into the thoracic, abdominal, or pelvic cavities. Estimated blood loss must therefore take into account both visible hemorrhage (at the injury scene and hospital) and potential hemorrhage into one of these three cavities. Significant blood volume can also be lost into the thigh with certain femoral injuries. Identification of pelvic injuries or femur fractures, with subsequent placement of pelvic binders or long bone splints, helps to limit hemorrhage into the pelvis and thigh, respectively. (683)

17. Operative intervention is required if more than 1500 mL of blood comes out at the time of thoracostomy tube placement, or 200 mL per hour thereafter. This degree of chest tube output suggests active intrathoracic hemorrhage and is defined as a massive hemothorax. Massive hemothorax should also be assumed, until proven otherwise, in any patient with a penetrating thoracic injury that is hemodynamically unstable. (683)

18. Persistence of hematuria in a trauma patient may be an indication of bladder injury or injury to the genitourinary system. (683)

19. The primary treatment of hypovolemic shock is to stop any active bleeding. Delays in identification and control of hemorrhage can be deadly and should therefore be avoided. Fluid resuscitation is the mainstay of supportive therapy for patients with hypovolemic shock after injury. Warmed isotonic crystalloid can be used initially for volume resuscitation, but patients with persistent shock should be given blood products to maintain minimum perfusion pressures until hemorrhage is controlled. Vasopressors may be helpful in patients not responding to fluid therapy or to induce higher blood pressure for spinal cord or cerebral perfusion. (683-684)

20. Massive transfusion is traditionally defined as: greater than or equal to 10 units of blood transfused in 24 hours, equivalent to the replacement of one blood volume in an average size patient. The unit ratios of blood products transfused may affect the likelihood of hemorrhage control and survival in injured patients requiring massive transfusion. During a massive transfusion, many trauma centers use blood product ratios to help providers administer fluids that more closely replace the functions of a patient's lost blood. (684)

21. The GCS is used during the initial assessment of a trauma patient to rapidly evaluate neurologic status. The GCS is calculated by assigning points based on a patient's eye opening (1 to 4), verbal response (1 to 5), and motor response (1 to 6) to compute a total score between 3 (worse) to 15 (best). The GCS can then be used to categorize the severity of traumatic brain injury (TBI). A GCS score of 8 or less is classified as "severe" TBI. Patients with severe TBI have a high likelihood

of intracranial hypertension, possibly with midline shift or brain herniation. Endotracheal intubation and control of ventilation is therefore needed to quickly diagnose and treat any life-threatening intracranial hemorrhage. (684, Table 42-4)

22. Hypotension, hypoxia, hyperthermia, and sustained intracranial hypertension should be avoided in traumatic brain injury patients, as these secondary insults are associated with worse outcomes in brain-injured patients. Hyperglycemia is also neurotoxic in models of brain injury and should be avoided. (684)

23. Treatment of an elevated ICP is frequently recommended when the pressure exceeds 20 mm Hg for a sustained period of time. There are several methods by which elevations in ICP can be treated. These include positioning of the head up and neutral, hyperosmolar therapy, osmotic and loop diuretics, cerebrospinal fluid drainage, and the administration of drugs such as barbiturates that decrease both cerebral blood flow and cerebral metabolism. (684)

24. Mannitol is the osmotic diuretic that is most frequently administered to decrease ICP. Osmotic diuretics decrease ICP by drawing water out of tissues and into the intravascular space. Osmotic diuretics do so by transiently increasing the osmolarity of plasma. The dose of mannitol that is administered is 0.25 to 1.4 g/kg over 15 to 30 minutes. (684)

25. Glucose-containing intravenous solutions should be avoided in traumatic brain injury patients because of the potential for hyperglycemia and hypotonicity, both of which can be neurotoxic. (684)

26. Though corticosteroids are often administered to patients with an elevated ICP, they are most effective in decreasing focal cerebral edema such as that which develops after brain tumor resection. Steroids have no demonstrated benefit in traumatic brain injury patients, increase the risk of hyperglycemia, and should not be given routinely to TBI patients. (684)

27. Deliberate hyperventilation should only be instituted if there is ongoing or imminent brain herniation and rescue measures are needed prior to decompressive craniectomy. Prolonged hyperventilation ($Paco_2$ 25 to 30 mm Hg) is associated with worse outcomes in TBI patients. Excessive hyperventilation in adults (<25 mm Hg) and children (<20 mm Hg) creates even greater potential for cerebral ischemia, as cerebral blood flow decreases in response to alkalosis. (684)

28. All trauma patients with a loss of consciousness, an unclear history, or a mechanism of injury suggestive of neck injury should be placed in a rigid cervical spine collar at the time of initial assessment, if not already done. Mechanisms of injury with a higher likelihood of cervical spine injury include: front-end motor vehicle accident without a seat belt, head-first fall, and blunt maxillofacial trauma. "Clearing" the cervical spine (i.e., declaring that cervical spine stabilization is no longer necessary) occurs when a patient reliably denies pain with neck palpation and neck movement. This should not be done if the patient has a distracting injury or altered mental status. If physical examination is unreliable, computed tomography and MRI are commonly used to diagnose cervical spine fractures and ligamentous injuries. (683-685)

29. The final component of the "ABCDEs" of trauma assessment is Exposure/Environment. This begins with the removal of all clothing and prehospital dressings, a practice that allows for a complete examination of the entire body to ensure that no injuries are missed. Contaminated and cold clothing are also removed at the same time, transitioning to a safer and warmer environment for the patient. Once examined, a hypothermic patient should be rewarmed with blankets, forced air blankets, and warmed intravenous fluids. (685)

30. Special considerations for a burn injured patient include the administration of 100% oxygen regardless of airway examination due to risk of carbon monoxide poisoning, calculation of total body surface area burned, and assessment for signs of inhalational injury (e.g., singed nasal hair, voice changes, carbonaceous sputum). (682, 685)

31. For the burn injury patient arriving to a trauma center, a history of closed space fire or explosion, and the presence of facial burns, singed nasal hair or eyebrows, and/or carbonaceous sputum are all risk factors for significant inhalational injury and need for endotracheal intubation. Stridor, hoarseness, or visualized periglottic swelling/soot are signs of imminent loss of airway and indications for immediate endotracheal intubation. Patients with inhalational injury can rapidly develop facial and glottic edema that completely obstructs the airway, making oral intubation of the trachea difficult or impossible. (685)

32. A patient's percentage of body surface area (BSA) burned is estimated using the "rule of nines": (685)

Head and neck region:	9%
Upper extremities:	18% (left and right: each 9%)
Lower extremity:	36% (front and back: each 9%)
Torso:	18% (front and back: each 9%)
Perineal area	1%
Total:	100%

33. Burn injury victims may have suffered from smoke inhalation injury with associated carbon monoxide inhalation, particularly if the patient had been exposed to smoke in a closed space. Carbon monoxide has a binding affinity for hemoglobin that is about 200 times greater than that of oxygen. The presence of high carbon monoxide levels therefore creates a functional anemia by reducing the oxygen content and delivery of a patient's hemoglobin, despite the presence of a normal Pa_{O_2}. In addition, the binding of carbon monoxide to hemoglobin shifts the oxyhemoglobin dissociation curve to the right, making the remaining oxygen bind more tightly to hemoglobin and decreasing the ability of hemoglobin to unload oxygen at the tissues. A pulse oximeter will have normal readings despite carbon monoxide toxicity. Carbon monoxide toxicity should be treated with the administration of 100% oxygen. A high Pa_{O_2} will lead to the removal of carbon monoxide from hemoglobin with greater rapidity. (685)

34. The burn injury patient often requires large volumes of fluid for volume resuscitation after his or her injury secondary to huge volume shifts into burned tissue, increased vascular permeability, evaporative losses, and increased metabolism. The Consensus formula (traditionally known as the Parkland formula) is used to calculate the initial rate of fluid administration. Lactated Ringer solution should be given at 4 mL/kg in the first 24 hours for every 1% of the patient's body surface area that is burned, with one half of the calculated volume administered in the first 8 hours after injury. The remaining half should be administered in the subsequent 16 hours, though the fluid rate should be continually adjusted to maintain adequate organ perfusion. (685)

35. Warmed isotonic solution such as lactated Ringer solution should be used for fluid resuscitation in burn patients. Colloids have no demonstrated advantage over crystalloid and may actually worsen outcomes. While the Consensus formula is used to determine the initial fluid requirements of burn patients, the fluid rate is typically adjusted continuously, based on a urine output goal of 0.5 mL/kg/hr, to avoid overresuscitation or underresuscitation of patients. (685)

36. Patients suspected of having a closed-head injury can be evaluated by history, physical examination, and radiologic studies. The hallmark clinical sign of a closed-head injury is loss of consciousness. A GCS score should be calculated based on eye opening and verbal and motor responses. A noncontrast computed tomographic scan of the head should be performed as early as possible to assess for intracranial hypertension or a need for emergent operative intervention. Midline shift, brain herniation, skull fractures, and any intracranial bleeding can be quickly assessed with computed tomography. (684, Table 42-4)

37. A plateau wave in the ICP wave tracing refers to an abrupt increase in the ICP observed during continuous monitoring. This can occur following painful stimuli even in an otherwise unresponsive patient. The plateau wave is usually sustained for 10 to 20 minutes, followed by a rapid decrease in the ICP. The presence of plateau waves on an ICP wave tracing may indicate that the intracranial compliance is low. Some providers administer opioids and/or lidocaine to blunt this effect, though the efficacy of such measures is unclear. (683, Figure 42-1)

EMERGENCY SURGERY FOR TRAUMA

38. In general, rapid sequence intubation of the trachea should be performed for all emergency trauma procedures, so the time since a patient's last meal has no impact on airway management. Because gastrointestinal motility decreases following trauma, providers assume that all trauma patients have full stomachs and are at risk for the aspiration of gastric contents. Rapid sequence intubation of the trachea reduces this risk by minimizing the time between loss of airway reflexes and placement of a secure airway. (682, 686, Table 42-3)

39. In emergency surgery for trauma, the risks of preexisting hypovolemia, massive hemorrhage, and hemodynamic instability are higher; therefore general anesthesia is maintained with lower than usual doses of inhaled volatile anesthetics or benzodiazepines to optimize hemodynamic stability. Ketamine can also be used for this purpose. Nitrous oxide is generally avoided in patients with a potential for pneumothorax or for abdominal procedures. (682-683, 686)

40. If a trauma patient is unable to tolerate high levels of general anesthetics, neuromuscular blocking drugs are needed to prevent skeletal muscle movement and facilitate the surgical procedure. Small doses of a benzodiazepine or scopolamine can be used under these circumstances in an attempt to prevent recall. Under these critical conditions, patients may experience some recall of the intraoperative events, making it important for the anesthesiologist to communicate with the patient during and after the procedure. (686)

41. Intraoperative fluid management for trauma patients follows the same principles as the initial management of the acute trauma patient, with the goals of maintaining adequate circulating volume while optimizing conditions for hemorrhage control. Fluid resuscitation may be initiated with isotonic crystalloid solutions, with early transition to blood products and permissive hypotension if hemorrhaging is uncontrolled. Hypothermia, coagulopathy, and severe acidosis should be actively prevented and corrected. Rapid fluid infusion, fluid warmers, and autotransfusion systems should be used if appropriate and available. (683-684, 686, Table 42-5)

42. Arterial blood gases, hematocrit and platelet count, coagulation tests, and electrolytes are followed regularly to assess the progress of resuscitation and surgery. Invasive monitoring, such as arterial pressure variability, central venous pressure, and echocardiography, is also commonly used to guide therapy. Use of newer technologies such as thromboelastography and central venous oxygen saturation can also provide real-time measurements of coagulopathy and shock, respectively. (683-684, 686, Table 42-5)

43. Opening of any anatomic compartment containing recent blood loss can remove external pressure on injured vessels and precipitate uncontrolled hemorrhage. Opening of the peritoneum in a patient with recent intraabdominal hemorrhage should not occur until the preparations have been made for adequate large-bore intravenous access, monitoring, fluid products, and vasoactive medications. Surgical equipment such as vascular clamps and wound packing supplies should also be immediately available. The same principles apply to opening of the dura during craniotomies, opening of the pleura during thoracotomies, etc. (686)

44. Injuries that may be sustained in abdominal trauma include soft tissue contusions or avulsions, rupture of visceral organs, or laceration of the spleen or liver. Injury to the spleen or liver can result in significant hemorrhage. The diagnosis of intraabdominal hemorrhage is made by FAST (focused assessment with sonography in trauma) examination, peritoneal lavage, and/or computed tomography. (683, 686)

45. "Damage control" surgery for trauma patients refers to the practice of focusing the initial surgical intervention on hemorrhage control and abbreviated surgery, with a plan to delay extensive examination and definitive repair of all injuries until after the patient is fully resuscitated and stabilized in the ICU. This practice allows for shorter operating and general anesthesia time initially, achieves hemorrhage control and shock reversal sooner, and reduces the risk of developing acidosis, coagulopathy, and hypothermia. (686)

46. After establishing that the airway and breathing are stable, the pelvic ring should be initially closed with a pelvic binder device, followed by angioembolization of pelvic vessels in the interventional radiology suite. If interventional radiology services are not available, extraperitoneal packing can be performed to achieve hemorrhage control, with external fixation of the pelvis performed once the patient is fully resuscitated and hemodynamically stable. (687)

47. Abdominal compartment syndrome is defined as an intra abdominal pressure greater than 20 mm Hg with associated organ dysfunction. Trauma patients with abdominal injury and/or large volume resuscitation should be closely monitored for abdominal compartment syndrome. (687)

MASS CASUALTY DISASTERS

48. Mass casualty disasters are events that require more resources than the local community can provide. Disasters can be natural (e.g., floods and earthquakes), unintentional (e.g., industrial or multivehicle accidents), or intentional. Intentional disasters are acts of terrorism or warfare, and can be explosive, nuclear, biologic, or chemical disasters. (687, Table 42-6)

49. Additional resources are unlikely to arrive for at least 24 to 72 hours after a disaster, so hospitals should have enough resources within the local community to respond for this period of time. Community emergency preparedness plans should be in place and coordinated among local health care providers, law enforcement agencies, fire and rescue services, and local governments. (687-688, Table 42-8)

50. In the event of a mass casualty disaster, anesthesia providers may be required to fulfill many roles including assistance with triage, stabilization of patients in the emergency department, resuscitation and life support in the intensive care unit, as well as intraoperative patient management. Like all clinicians, anesthesia providers should also be able to fulfill their duties within the local emergency response plan, recognize and report any suspected cases of mass casualty events, and be familiar with available exposure prophylaxis. (687, Table 42-9)

51. The goals of patient triage in mass casualty events are to quickly prioritize injuries based on severity of injury and likelihood to survive, so that limited resources can be used to achieve the greatest population benefit. This concept of

population-based resource allocation can be difficult for providers used to utilizing every possible resource for each patient under their care. While multiple mass casualty triage systems exist, nearly all divide patients into groups requiring immediate, delayed, minimal, or no treatment. "Expectant" patients are those who are expected to die of their injuries, even if life-saving surgery were attempted. Expectant patients are separated from the main patient flow and placed in a quiet area with an emphasis on analgesia and comfort. (688-689, Table 42-10)

52. Decontamination of mass casualty patients is typically performed at the scene before transportation. Hospitals set up a secure area outside of the main hospital area to complete decontamination and triage of patients. Out-of-hospital decontamination reduces ongoing exposure injuries and minimizes the risk of secondary exposure to health care providers and other patients. (689)

53. Mass casualty events create situations where patients outnumber resources, including airway equipment and ventilators. Maintaining spontaneous ventilation and hemodynamic stability can therefore be critical in such patients. Ketamine is a useful and commonly used anesthetic agent in such scenarios—including prehospital procedures such as limb amputation—because it provides analgesia and hypnosis with minimal depression of respiratory or cardiovascular function. (689)

54. Neuraxial blockade (i.e., epidural or spinal anesthesia) is generally avoided in mass casualty patients due to the risk of severe hypotension due to hypovolemia and underlying injury. Coagulopathy and need for immobilization are also common reasons to avoid neuraxial blockade for emergency trauma surgery. (690)

NUCLEAR EXPOSURE

55. Transmission of radioactive material from victim to health care provider is low, so standard trauma protocols should be followed during the initial evaluation of a nuclear exposed trauma patient, progressing from "A" through "D": airway, breathing, circulation, disability (neurologic status). Decontamination is then performed as part of the assessment and treatment of "E," or exposure. (690)

56. As part of the exposure assessment, nuclear disaster victims are externally decontaminated by removing all clothing and rinsing the skin with warm soapy water. Once stabilized and externally decontaminated, internal decontamination is performed with methods such as gastric lavage, emetics, laxatives, and diuretics, as well as copious irrigation of any open wounds. These measures are necessary to prevent continued injury from retained nuclear material. (690)

57. Acute radiation syndrome is characterized by thrombocytopenia, granulocytopenia, nausea, and vomiting. Once stabilized, the patient should be monitored continuously for such signs. Prevention involves minimizing the duration of exposure through both external and internal decontamination. Medications can be given to facilitate renal excretion and chelation. Potassium iodide can also be given within the first 24 hours to prevent radiation-induced thyroid abnormalities. (690)

CHEMICAL AND BIOLOGIC TERRORISM

58. Category A bioterrorism agents, as classified by the United States Centers for Disease Control and Prevention, are agents thought to be mass-engineered by terrorist groups, easily disseminated or transmitted to victims, have a high mortality rate, and/or create public panic if released. Examples of category A agents are anthrax, smallpox, and Ebola virus. (691, Table 42-12)

59. Any clustering of unusual illness should be treated as victims of bioterrorism until proven otherwise. In this case, the history of flulike symptoms followed by chest pain and profound respiratory distress suggests inhalational anthrax. Shock and meningitis may also be present. A widened mediastinum, due to mediastinal

adenopathy, can be seen on chest radiograph of inhalational anthrax patients. When profound dyspnea develops, death can ensue within 2 days; therefore treatment and supportive measures should be instituted immediately (e.g., antibiotic therapy, endotracheal intubation, and mechanical ventilation). Either ciprofloxacin or doxycycline can be used to effectively treat weaponized anthrax. Although inhalational anthrax presents little to no risk of secondary spread from patients with established infection, such patients should initially be isolated and health care officials should be notified. Prophylaxis for exposed individuals can be done with either a fluoroquinolone alone for 60 days or a vaccination plus a fluoroquinolone for 30 days. (691-692, Table 42-13 through Table 42-16, Figure 42-2)

60. Smallpox produces cutaneous lesions 72 to 96 hours after a fever, whereas patients with varicella zoster infection, or "chickenpox," develop their rash at the same time as a fever. In addition, smallpox lesions appear all at once and will therefore all be at the same stage. In contrast, chickenpox lesions appear at different times, so physical examination reveals lesions with different stages of lesion development (papules, vesicles, pustules, scabs). (692)

61. Aerosolized plague (*Yersinia pestis*) is viable for approximately 60 minutes. If an individual develops pneumonic plague, management includes strict isolation and exposure precautions because pneumonic plague is highly contagious. Early antibiotic treatment is also critical, as the mortality of untreated individuals approaches 100%. Streptomycin, gentamicin, tetracycline, and chloramphenicol are all effective therapies for plague. (692, Table 42-18)

62. Clostridium botulinum toxin is a category A agent that causes skeletal muscle weakness between 12 to 36 hours after ingestion or inhalation of the toxin. Botulism results from inhibition of acetylcholine release, and can be treated with trivalent antitoxin. Endotracheal intubation and mechanical ventilation may also be required. The toxin is not contagious, however, therefore health care providers do not need to follow any additional special precautions. While botulism leads to decreased salivation, ileus, and urinary retention, nerve agents (e.g., sarin) are acetylcholinesterase inhibitors and cause cholinergic effects in addition to skeletal muscle weakness. (691, 693-696, Table 42-12, Table 42-20, Table 42-22)

63. Nerve agents are military-grade chemicals that act, similar to organophosphate pesticides, by inhibiting acetylcholinesterase and produce cholinergic effects including muscle fasciculations, weakness, incontinence, and hypersecretion. They are typically lipophilic clear liquids that vaporize at room temperature and are absorbed through the skin, mucous membranes, lungs, or gastrointestinal tract. (695)

64. Sarin is a potent nerve agent that has been used recently in chemical terrorist attacks. It is also referred to by the two-letter NATO military code "GB." Like other nerve agents, exposure to sarin should be treated with atropine (2 to 6 mg IM) and pralidoxime (600 to 1800 mg IM), with atropine redosed every 5 to 10 minutes until secretions begin to decrease. Pyridostigmine is a medication that reversibly binds to AChE. Administration of pyridostigmine 30 minutes before exposure therefore provides protection by occupying the binding sites that the nerve agents target. It then dissociates from the AChE enzyme after the exposure risk has passed. (695-696, Table 42-22)

Chapter

40 CHRONIC PAIN MANAGEMENT

Pankaj Mehta, James P. Rathmell

MULTIDISCIPLINARY CHRONIC PAIN MANAGEMENT

1. Why is multidisciplinary teamwork necessary for managing chronic pain? What are the components of such a multidisciplinary team? How are patients usually referred to a pain clinic?
2. How should the initial evaluation of a patient be carried out in the pain clinic? How is a treatment plan established for a patient evaluated in a chronic pain clinic?
3. Name some treatment modalities for the management of chronic pain.
4. List some of the psychological components of the chronic pain disease process. What is the potential value of the Minnesota Multiphasic Personality Inventory when evaluating patients with chronic pain?

COMMON PAIN SYNDROMES

5. What is meant by the term low back pain? What is the usual pattern of recovery for patients presenting with low back pain?
6. How does the typical patient with low back pain present to a pain physician?
7. What are the pathophysiologic mechanisms which commonly contribute to low back pain?
8. How can chronic low back pain arising from the lumbar facet joints be distinguished from lumbar radiculopathy?
9. What are some warning signs on the initial history and physical when evaluating a patient with low back pain that may indicate significant physical comorbidity that should be promptly investigated?
10. How should a physician approach medical therapy for the most common presentations of low back pain?
11. What are the socioeconomic considerations of low back pain and its treatment? What are some risk factors for developing chronic low back pain?
12. What is neuropathic pain? What are some of the typical signs and symptoms of neuropathic pain?
13. What is postherpetic neuralgia?
14. What treatment modalities have been used for the treatment of postherpetic neuralgia?
15. What are some of the side effects of tricyclic antidepressants that may limit their usefulness in elderly patients with postherpetic neuralgia?
16. What is diabetic peripheral neuropathy? How does it present?
17. What is complex regional pain syndrome? What differentiates type I and type II complex regional pain syndromes?
18. What are the clinical manifestations of complex regional pain syndrome?
19. How is the diagnosis of complex regional pain syndrome of the upper or lower extremity made?

20. What is the treatment for complex regional pain syndrome? How does the time delay to diagnosis and treatment affect treatment outcome?
21. What pharmacologic agents are commonly used for intravenous regional sympathetic nerve blockade? How is this technique believed to work?

CANCER-RELATED PAIN

22. What are the various ways in which cancer can cause pain? What is the primary treatment for cancer pain?
23. What are some oral analgesics used to treat persistent cancer pain? What is the World Health Organization stepwise approach to managing cancer-related pain?
24. When oral intake by patients is limited, what are some alternative routes of analgesic drug delivery used to manage persistent cancer pain?
25. What are some neurosurgical procedures for the treatment of chronic pain that may be useful in cancer patients in whom less invasive procedures have been unsuccessful in providing pain control?
26. Which is the most common uniformly efficacious neurolytic block for visceral malignancy? What are the limitations of such a block?

PHARMACOLOGIC MANAGEMENT OF CHRONIC PAIN

27. What are some of the pharmacologic agents used for pain management?
28. What are simple analgesics and how can they be useful in chronic pain management? How are cyclooxygenase-2 selective drugs useful for chronic pain management and how do they differ from nonselective drugs?
29. How do antidepressants exert their actions? List some antidepressants commonly used for pain management and their side effects.
30. Which anticonvulsants are commonly used for pain management? What are the most common side effects associated with each agent? What are the first-line treatments for neuropathic pain?
31. What potential problems are encountered by physicians when prescribing opioids?
32. What basic principles guide the use of opioids in terminally ill patients as compared with those with nonmalignant chronic pain?
33. What are the current guidelines for the stepwise pharmacologic management of neuropathic pain?

INTERVENTIONAL PAIN THERAPIES

34. What is meant by the term *interventional pain therapy*? Name some of the commonly performed interventional procedures used to treat pain.
35. How is an epidural steroid injection useful as an interventional therapeutic procedure? What side effects should patients be informed about?
36. What are the different techniques used to inject steroids into the epidural space? What is the rationale for using one technique over another?
37. When should a physician suspect the facet joint as a cause of low back pain? How can a facet joint block be useful as a diagnostic tool?
38. What is the role of radiofrequency ablation in the long-term management of persistent facet-related pain?
39. What is the current role of lumbar diskography in the management of lumbosacral pain?
40. What is minimally invasive disk decompression? How does it work and what is a limitation of this procedure?
41. How are sympathetic nerve blocks useful as a diagnostic tool in chronic pain management? What is the current evidence of their role in managing chronic pain syndromes?
42. What is the anatomical location of stellate ganglion? How is a stellate ganglion block useful in the management of chronic pain?
43. How is a stellate ganglion block performed? Describe a safer alternative to the conventionally performed stellate ganglion block.
44. List the common conditions for which stellate ganglion block is used in treatment.
45. What are the signs of a successful stellate ganglion block?

46. What are the complications of stellate ganglion block?
47. What is the anatomic location of the celiac plexus and what are the structures that lie immediately adjacent to the celiac plexus?
48. What are the most common techniques by which a celiac plexus block can be performed?
49. What is the clinical indication for a celiac plexus block?
50. How does a celiac plexus block differ from a splanchnic nerve block?
51. What are the complications associated with celiac plexus block?
52. Describe the applied anatomy of the lumbar sympathetic chain.
53. What are some of the clinical uses of a lumbar sympathetic block? List the complications that may be encountered while performing a lumbar sympathetic block.
54. What fundamental physiologic principle forms the basis of spinal cord stimulation?
55. What is the current role of spinal cord stimulation in managing chronic pain syndromes?
56. What are the complications of spinal cord stimulation?

ANSWERS*

MULTIDISCIPLINARY CHRONIC PAIN MANAGEMENT

1. Chronic pain is a complex disorder and patients suffering from chronic pain usually have biologic disease that coexists with cognitive, affective, behavioral, and social factors. Hence, management of such a disease process requires the expertise of health care providers from a range of medical specialties. The team at most centers consists of a physician, often an anesthesiologist, a psychologist, and a physical therapist working together. Patients are usually referred to a chronic pain clinic by their primary care physicians for a problem with chronic pain that has not responded to conventional medical therapy.

   In the pain clinic, the physician coordinates the diagnosis and medical treatment, the psychologist incorporates patient education and cognitive behavioral therapy, and the physical therapist plans an appropriate exercise regimen for the patient aimed at improving function. Thus the team members interact to manage the chronic pain problem using a multimodal approach. (699)

2. On his or her arrival to a chronic pain clinic, the patient should be evaluated by a physician with expertise in pain medicine. During the initial evaluation, the potential psychological, medical, and social contributions to the patient's pain should be evaluated. While it would be ideal for a psychologist and a physical therapist to also evaluate each new patient and then this multidisciplinary team meet to discuss the various aspects of the patient's history, as well as a probable diagnosis, this is seldom possible in today's constrained health care environment. Nonetheless, the physician who conducts the initial evaluation must devise a treatment plan for each patient that takes into consideration all aspects of the patient's care and arranges for appropriate referral to other members of the team when needed. (699)

3. Treatment modalities available in most chronic pain clinics include oral pharmacotherapy, diagnostic and therapeutic nerve blocks, the neuraxial administration of opioids, neurostimulation techniques, biofeedback, and physical therapy. (699)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

4. Chronic pain as a disease process may include psychiatric and psychological manifestations, some of which include depression, insomnia, and avoidance of social and vocational obligations. Dependence on analgesics and visits to multiple physicians are common among patients with chronic pain. The Minnesota Multiphasic Personality Inventory is a useful test for the detection of many of these common comorbidities that often coexist in those suffering with chronic pain. (699)

COMMON PAIN SYNDROMES

5. Low back pain (LBP) is the most common reason why people seek medical attention and is also known as lumbosacral pain. This refers to pain in either the lumbar or the sacral spinal region. Anatomically, the region is defined as the area of the back between the tip of the twelfth thoracic spinal process up till the sacrococcygeal joint. Most people presenting with low back pain recover with no treatment. A majority recover by 6 weeks (60% to 70%) or mostly by 12 weeks (90%). The recovery after 12 weeks, however, is slow and uncertain. (699, Figure 43-1)

6. Patients presenting with low back pain usually have pain either localized to the back region (acute or chronic lumbosacral pain) or distributed in the area of nerve (acute or chronic radicular pain). *Acute radicular pain* is typically caused by a herniated nucleus pulposus in younger patients. Signs of radiculopathy include numbness, weakness, or loss of deep tendon reflexes in the area of the affected nerve. In the elderly, foraminal narrowing may affect the spinal nerve leading to acute radicular pain. Patients presenting with *chronic radicular pain* require a detailed search for a reversible cause of nerve root impingement. MRI or electrodiagnostic testing could give some clues to the cause of pain in patients who have had prior surgery. *Acute lumbosacral pain* with no radicular symptoms in most cases may be myofascial in origin and require no further radiologic investigation. *Chronic lumbosacral pain* may arise from many parts of the vertebral unit; most commonly implicated are the sacroiliac joint, lumbar facets, and the intervertebral disks. Diagnostic nerve blocks involving injection of local anesthetic at these anatomic sites leading to temporary pain relief can aid in localizing the origin of pain. Diagnosis and treatment of the patient with low back pain rely on the location of pain (primarily radicular or lumbosacral) and the duration of symptoms (acute or chronic). (700-701)

7. The following pathophysiologic mechanisms result from degenerative changes in the spinal functional unit due to aging and injury, and can give rise to lumbosacral and/or lumbar radicular pain:
   - Synovitis in the facet joints leading to capsular laxity and subluxation; facet-related pain is predominantly localized over the lumbosacral junction.
   - Degeneration in the intervertebral disks leading to loss of hydration of the nucleus pulposus. Further compromise with tears within the annulus fibrosis is termed internal disk disruption; discogenic pain is predominantly localized over the lumbosacral junction.
   - Internal disruption of the disk may also lead to herniated nucleated pulposus, which is an extension of nuclear material beyond the disk margin. These disk herniations often extend posterolaterally to involve the spinal nerve inciting an intense inflammatory reaction and producing acute radicular pain ("sciatica"). (700)

8. Pain arising from the lumbar facet joint is predominantly localized near the lumbosacral junction, while lumbar radicular pain is localized within the leg. The pain arising from facet joints is usually diagnosed by the injection of a small volume of local anesthetic into the joint under fluoroscopic guidance. Substantial pain relief suggests that pain originates from inflammation of that particular joint. However, a substantial number of patients will report pain reduction even when a nonactive agent such as normal saline is injected. This placebo response can complicate certain diagnosis using diagnostic injections. (700)

9. When first evaluating a patient with back pain, the physician should be aware of certain conditions that may indicate significant physical comorbidity, prompting further investigation. In the patient's history, these include new onset or worsening pain after trauma, infection, or previous malignancy. Patients who report worsening neurologic deficits, or bladder or bowel dysfunction, warrant early radiologic imaging to rule out neural compression. (700)

10. Medical therapy for the most common presentations of low back pain is based on how a patient presents to the pain physician and on the duration of pain symptoms. *Acute radicular pain*: Therapy is usually started with a 7-day course of simple analgesics alone or in combination with an opioid analgesic and a muscle relaxant for associated muscle spasm. *Chronic radicular pain*: Therapy usually begins with a trial of antidepressants or anticonvulsants since opioids are less effective for neuropathic pain. Patients who are poor responders to combination medical therapy are offered a trial of spinal cord stimulation. *Acute lumbosacral pain* is usually managed with a short course of a simple analgesic alone or in combination with an opioid and a muscle relaxant as needed. Pharmacotherapy is usually followed by physical therapy for patients with persistent pain. First-line management for patients with *chronic lumbosacral* pain involves diagnostic medial branch nerve blocks to rule out facet joint pain. If positive, radiofrequency treatment may prove beneficial. For patients with continued pain, a formal physical and behavioral therapy program is usually recommended. (705, Table 43-4)

11. Low back pain and its treatment place a huge socioeconomic burden on society. Only 40% to 45% of the patients who are disabled for 6 months will ever return to work. The return to work rate for patients absent for 2 years is close to zero. The risk factors for developing chronic low back pain include age, gender, socioeconomic status, body mass index, tobacco use, general health status, strenuous physical activities, job dissatisfaction, depression, and anatomic variations. (699)

12. Neuropathic pain is persistent following injury to the nervous system. The three most common types of neuropathic pain include postherpetic neuralgia, diabetic peripheral neuropathy, and complex regional pain syndrome. Patients with neuropathic pain often report:
    - Spontaneous pain—that is, it occurs without any stimulus.
    - Hyperalgesia—an exaggerated painful response to a mildly noxious stimulus.
    - Allodynia—a painful response to a normally nonnoxious stimulus. (702)

13. Postherpetic neuralgia refers to pain that persists for extended periods of time (more than 3 to 6 months) after an acute infection of herpes zoster. Postherpetic neuralgia usually occurs in elderly or immune compromised patients due to a secondary infection of varicella zoster virus (called shingles) leading to damage to small unmyelinated nerve fibers. The pain is characterized by episodic lancinating pain accompanied by severe allodynia in the affected dermatome. In recent years the availability of a vaccine has reduced the incidence of postherpetic neuralgia. (702)

14. Postherpetic neuralgia has been treated with occasional success with sympathetic nerve blocks in patients who have sought early treatment, but sympathetic blocks are ineffective in those with established postherpetic neuralgia. Treatment of established postherpetic neuralgia is challenging. Tricyclic antidepressants and anticonvulsants remain the mainstay of treatment. Topical lidocaine is useful to reduce the painful allodynia. (702)

15. Side effects of tricyclic antidepressants include orthostatic hypotension, sedation, urinary retention, and an increase in appetite. Tricyclic antidepressants may also cause worsening of preexisting heart block. These side effects may limit the usefulness of tricyclic antidepressant medication therapy in elderly patients suffering from postherpetic neuralgia. (704)

16. Diabetic peripheral neuropathy, the most common cause of neuropathic pain, occurs as a result of damage to small unmyelinated nerve fibers. The symptoms are numbness associated with paresthesias, dysesthesias, and pain commonly described as burning or deeply aching. Symptoms can progress slowly over many years, and may affect the hands as well as the lower extremities. Diabetic patients with poor glucose control are at the greatest risk for developing diabetic peripheral neuropathy. (702)

17. Complex regional pain syndrome (CRPS) refers to signs and symptoms that emerge in certain patients after injury to peripheral nerves, typically after trauma to an extremity. After the initial trauma, and during healing, persistent neuropathic pain associated with sympathetic nerve dysfunction develops and is characterized by swelling, edema, erythema and temperature changes. The term CRPS type I, also called reflex sympathetic dystrophy, is used when pain occurs without an identifiable injury to a major nerve (e.g., ankle sprain). CRPS, type II, also called causalgia, presents with the same signs and symptoms but following an identifiable nerve injury (e.g., a pelvic fracture with a partial sciatic nerve transection). (702-703)

18. Clinical manifestations of complex regional pain syndrome include chronic, severe burning pain, hyperalgesia, bone demineralization, joint stiffness, and atrophic changes. Patients typically have localized sympathetic nervous system dysfunction, which is manifest as warm, erythematous, dry, and swollen skin early in the disease process, followed by vasoconstriction, with cool, pale, and edematous skin later in the course. Patients usually characterize the pain in these syndromes as aching, intense, and/or agonizing. The pain appears to be enhanced by mechanical stimulation, movement, and the application of heat or cold. (702, Table 43-1)

19. The diagnosis of complex regional pain syndrome is based on the appearance of the typical signs and symptoms after injury and the absence of any other underlying condition. Some practitioners have suggested that the diagnosis can be made by performing sympathetic nerve blocks in the affected extremity and evaluating the patient for relief of the pain. For the upper extremity a stellate ganglion block may be performed, while for the lower extremities lumbar sympathetic blocks are usually performed. However, there is a significant placebo response to diagnostic blocks, and the true role of sympathetic blocks in the diagnosis and management of CRPS remains in question. (703)

20. The management of CRPS requires a multimodal approach. The primary goal of managing patients diagnosed with CRPS is maintenance and restoration of function through aggressive physical therapy, which is possible only with adequate pain reduction. Sympathetic nerve blocks often aid in short-term pain reduction and hence facilitation of physical therapy. Tricyclic antidepressants and anticonvulsants usually form the first line of analgesic therapy. Spinal cord stimulation is now used more commonly and may provide a more effective long-term means to produce pain reduction, hence facilitating long-term physical therapy aimed toward functional restoration of the affected extremity. A delay in the diagnosis and treatment of complex regional pain syndrome may result in poorer outcome. (703)

21. Intravenous regional sympathetic nerve blockade has been used for the treatment of complex regional pain syndromes. Pharmacologic agents that have been used for intravenous regional sympathetic nerve blockade include guanethidine and bretylium. Guanethidine is taken up by presynaptic sympathetic nerve terminals where it is concentrated in norepinephrine neurotransmitter vesicles and replaces norepinephrine, thereby blocking norepinephrine release. Bretylium blocks norepinephrine release from nerve terminals. These agents are believed to exert their analgesic effects in sympathetically maintained states by blocking norepinephrine release from sympathetic nerve terminals. Neither agent is now commonly used: guanethidine is not available for clinical use in the United States and bretylium is associated with profound hypotension. More commonly,

intravenous regional blocks are conducted with local anesthetic alone, typically 0.5% lidocaine; careful attention must be paid to avoid toxic levels of local anesthetic. The relative effectiveness of intravenous regional blockade versus sympathetic ganglion blocks is unknown. (703)

CANCER-RELATED PAIN

22. Pain is the most common presenting symptom of undiagnosed malignancy. Cancer pain may be due to direct invasion of the malignancy or treatment. Local tumor infiltration or metastases to bone or nerves are especially painful. Patients may also experience pain as a side effect of chemotherapy, irradiation, or surgical treatment. Examples include phantom limb pain, peripheral neuropathy, and radiation fibrosis. Approximately 40% of patients with cancer experience chronic pain. The primary focus of pain reduction in patients with cancer is direct treatment of the malignancy, with successful treatment often leading to complete pain resolution. (703)

23. The mainstay of treatment of chronic pain for cancer patients is opioid therapy. Other analgesics which are commonly used are tricyclic antidepressants, anticonvulsants, and corticosteroids. Tricyclic antidepressants may have additional benefits of treating depression (common among cancer patients), potentiating the effect of opioids, facilitating nocturnal sleep, and improving mood. Anticonvulsant medications may be useful in neuropathic pain. Corticosteroids play a role in decreasing the sensation of pain, improving mood, and increasing appetite, all of which are ongoing problems in patients with chronic cancer pain. The World Health Organization's analgesic approach has been adopted worldwide to promote the aggressive treatment of cancer-related pain by tailoring analgesic use to the severity of pain. It comprises a simple three-step analgesic ladder starting with nonopioids and moving toward more potent opioid analgesics as necessary to control pain. (703, Table 43-2)

24. Intravenous, neuraxial, transdermal, and transmucosal routes of administration are alternative routes of analgesic drug delivery for the cancer patient with chronic pain in whom the oral administration of medicines is not possible. Implantable intrathecal drug delivery systems using intrathecal opioids, local anesthetics, clonidine, and other agents are now often used in managing intractable cancer pain. (703)

25. Patients with chronic pain secondary to cancer who have not had success with pain control with less invasive procedures may benefit from some neurosurgical procedures for the treatment of the pain. Neurosurgical procedures that may be useful in these cancer patients include a cordotomy or dorsal rhizotomy. A cordotomy is the open or percutaneous interruption of the spinothalamic tract. A dorsal rhizotomy is the interruption of the sensory nerve root.

26. One of the most common nerve blocks that successfully treats abdominal visceral malignancy is the neurolytic celiac plexus block. The neurolytic celiac plexus block (NCPB) may be useful to treat pain associated with cancer of the pancreas or upper abdominal viscera. One limitation of this block is the inability to treat pain from the left colon and pelvic viscera as the sensory and autonomic nervous system fibers only from the abdominal viscera are carried by the celiac plexus. NCPB has a long-lasting benefit for 70% to 90% of patients with abdominal visceral malignancies. (710)

PHARMACOLOGIC MANAGEMENT OF CHRONIC PAIN

27. Pharmacologic agents used for pain management include nonsteroidal antiinflammatory agents, antidepressants, anticonvulsants, muscle relaxants, and opioids. Opioid analgesics are the most common agents used in the management of cancer-related pain, but their long-term benefit in managing patients with noncancer pain remains unclear. The antidepressants and anticonvulsants are the most common agents used for the long-term treatment of chronic neuropathic pain.

Nonsteroidal antiinflammatory drugs and muscle relaxants are useful in the management of acute pain, but the risk/benefit ratio of long-term use is less clear. (704, Table 43-3)

28. The term simple analgesic has been traditionally reserved for acetaminophen and the nonsteroidal antiinflammatory drugs (NSAIDs). They are the most common agents used to treat mild to moderate pain. Even though poorly supported by evidence for use in chronic illnesses such as low back pain, the use of NSAIDS remains fairly common. They may be useful in conjunction with opioids for the treatment of chronic pain in patients with pain that involves an inflammatory process or in patients with bone pain such as arthritis. They also constitute the first step of the WHO analgesic ladder and are used to treat mild to moderate cancer-related pain. Enzyme selective NSAIDs (i.e., the COX-2-selective inhibitors) have a lower risk of GI bleeding as compared to nonenzyme selective drugs, even though they are comparable in their analgesic efficacy. (703)

29. Antidepressants are thought to exert their effect by normalizing sleep patterns, decreasing anxiety, and decreasing the patient's perception of the pain. Antidepressants may enhance neurotransmitters acting on descending efferent inhibitory pain pathways, thus producing analgesia that is independent of their antidepressant effects. Antidepressants commonly used for the management of chronic pain include tricyclic antidepressants and newer selective norepinephrine reuptake inhibitors (SNRIs). Examples of tricyclic antidepressants include the secondary amine agents (nortriptyline and desimipramine) and tertiary amine agents (amitriptyline and imipramine), which are more poorly tolerated. Side effects of tricyclic antidepressants include dry mouth and urinary retention, and potentially worsening of preexisting heart block. The newer SNRIs (venlafaxine, duloxetine) are effective in treatment of neuropathic pain, such as painful diabetic peripheral neuropathy. Though SNRIs have a similar analgesic efficacy as tricyclic antidepressants, they are better tolerated because of a favorable side effect profile. (704)

30. The anticonvulsant drugs gabapentin and pregabalin are effective for pain management. These drugs are commonly used as they are fairly well tolerated with mild to moderate side effects like somnolence, drowsiness, and peripheral edema. They are also commonly used to treat all types of neuropathic pain. The choice of neuropathic agent should be guided by the severity of the pain and the side effect tolerability by each patient. (704)

31. Use of long-term opioid therapy for the treatment of chronic noncancer pain remains controversial. The most common problems encountered by physicians when prescribing opioids are aberrant drug-related behavior (e.g., losing prescriptions, unauthorized escalation of drug dose) and opioid tolerance (need for increasing drug dose to produce the same effect). Overt addiction (i.e., preoccupation with use of the opioid despite negative consequences like job loss) is uncommon. (704)

32. Opioid analgesic prescribing for nonmalignant chronic pain is adapted from cancer pain management. This practice involves using a long-acting opioid for continuous analgesia while a short-acting analgesic is used to cover intermittent spikes in pain intensity, or breakthrough pain. However, the long-term use of opioids has come under increasing scrutiny for managing noncancer pain, thus adopting more stringent guidelines is wise. Most practitioners agree that opioids should be used only when other, more conservative measures have failed. Patients should receive these medications from a single prescriber and they should only be continued when they lead to less pain and improvement in function. Many practitioners have adopted routine use of random urine drug testing to help ensure that patients remain compliant with chronic opioid therapy and that they are not using other prescription or illicit drugs. (704)

33. Evidence-based guidelines for the pharmacologic management of neuropathic pain recommend a stepwise pharmacologic approach. Following initial assessment

and diagnosis, realistic goals should be discussed with the patient. Therapy is usually begun with a tricyclic antidepressant, SNRI, or anticonvulsant as the first-line drug, followed by opioids or tramadol, alone or in combination (second-line drugs). Serial follow-ups are conducted to evaluate response to therapy and alternative first- or second-line drugs are commenced based on the response. Certain antiepileptics, antidepressants, and NMDA receptor antagonists can be used as a third line of drugs for a selective group of patients who respond poorly to the previous therapy. (704, Table 43-3)

INTERVENTIONAL PAIN THERAPIES

34. The term *interventional pain therapy* encompasses a variety of treatments used for specific pain syndromes and these range from diagnostic nerve blocks to therapeutic injections of steroids and sympathetic nerve blocks. Some of the commonly performed procedures in the pain clinic include: epidural steroid injections, facet joint nerve blocks, and radiofrequency ablation. (705)

35. The injection of steroid into the epidural space is aimed at the inflammatory response that is associated with acute disk herniation. Epidural steroids are most useful for treating acute radicular pain, where a steroid injection if given within 6 weeks can accelerate the resolution of leg pain. Patients should be informed about pain at the injection site and transient worsening of any radicular pain if present on presentation. Infection, bleeding, and neural injury are all uncommon and discussions about these rare complications should be based on individual patient concerns. (705-706)

36. Epidural injection of steroids can be done using either the interlaminar or transforaminal approach. The transforaminal approach may be more effective as it allows the concentrated steroid solution to be injected directly adjacent to the spinal nerve close to the site of the inflammation, yet there is little scientific evidence to guide the choice between these two approaches. (706, Figures 43-4, 43-5)

37. One of the many causes of low back pain is pain arising from the facet joints. Facet-related pain should be suspected in patients who have persistent pain over in the lumbosacral area, and have typical patterns of referred pain with maximal tenderness directly over the facet joints. Facet joint blocks are commonly used as a diagnostic tool and involve intraarticular injections of a mixture of local anesthetic and corticosteroids. Intermediate pain relief lasting weeks to months is common and supports the diagnosis of facet-related pain. (706)

38. Radiofrequency denervation of the lumbar facet joints can provide longer duration of pain relief than intraarticular injections in some patients with facet-related pain. About 50% of patients will respond with a 50% reduction of pain lasting for up to 12 months. Radiofrequency denervation involves the delivery of energy adjacent to the sensory nerve in the facet joint. The procedure can be repeated with similar efficacy after repeat treatment. (706, Figure 43-6)

39. The use of lumbar diskography is based on the hypothesis that the intervertebral disk is the source of ongoing pain in about 30% to 40% of the patients presenting with lumbosacral pain. Provocative diskography is currently used to select patients for surgical fusion but has largely remained a controversial test because of the subjective nature of the test and the lack of convincing evidence that use of diskography improves surgical outcome. Diskography has also been used to select patients for intradiscal electrothermal therapy (IDET), a treatment that uses thermal energy to treat discogenic pain. Evidence for use of IDET is mixed; in some reports, 30% to 50% of patients showed long-term pain reduction and improvement in standing and sitting tolerance. The use of both diagnostic diskography and IDET has declined in recent years. (706)

40. Percutaneous plasma disk decompression (PDD) is a minimally invasive procedure used to treat chronic radicular pain due to a focal disk bulge identified on imaging studies, usually MRI. PDD reduces pain and improves long-term functional status in highly selected patients—those with ongoing leg pain and small disk protrusions. The procedure uses radiofrequency energy to remove a portion of nucleus pulposus, which eases the pressure of the disk and hence decompresses any pressure on the spinal nerve causing pain. A major limitation of this technique is that it is only useful for patients with herniations smaller than 3 mm, and this comprises less than 5% of patients with low back pain. (707)

41. Certain pain syndromes such as CRPS and microvascular insufficiency causing ischemic extremity pain are believed to be maintained by hyperactivity of the sympathetic nervous system and are termed sympathetically maintained pain syndromes. Blockade of the sympathetic nerve fibers produces pain relief in these disease states and these nerve blocks are hence often used to diagnose CRPS and related syndromes. There is a paucity of evidence supporting the use of repeated sympathetic blocks to provide long-term pain relief or improvement in function; however, these nerve blocks are still used to provide short-term pain relief and facilitate physical therapy. (707-708)

42. The stellate ganglion is formed by the fusion of the inferior cervical and the first thoracic sympathetic ganglia. There is significant anatomic variation in the cervical and thoracic sympathetic chain and in many individuals the superior thoracic and inferior cervical ganglia are separate structures. On the medial side of the ganglion is the lateral border of the longus colli muscle. Posteriorly are the neck of the first rib and the transverse process of the seventh cervical vertebra. Anteriorly lay the first part of the subclavian artery and the origin of the vertebral artery behind the dome of the lung. Anatomically, the sympathetic supply of the head, neck, and the arms passes through the stellate ganglion on each side. Hence a stellate ganglion block is performed to diagnose and treat sympathetically maintained pain of the head, neck, and the upper extremity. (708, Figure 43-7)

43. The most common approach to the stellate ganglion is the anterior paratracheal approach guided by surface anatomy of the C6 vertebra. When performing the block without radiographic assistance, the operator palpates the anterior tubercle of the transverse process of the C6 vertebra then retracts the overlying carotid artery and jugular vein laterally. A needle is advanced until seated on the anterior tubercle of C6, where about 10 mL of local anesthetic is injected incrementally. The local anesthetic spreads along the prevertebral fascia in the caudal direction to bathe the stellate ganglion. Another approach that has been used is approaching the ganglion at the level of C7; however, this carries a substantial risk of pneumothorax because the dome of the lung lies in close approximation to the needle injection site. When performed under radiographic assistance, the needle is placed just inferior to the uncinate process of the C6 or C7 vertebra near the junction of the transverse process and the vertebral body. (708)

44. A stellate ganglion block is used to diagnose and treat painful syndromes involving the upper extremity, most commonly CRPS. There is some evidence that it may also be useful for treating neuropathic pain arising from ischemia, herpes zoster, early postoperative neuralgia, and postradiation neuritis. Stellate ganglion block has also been used in the treatment of some disease states associated with vascular compromise, including intractable angina pectoris, Raynaud disease, frostbite, vasospasm, and occlusive or embolic phenomena. Stellate ganglion block has shown usefulness in controlling hyperhidrosis of the upper extremity. (709)

45. Successful stellate ganglion block is signaled by the appearance of Horner syndrome, a constellation of signs and symptoms which includes miosis (pupillary

constriction), ptosis (drooping of the upper eyelid), and enophthalmos (sunken eyeball). Other signs of a successful block include nasal congestion, anhidrosis (lack of sweating), and venodilation in the involved extremity. There will also be an increase in local temperature by at least a degree Celsius in the affected extremity. Thus there are several signs the clinician should look for to confirm success of a stellate ganglion block. (708)

46. Stellate ganglion block is associated with the following minor and major complications. Minor complications include a recurrent laryngeal nerve block causing hoarseness, phrenic nerve blockade leading to unilateral diaphragmatic paresis, and somatic blockade of the upper extremity (brachial plexus block) characterized by sensory and motor loss on the ipsilateral side. Major complications include intravascular injection of local anesthetic causing immediate seizures, and epidural or intrathecal injection of the local injection causing a neuraxial block. The complication of a neuraxial block can be a high epidural or spinal with loss of consciousness and apnea, for which immediate resuscitation would be required. (709)

47. The celiac plexus is comprised of a diffuse network of nerve fibers that lie over the anterior surface of the aorta at the T12-L1 vertebral level surrounding the origin of the celiac artery from the aorta. Presynaptic nerve fibers travel from the sympathetic chain toward the ganglion over the anterolateral aspect of the inferior thoracic vertebra as the greater, lesser, and least splanchnic nerves. Postsynaptic fibers innervate all the abdominal viscera, including the gastrointestinal tract between the gastroesophageal junction and the splenic flexure of the colon. Sympathetic fibers to the descending and sigmoid colon, the rectum, and the pelvis do *not* travel through the celiac plexus. (710, Figure 43-8)

48. A neurolytic celiac plexus block (NCPB) can be performed using either a transcrural or a retrocrural approach. The transcrural technique consists of placing the neurolytic agent directly on the celiac ganglion anterolateral to the aorta. This approach reduces the chance of nerve root involvement. The retrocrural approach involves positioning the needles posterior to the diaphragmatic crura in close apposition to the T12 vertebral body. The percutaneous posterior approach is performed using surface anatomic landmarks to position needles in the vicinity of the celiac plexus. NCPB is then achieved with the injection of 20 to 30 mL of either alcohol (50% to 100%) or phenol (10% to 12%). The position of the needle can be verified by computed tomography (CT), fluoroscopy, or ultrasound (using an endoscopic ultrasound-guided transgastric approach). No single technique has proven superior to the other. (710)

49. A neurolytic celiac plexus block is used to control pain arising from intraabdominal structures, including the pancreas, liver, gallbladder, omentum, mesentery, and the gastrointestinal tract from the stomach to the transverse colon. Most often the source of the pain is malignancy, particularly pancreatic cancer. The pain relief for these patients can be dramatic, and has long-lasting benefit for 70% to 90% of patients. The use of the NCPB for nonmalignant pain, such as those with chronic pancreatitis, is debatable. (711)

50. During NCPB, a transcrural approach places the neurolytic agent directly on the celiac ganglion, anterolateral to the aorta, while a retrocrural approach places the solution posterior to the diaphragmatic crura in close apposition to the T12 vertebral body. A splanchnic nerve block is a minor modification to the classic retrocrural celiac plexus block; the only difference being that for a splanchnic nerve block, the needles are placed in the midportion of T12 rather than in the cephalad portion of L1 as is done for a celiac plexus block. (710)

51. The normal and expected physiologic effects of producing a sympathetic block to the abdominal viscera are diarrhea from unopposed parasympathetic stimulation of the bowel and orthostatic hypotension from splanchnic vasodilation.

There are other potential complications of a neurolytic celiac plexus block. Intravascular injection of 30 mL of 100% ethanol results in a blood ethanol level high enough to produce intoxication. Intravascular injection of 30 mL of 10% phenol will cause clinical manifestations similar to local anesthetic toxicity, including seizures, cardiac arrhythmias, and even cardiovascular collapse. Perhaps the most feared complication of NCPB is paraplegia. Segmental spread at the level of T12 or L1 may cause spasm or even necrosis of the artery of Adamkiewicz, which compromises the blood supply of the anterior two thirds of the spinal cord in the low thoracic region. Best available estimates of the incidence of paraplegia place the risk at less than 1:1000. (711)

52. The lumbar sympathetic chain consists of four to five paired ganglia that lie over the anterolateral surfaces of the L2-L4 vertebra. Their cell bodies lie in the anterolateral region of the spinal cord from T11 to L2, where the preganglionic fibers exit the spinal canal with the corresponding spinal root, join the sympathetic chain, and then synapse with the appropriate ganglion. Postganglionic fibers exit the ganglion to form a diffuse network of perivascular fibers surrounding the vessels in the lower extremities; postganglionic fibers also travel within the nerves of the lumbosacral plexus. (711, Figure 43-9)

53. Lumbar plexus block is used in the diagnosis and treatment of sympathetically maintained pain of the lower extremities (e.g., CRPS types I and II). It is also used clinically to treat ischemic pain from small vessel occlusion in the lower extremities. There is some evidence supporting the usefulness of lumbar sympathetic block for treating painful neuropathic states of the lower extremities, including early postherpetic neuralgia and acute herpes zoster. Complications are uncommon with proper use of a lumbar sympathetic block. Toxic levels of local anesthetic can result from an inadvertent intravascular injection while performing a lumbar sympathetic block, and if large volumes of concentrated local anesthetic are used, the local anesthetic toxicity could be catastrophic. Some other complications which could be encountered include hematuria caused by direct needle placement through the adjacent kidney, spinal nerve injury, and epidural or intrathecal injection of local anesthetic. All are uncommon complications when the procedure is performed under radiographic guidance. Following neurolysis of the lumbar sympathetic chain, postsympathectomy pain in the distribution of the L1 spinal nerve (anterior thigh) occurs in about 10% of patients. (712)

54. Spinal cord stimulation is based on the hypothesis that a nonnoxious stimulus interferes with the perception of pain. This input of a nonpainful stimulus directly activates the ascending fibers within the dorsal columns of the spinal cord that transmit nonpainful stimuli and this principle is used to treat chronic back pain. A typical spinal cord stimulator system is comprised of a pacemaker-like implanted pulse generator connected to an electrode positioned over the dorsal columns of the spinal cord in the posterior epidural space. (712)

55. Current evidence supports the use of spinal cord stimulation (SCS) to treat pain, in particular for patients presenting with chronic lumbosacral pain or radicular pain after prior lumbar surgery. The evidence for the use of SCS for lumbosacral pain has been inconclusive, but with the advent of new dual lead systems and electrode arrays providing a broader area of stimulation, SCS may become more useful for treating pain in these patients. Management of chronic radicular pain using SCS is the best studied indication with the highest overall rate of successful long-term pain reduction. SCS has proven to be less expensive and more successful than repeat surgery in the management of persistent pain after prior lumbar surgery. (712)

56. The most common complication associated with SCS is lead displacement with the need for reoperation to reposition the lead(s). In modern case series, less than 5% of patients experienced wound infection or dehiscence. (712)

Chapter

41 CARDIOPULMONARY RESUSCITATION

David Shimabukuro

1. What is cardiopulmonary resuscitation (CPR)? What is basic life support (BLS)? What is advanced cardiac life support (ACLS)?
2. Who developed the Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care?

BASIC LIFE SUPPORT (BLS)

3. What are the four major components of BLS? What major change was recommended in 2010 regarding the sequence of attention to airway, breathing, and circulation during BLS?

Closed-Chest (External) Cardiac Compressions

4. Where should the rescuer's hands be placed on the adult patient to maximize blood flow when performing closed-chest cardiac compressions? What are some risks to the patient when the rescuer's hands are placed incorrectly?
5. How should the rescuer be positioned relative to the patient when performing closed-chest cardiac compressions? By how much is the sternum of an adult patient depressed during each compression?
6. What is the minimum rate (number of compressions per minute) for adult BLS? What is the ratio of cardiac compressions to ventilation during one-rescuer CPR? What is the ratio of cardiac compressions to ventilation during two-rescuer CPR?
7. What are the two proposed mechanisms for blood flow during closed-chest cardiac compressions? Which of these is thought to be the most important?
8. How can the effectiveness of closed-chest cardiac compressions be verified? What should the goal be for end-tidal CO_2 if an end-tidal CO_2 monitor is available?

Provision of a Patent Upper Airway

9. What is the head-tilt/jaw thrust maneuver? What is its goal? How can it be modified in a patient with a possible neck injury?

Specialized Equipment to Maintain the Airway

10. What are the advantages of a cuffed endotracheal tube for ventilation of the lungs in a patient receiving CPR?

External Defibrillation

11. What is the definitive treatment for pulseless ventricular tachycardia (VT) and ventricular fibrillation (VF)? What is the most important determinant of return of spontaneous circulation in a patient with VT/VF when performing external defibrillation?
12. How many joules of electricity should be delivered during an initial attempt at external defibrillation? How many joules should be delivered in subsequent defibrillation attempts, provided they are necessary?
13. Where on the chest is the appropriate placement of paddles/pads for external defibrillation?
14. What is the risk of external defibrillation in the patient with a cardiac pacemaker?

ADVANCED CARDIAC LIFE SUPPORT

15. What are the three advanced cardiac life support (ACLS) algorithms most likely to be used in the operating room?

Ventricular Fibrillation/Pulseless Ventricular Tachycardia

16. What are some causes of VF/pulseless VT?
17. What is the appropriate treatment for VF/ pulseless VT?
18. What is torsades de pointes? What are some causes of torsades de pointes?
19. What is the treatment for torsades de pointes?

Pulseless Electrical Activity

20. What are some causes of pulseless electrical activity (PEA)?
21. What is PEA? How should it be treated?

CARDIAC ASYSTOLE

22. What are some causes of cardiac asystole? How should it be treated?

Bradycardia

23. Bradycardia is defined as what heart rate?
24. What is the appropriate treatment for bradycardia?

Narrow-Complex Tachycardias

25. What is the appropriate treatment for narrow-complex tachycardias?
26. What are some side effects of the administration of adenosine?
27. What is the risk of cardioversion when it is performed without synchronization?

Wide-Complex Tachycardias

28. What is the appropriate treatment for wide-complex tachycardias?
29. When should adenosine be administered? How should β receptor blockers and calcium channel blockers be administered?
30. What is the risk of cardioversion when it is performed without synchronization?

Precordial Thump

31. What is a precordial thump? When is a precordial thump recommended in adult patients?

DRUG THERAPY

32. What is the goal of initial drug therapy during CPR? What are the mainstays of treatment for the patient in cardiac arrest?

33. What actions of epinephrine are thought to be responsible for its beneficial effects during cardiac arrest?
34. What actions of vasopressin are thought to be responsible for its beneficial effects during cardiac arrest?
35. When is amiodarone administered during cardiac arrest?
36. What is the advantage of the delivery of drugs by a centrally placed intravenous catheter during CPR? How long should the rescuers wait for drug administered via a peripheral vein to reach the central circulation?
37. What are two alternatives for drug delivery when vascular access is not available?

RESUSCITATION OF INFANTS AND CHILDREN

38. Where should the pulse be palpated in infants up to 1 year of age? Where should it be palpated in children?
39. How should closed-chest cardiac compressions be performed in infants?
40. How should closed-chest cardiac compressions be performed in children?
41. What energy setting, in joules, should be applied for optimal success for a return of spontaneous circulation when using an external defibrillator? If the initial attempt at defibrillation is unsuccessful, what energy setting should be used for the subsequent attempts?

POSTRESUSCITATION CARE

42. How should a cardiac arrest patient be managed after the return of spontaneous circulation?
43. What glucose and arterial carbon dioxide levels should be maintained in a patient after resuscitation from cardiac arrest?

SPECIAL PERIOPERATIVE CONSIDERATIONS

44. What are some of the more common drugs used in the operating room that can precipitate an anaphylactic reaction? In addition to removing or stopping the inciting agent, what is the primary treatment for anaphylaxis?
45. What is the treatment for an intraoperative venous gas embolism?
46. What is the primary treatment for local anesthetic toxicity? How long should the resuscitation continue in the event of complete cardiovascular collapse?
47. How should one manage cardiovascular collapse in a patient who has received neuraxial anesthesia?

ANSWERS*

1. CPR is the institution of artificial circulation and ventilation until spontaneous cardiopulmonary function returns, extracorporeal life support is initiated, or resuscitation efforts are discontinued. It consists of BLS and ACLS. BLS is the rapid evaluation of an unresponsive individual with the activation of the emergency medical system and the acquisition of an automated external defibrillator (AED) or a regular defibrillator. Artificial circulation is achieved through closed-chest cardiac compressions and ventilation is performed via mouth-to-mouth, mask-to-mouth, or bag-valve mask. Any individual (including nonhealth care personnel) who has had the appropriate training and certification can perform BLS. ACLS, based on BLS, can only be performed by health care workers and adds advanced airway management, cardiovascular drugs, cardiac rhythm analysis, and postresuscitation management. ACLS also includes recognition, diagnosis, and initial treatment of acute myocardial infarction and acute stroke. (715)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

2. The International Liaison Committee on Resuscitation publishes the guidelines based on evidence from the medical and basic science literature. This multinational committee, primarily represented by the American Heart Association and European Resuscitation Council, meets every few years to evaluate and/or revise the guidelines. (715)

BASIC LIFE SUPPORT (BLS)

3. The four major components of BLS are the recognition of an unresponsive patient that is not breathing, activation of the emergency medical system and acquisition of an AED, closed-chest cardiac compressions with ventilations, and actual defibrillation. In 2010 a major change occurred in the recommendation for the sequence of attention by the rescuer in airway, breathing, and circulation. The old mnemonic of ABCD (airway, breathing, circulation, and defibrillation) was changed to CAB (compression, airway, breathing). In the hospital setting, ventilation is expected in cardiopulmonary resuscitative efforts, although large out-of-hospital studies have shown no difference in outcome between patients who had chest compression alone CPR versus those who had chest compression and ventilation CPR. (716, Figure 44-1)

Closed-Chest (External) Cardiac Compressions

4. For closed-chest cardiac compressions in the adult patient, the rescuer's hands should be placed in the middle of the patient's sternum. This provides for maximum compression to the underlying cardiac ventricles and optimizes blood flow produced by the compressions. If the rescuer's hands are placed incorrectly during closed-chest cardiac compression, not only is blood flow not optimized, but the patient may suffer from internal injury as well. For example, pressure over the xiphoid process or rib cage can result in damage to abdominal organs, especially the liver, or cause rib fractures. Rib fractures can result in damage to the heart and lungs. (716, Figure 44-2)

5. During closed-chest cardiac compressions, the rescuer's upper body should be directly over the patient's chest. The shoulders are positioned directly over the hands and the elbows are kept straight. This position enables the rescuer to use the weight of his or her upper body for compression and may prevent fatigue. The sternum of an adult patient should be depressed at least 2 inches (5 cm) during closed-chest cardiac compression. (716, Figure 44-2; 725, Table 44-3)

6. The rate for closed-chest compressions for an adult is at least 100 compressions per minute. The rescuer needs to push hard and push fast, but allow for full chest recoil. The ratio of cardiac compressions to ventilation during CPR is 30:2, regardless of the number of rescuers. (716, Figure 44-1; 725, Table 44-3)

7. There are two proposed mechanisms for blood flow during closed-chest cardiac compression: (1) the cardiac pump mechanism and (2) the thoracic pump mechanism. The cardiac pump mechanism theorizes that the direct compression of the cardiac ventricles between the sternum and the spine results in an increase in intracardiac pressures, closure of the tricuspid and mitral valves, and the forward flow of blood into the pulmonary arteries and aorta. During relaxation, the aortic and pulmonary valves close to ensure unidirectional movement of blood. The second proposed thoracic pump mechanism for forward blood flow revolves around the alternating increase in intrathoracic pressure that accompanies closed-chest compressions and decrease in intrathoracic pressure during relaxation. During compressions, the increase in intrathoracic pressure ejects blood out of the chest; during relaxation, the drop in intrathoracic pressure promotes venous return back into the thoracic cavity. Evidence for the thoracic pump mechanism can be seen with forceful coughing, which can sustain consciousness for as long as 1.5 minutes. The dominant mechanism for forward blood flow during closed-chest

compression is unclear, but most believe it to be the cardiac pump mechanism. However, heart size, the anterior-to-posterior chest distance, and thoracic compliance are believed to influence which of these mechanisms eventually dominates.

8. Verification of the effectiveness of closed-chest cardiac compressions can be estimated by the palpation of peripheral pulses and, if an arterial line is present, a diastolic blood pressure of at least 20 mm Hg. If an endotracheal tube is in place, a capnogram should be used to guide the effectiveness of closed-chest cardiac compression. When ventilation and CO_2 production are constant, alterations in the end-tidal CO_2 are reflective of alterations in pulmonary blood flow and cardiac output. When end-tidal CO_2 monitors are available during closed-chest cardiac compression, an end-tidal CO_2 of 20 mm Hg or more suggests effective CPR. Conversely, an end-tidal CO_2 of 10 mm Hg or less is suggestive of poor CPR or a grave prognosis. (718-720, Figure 44-5)

Provision of a Patent Upper Airway

9. Upper airway obstruction in an unconscious patient is due to the tongue falling against the posterior pharynx. The head-tilt/jaw thrust maneuver involves extension of the head and displacement of the mandible to an anterior position thereby moving the tongue forward away from the posterior pharynx. For many individuals, this is adequate to provide a patent airway. For patients with suspected neck trauma, the rescuer needs to modify the head-tilt/jaw thrust maneuver to avoid exacerbating a potential spinal cord injury. The head-tilt should be excluded from the maneuver and only the jaw thrust performed in these patients. (717, Figure 44-3)

Specialized Equipment to Maintain the Airway

10. There are several advantages of a cuffed endotracheal tube for ventilation of the lungs in a patient receiving CPR. First, it allows for proper ventilation and end-tidal carbon dioxide ($ETco_2$) monitoring. Second, compressions and ventilations are no longer synchronous. Compressions are performed non-stop, while breaths are given once every 6 to 8 seconds. This allows for more time with an adequate perfusion pressure. Third, it also allows for the addition of supplemental oxygen in a reliable manner. Finally, a cuffed endotracheal tube provides the lungs with some protection against the aspiration of gastric contents. (718-720, Figure 44-5)

External Defibrillation

11. The definitive treatment for pulseless VT and VF is external defibrillation. The most important determinant of the success of external defibrillation is the duration of the time lapse between cardiopulmonary arrest and external defibrillation. For this reason, the current recommendation is to apply external defibrillation as soon as possible in these patients. (718-719, Figures 44-1 and 44-5)

12. The initial, and subsequent, attempts at external defibrillation require a shock of 120 to 200 J (biphasic) for adult patients. If the amount of energy needed to terminate VF is not known for the specific device, then 200 J (biphasic) should be used. (718-719, Figure 44-5)

13. The paddles/pads should be applied to the chest with firm pressure ensuring good skin contact in a position that will reduce impedence or resistance and maximize the flow of electrical current through the myocardium. The standard placement is with one paddle/pad below the right clavicle and to the right of the sternum; the second paddle/pad is applied at the level of the apex of the heart in the midaxillary line. Poor skin contact can lead to an increase in the resistance or impedence to current flow during shock delivery or arcing of the current. (718, Figure 44-4)

14. The risk of external defibrillation in the patient with a cardiac pacemaker is the malfunction of the pacemaker. It is recommended that the paddles/pads be placed 1 to 2 cm away from the pacemaker generator. (718)

ADVANCED CARDIAC LIFE SUPPORT

15. Every anesthesiologist should be familiar with pulseless arrest, bradycardia, and tachycardia algorithms.

Ventricular Fibrillation/Pulseless Ventricular Tachycardia

16. Possible causes of VF/pulseless VT include hypovolemia, hypoxia, hydrogen ion (acidosis), hypokalemia/hyperkalemia, hypothermia, tension pneumothorax, cardiac tamponade, toxins, thrombosis (pulmonary), and thrombosis (coronary). (719, Figure 44-5, 723, Table 44-2)

17. Patients in VF/pulseless VT should receive immediate defibrillation of 120 to 200 J with a biphasic defibrillator. Good quality CPR should also be instituted and maintained throughout the resuscitation. Vasoactive medications, such as epinephrine and vasopressin, are to be given at the appropriate times. Amiodarone, an antiarrhythmic, should be considered as well. (718-722, Figure 44-5 and Table 44-1)

18. Torsades de pointes is an atypical form of VT with a characteristic twisting of the QRS around the baseline such that it appears as a sine wave. Causes of torsades de pointes include drugs that prolong the QT interval, such as quinidine, procainamide, disopyramide, phenothiazines, and tricyclic antidepressants; other causes include bradycardia, hypokalemia, hypomagnesemia, and acute myocardial ischemia or infarction.

19. The treatment for torsades de pointes may include overdrive pacing of the cardiac atria or ventricles and/or treatment with magnesium sulfate for stable patients. Patients whose condition is unstable should undergo defibrillation.

Pulseless Electrical Activity

20. Causes of PEA are identical to those of VF or pulseless VT. (719, Figure 44-5 and 723, Table 44-2)

21. PEA is a term used to describe the presence of a normally perfusing cardiac rhythm on the electrocardiogram with little or no cardiac output. In patients with PEA, there is an absence of peripheral pulses or systemic blood pressure. Cardiac rhythms that may be present include organized electrical activity, idioventricular rhythms, and/or ventricular escape rhythms. PEA should be treated with closed-chest compressions and the rapid administration of epinephrine and/or vasopressin. There should also be a search for, and correction of, possible causes. (719-723, Figure 44-5 and Table 44-1)

CARDIAC ASYSTOLE

22. Causes of cardiac asystole are identical to those of PEA, VF, or pulseless VT. It is treated identically to PEA. (719, Figure 44-5 and 723, Table 44-2)

Bradycardia

23. Typically, bradycardia is defined as a heart rate of less than 60 beats/min. (720, Figure 44-6)

24. Treatment for bradycardia depends on symptoms and underlying rhythm. Asymptomatic patients can be monitored and observed. Symptomatic patients or those with a high degree block need more definitive pharmacologic therapy

(atropine, dopamine infusion, epinephrine infusion) or cardiac pacing. (720, Figure 44-6, 722, Table 44-1, 723)

Narrow-Complex Tachycardias

25. The factor that determines the appropriate method of treatment for narrow-complex tachycardias is the amount of hemodynamic compromise that occurs as a result of the cardiac dysrhythmia. Patients who are hemodynamically unstable should undergo immediate synchronized cardioversion. The amount of energy used is dependent upon the regularity of the QRS complex and likelihood of a type of dysrhythmia. The treatment of patients with narrow-complex tachycardias whose condition is stable includes vagal maneuvers, adenosine, β-blockers, calcium channel blockers, and amiodarone. (721, Figure 44-7, 722, Table 44-1, 723)

26. Side effects of the administration of adenosine include flushing, dyspnea, chest pain, and bronchospasm.

27. The risk of cardioversion that is not synchronized is VF. VF results if the cardioversion shock occurs on the relative refractory period of the cardiac cycle. (723)

Wide-Complex Tachycardias

28. The appropriate treatment for wide-complex tachycardias is determined by the hemodynamic stability of the patient. Pulseless patients should receive immediate defibrillation of 120 to 200 J with a biphasic defibrillator. Hemodynamically unstable patients with evidence of acute myocardial ischemia or infarction, who have acute pulmonary edema, or who have other evidence of end-organ hypoperfusion should undergo immediate synchronized or unsynchronized cardioversion with a shock of 100 to 200 J (biphasic) depending on the regularity of the QRS complex and the likelihood of the type of dysrhythmia. Sedation will likely be needed in awake patients. Hemodynamically stable patients can undergo drug treatment. Drug therapy includes amiodarone, sotalol, or procainamide. A cardiologist should be consulted before starting any of these drug therapies in a stable patient. (721, Figure 44-7, 722, Table 44-1, 723)

29. Adenosine should only be administered in a wide-complex tachycardia when the rate is regular and the QRS complex is monomorphic in nature. Adenosine has no effect on monomorphic VT. β receptor blockers and calcium channel blockers should be administered very cautiously and only if it is clear that the tachyarrhythmia is supraventricular in origin. (721, Figure 44-7, 722, Table 44-1, 723)

30. In a wide-complex tachycardia, the main risk of unsynchronized cardioversion is a change in rhythm to VF. However, with rapid ventricular rates, synchronization may not be possible and the defibrillator will fail to discharge.

Precordial Thump

31. A precordial thump is the delivery of a single, forceful blow by the rescuer with a closed fist to the middle portion of the patient's sternum. A precordial thump is recommended in adult patients for the initial treatment of VF or VT when a defibrillator is not immediately available. Immediate external defibrillation should not be delayed for a precordial thump. A precordial thump is not recommended in pediatric patients.

DRUG THERAPY

32. The goal of initial drug therapy during CPR is the increasing of coronary and cerebral perfusion pressures. The mainstay for treatment of the patient in cardiopulmonary arrest is the administration of oxygen and epinephrine. (718-723, Figure 44-5, Table 44-1)

33. Epinephrine is a nonspecific α receptor and β receptor agonist. During a resuscitation, its action on α_1 receptors is probably the most important. As mediated through the α receptor, there is an increase in cerebral and coronary perfusion pressure, intense arterial vasoconstriction in other vascular beds, and a selective redistribution of cardiac output. There is some evidence that epinephrine administered early in the resuscitative effort in a patient with cardiac arrest can possibly improve outcome. (723)

34. Vasopressin is a potent peripheral and mesenteric vasoconstrictor, yet a potent pulmonary artery and cerebral artery vasodilator. Its effects are mediated via the vasopressin receptor. Blood is redirected from the peripheral to the central circulation, thus, increasing blood to the brain and heart. (723-724)

35. Amiodarone, a class III antiarrhythmic, is used in the treatment of VF and VT (with and without a pulse). An initial dose of 300 mg IV push can be followed by a subsequent single dose of 150 mg IV push, if there has been no return of spontaneous circulation and resuscitation continues. In patients with stable VT with a pulse, 150 mg IV over 10 minutes can be administered in an effort to terminate the VT with conversion into sinus rhythm. (724)

36. The advantage of the administration of drugs by a centrally placed catheter during CPR is the rapid delivery of drugs to the heart. When a peripheral intravenous site is used for the administration of drugs during cardiopulmonary arrest, a period of 1 to 2 minutes should be allowed for drugs to reach the central circulation. In addition, drug administration should always be followed by at least 20 mL of normal saline. CPR should not be interrupted for placement of central venous access unless peripheral access and intraosseous access cannot be obtained. (720)

37. Two alternatives for drug delivery when vascular access is not available include an endotracheal tube or the placement of an intraosseous line. Drugs that can be absorbed across the alveolar epithelium include epinephrine and vasopressin. The intraosseous line should be treated as any other peripherally or centrally inserted intravenous line. (720)

RESUSCITATION OF INFANTS AND CHILDREN

38. In infants up to 1 year of age, the best location to check for a pulse is the brachial artery in the mid-upper arm. In children older than 1 year of age, the carotid artery is the preferred location for pulse palpation. (725, Table 44-3)

39. The heart in infants and children is positioned below the lower sternum, as in adults. Hand placement during closed-chest cardiac compressions in infants is with the rescuer's one hand to support the back while compressions are performed with two fingers of the other hand. Closed-chest cardiac compression in the infant should be performed at a rate of at least 100 per minute. The sternum of the infant patient during closed-chest cardiac compressions should be depressed by at least one third of the anterior-posterior diameter or 1.5 inches (4 cm). (724-725, Table 44-3)

40. Closed-chest cardiac compressions in children can be accomplished with the heel of one hand directly over the midsternum. The recommended rate of closed-chest cardiac compressions in children is at least 100 per minute, identical to infants and adults, and depression of the sternum should also be one third to one half the anterior-posterior diameter or 1.5 to 2 inches (4 to 5 cm). (724-725, Table 44-3)

41. The energy setting that should be used for the optimal success of external defibrillation of children is directly related to their body weight. The recommended initial energy setting is 2 to 4 J/kg. If the initial attempt at defibrillation is unsuccessful, the subsequent attempt should be made with at least 4 J/kg, but no more than 10 J/kg. (724-725)

POSTRESUSCITATION CARE

42. The management of the cardiac arrest patient after the return of spontaneous circulation should follow the algorithm for postresuscitation life support. Postresuscitation management should include close monitoring, supplemental oxygen to maintain an adequate oxygen saturation, and vasopressor drug therapy as needed to maintain an adequate perfusion pressure. Mild hypothermia should be immediately started and continued for the first 12 to 48 hours in comatose patients after resuscitation from cardiopulmonary arrest. (725-727, Figure 44-8)

43. In the postresuscitation phase, hypoglycemia and hyperglycemia have been shown to be deleterious for optimal neurologic outcome. Both hypoglycemia and hyperglycemia should be avoided. There is no evidence correlating specific values of the arterial partial pressure of carbon dioxide ($Paco_2$) to neurologic outcome. Hyperventilation is not recommended and may be harmful due to its effects on cerebral blood flow. The goal is normocapnia. (727)

SPECIAL PERIOPERATIVE CONSIDERATIONS

44. Common medications used in the operating room and associated with anaphylaxis are antibiotics and muscle relaxants. Intravenous contrast agents and latex may also be associated with intraoperative anaphylactic reactions. The main pharmacologic treatment for an anaphylactic reaction is epinephrine. (727, Table 44-4)

45. The treatment for intraoperative gas embolism is to stop insufflation, if it is being used, occlude open veins, and/or flood the field with saline. The patient should also be placed in a Trendelenburg position with the left side down. In case of cardiac arrest, CPR and ACLS need to be performed. (727)

46. The primary treatment for local anesthetic toxicity is the administration of intralipid. In the event of complete cardiac collapse, resuscitation should be continued for at least 60 minutes. (727-728, Table 44-5)

47. Cardiac arrest from neuraxial anesthesia is a rare event. Should it occur, it should be managed with CPR and ACLS. (728)

Chapter

42 AWARENESS UNDER ANESTHESIA

Daniel Cole

INCIDENCE

1. What is the difference between explicit and implicit memory?
2. Can the incidence of intraoperative awareness be reliably determined in the recovery room? By self-reporting?
3. What are the components of the "structured interview" as used to evaluate the occurrence of intraoperative awareness?
4. When studied prospectively, and when using a structured interview, what is the approximate incidence of intraoperative awareness?

ETIOLOGY AND RISK FACTORS FOR INTRAOPERATIVE AWARENESS

5. What are the three major causes of intraoperative awareness?
6. What are some risk factors for intraoperative awareness?
7. What procedures are associated with an increased risk of intraoperative awareness?

PSYCHOLOGICAL SEQUELAE

8. If a patient has an episode of intraoperative awareness, what is the approximate risk of late psychological sequelae?
9. What are the potential psychological sequelae of intraoperative awareness?

PREVENTION OF AWARENESS

10. What are some conventional monitors used to assess anesthetic depth?
11. What are some limitations of brain function monitors for assessing anesthetic depth and the risk for intraoperative awareness?
12. What measures can be taken to help prevent intraoperative awareness?
13. What are the elements that the Joint Commission recommends to prevent and manage intraoperative awareness?

BRAIN FUNCTION MONITORING

14. What does the best available data on brain function monitors suggest regarding the efficacy of these monitors to prevent intraoperative awareness?

THE ASA'S PRACTICE ADVISORY ON INTRAOPERATIVE AWARENESS AND BRAIN FUNCTION MONITORS

15. According to the Practice Advisory from the American Society of Anesthesiologists (ASA) on Intraoperative Awareness and Brain Function Monitoring, what should the preoperative evaluation include to minimize the risk of intraoperative awareness?
16. According to the Practice Advisory from the ASA on Intraoperative Awareness and Brain Function Monitoring, what should the preinduction phase include to minimize the risk of intraoperative awareness?

17. According to the Practice Advisory from the ASA on Intraoperative Awareness and Brain Function Monitoring, what should intraoperative monitoring include to minimize the risk of intraoperative awareness?
18. According to the Practice Advisory from the ASA on Intraoperative Awareness and Brain Function Monitoring, what should intraoperative and postoperative management include to minimize the risk of intraoperative awareness and associated sequelae?

MEDICOLEGAL SEQUELAE OF AWARENESS

19. Why is there a large disparity between the incidence of intraoperative awareness and associated malpractice claims?
20. What are the factors which influence a patient's decision to initiate a malpractice claim?

DATA FROM THE ASA CLOSED CLAIMS PROJECT

21. What is the percentage of claims for intraoperative awareness in the Closed Claims database?
22. What are the factors associated with a malpractice claim in the Closed Claims database?
23. What are the causes of intraoperative awareness in the Closed Claims database?

ANSWERS*

INCIDENCE

1. Explicit memory, or conscious memory, refers to the recollection of previous experiences and is equivalent to remembering (intraoperative awareness). Implicit memory, or unconscious memory, is the ability of a patient to respond to commands, yet lack conscious recall of intraoperative events. (737)
2. The incidence of intraoperative awareness is best estimated by formally interviewing patients postoperatively, well after discharge from the postanesthesia recovery room. Patients will not reliably, or voluntarily, report awareness if they were not disturbed by it, or if embarrassed to do so. A structured interview is recommended to evaluate the incidence of awareness. (738)
3. The structured interview consists of the following components: (738)
   - What was the last thing you remember before you went to sleep?
   - What is the first thing you remember after your operation?
   - Can you remember anything in between?
   - Can you remember if you had any dreams during your procedure?
   - What was the worst thing about your procedure?
4. The best estimate for the incidence of intraoperative awareness is 1 to 2 occurences/1000 patients undergoing a general anesthetic. (738)

EITOLOGY AND RISK FACTORS FOR INTRAOPERATIVE AWARENESS

5. The three major causes of intraoperative awareness include light anesthesia, increased patient requirements for anesthesia, and anesthetic delivery problems. (738)
6. Risk factors for intraoperative awareness include hemodynamic intolerance of anesthetic drugs; patients that are hypovolemic; patients with limited cardiovascular reserve; ASA Physical Statue 3–5; emergency surgery; administration of small doses of volatile anesthetics; a nitrous oxide or intravenous-based anesthetic; chronic use of alcohol, opioids, amphetamines, or cocaine; genetic resistance to anesthetics; and equipment problems. (738)

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

7. Cesarean delivery and open heart procedures are associated with an increased risk of intraoperative awareness. (738)

PSYCHOLOGICAL SEQUELAE

8. Approximately one third of patients who have an episode of intraoperative awareness have late psychological sequelae. (739)
9. Potential psychological sequelae of intraoperative awareness include flashbacks, anxiety/nervousness, loneliness, nightmares, and fear/panic attacks that vary from bothersome to distressing. Some patients develop severe, persistent symptoms (posttraumatic stress disorder) that profoundly interfere with interpersonal relationships and daily activities. (739)

PREVENTION OF AWARENESS

10. Conventional monitors of anesthetic depth include patient movement, tachycardia, hypertension, tearing, perspiration, and clinical instinct. One could also include anesthetic gas analyzers, which assess the dose of volatile anesthetic delivered to the patient. (739)
11. Limitations of brain function monitors include: (1) there is not a unitary mechanism of general anesthesia, and thus various anesthetics are likely to produce unique electrical activity at a given anesthetic depth. Consequently, a unique algorithm to each specific anesthetic regimen would likely be required for optimal correlation between electrical signals in the brain and anesthetic depth; (2) general anesthesia occurs on a continuum without a quantitative dimension, and there is considerable interpatient pharmacodynamic variability to a specific anesthetic. Attempting to translate a conscious or unconscious state into a quantitative number can at best be limited to the art of probability with an expectation of false positive and false negative data; and (3) there is less than an optimal likelihood of cortical electric activity having reliable sensitivity and specificity to a biochemical event which occurs at a distant subcortical structure. (739, 740, Figure 46-1, Figure 46-2)
12. Suggestions for the prevention of intraoperative awareness include premedication with an amnesic drug such as a benzodiazepine, giving adequate doses of drugs to induce anesthesia, avoiding muscle paralysis unless necessary, and administering a volatile anesthetic at a dose of 0.7 MAC or more with monitoring of end-tidal levels to ensure delivery of adequate levels of a volatile anesthetic. (740)
13. The Joint Commission's recommendations to prevent and manage intraoperative awareness include development and implementation of an anesthesia awareness policy, staff education, informed consent for high-risk patients, timely maintenance of anesthesia equipment, postoperative follow-up of all patients who have undergone general anesthesia, and postoperative counseling for patients with awareness. (740)

BRAIN FUNCTION MONITORING

14. The results of trials which evaluated the effect of brain function monitoring on the incidence of intraoperative awareness are mixed. The best evidence is derived from four sources: a randomized controlled trial in high-risk patients for which the incidence of awareness was reduced by 82% in patients monitored with a brain function monitor; a nonrandomized cohort comparison with historical control subjects for which the incidence of awareness was reduced by 77% in patients monitored with a brain function monitor; a prospective nonrandomized study for which there was no reported effect of a brain function monitor on the incidence of awareness; and a randomized trial that compared the bispectral index (BIS) to end-tidal gas monitoring and reported no difference in the incidence of definite awareness between the two groups. (740, 741)

THE ASA'S PRACTICE ADVISORY ON INTRAOPERATIVE AWARENESS AND BRAIN FUNCTION MONITORS

15. According to the ASA's Practice Advisory on Intraoperative Awareness and Brain Function Monitoring, the preoperative evaluation for preventing intraoperative awareness should include the identification of potential risk factors for intraoperative awareness, an interview of the patient and review of past medical records, and obtaining informed consent for those patients at high risk for intraoperative awareness. (741, Table 46-2)

16. According to the ASA's Practice Advisory on Intraoperative Awareness and Brain Function Monitoring, the preinduction phase of anesthesia should include the use of a checklist for machine/equipment function, verification of function of intravenous access and infusion equipment, and consideration of a preoperative benzodiazepine for the patient. (741, Table 46-2)

17. According to the ASA's Practice Advisory on Intraoperative Awareness and Brain Function Monitoring, intraoperative monitoring should include multiple modalities to monitor the depth of anesthesia (clinical, conventional monitors, and brain function monitoring on a case-by-case basis). (741, Table 46-2)

18. According to the ASA's Practice Advisory on Intraoperative Awareness and Brain Function Monitoring, intraoperative and postoperative management should include consideration of a benzodiazepine if the patient unexpectedly becomes conscious, a postoperative visit, consideration of a structured interview to determine the patient's anesthetic experience, an occurrence report to continuous quality improvement, and offering the patient psychological counseling. (741, Table 46-2)

MEDICOLEGAL SEQUELAE OF AWARENESS

19. The large disparity between the incidence of awareness and actual malpractice claims is multifactorial and includes the nature and severity of the injuries associated with awareness, as well as the medicolegal and injury compensation system. (742)

20. Factors influencing a patient's decision to initiate a malpractice claim are poor communication between the patient and physician, unmet expectations, and financial pressure on the patient. One study reported that 50% of potential plaintiffs had a poor relationship with their physician. (742)

DATA FROM THE ASA CLOSED CLAIMS PROJECT

21. Claims for intraoperative awareness represent a small fraction (2%) of all malpractice claims in the Closed Claims database. (742)

22. Factors associated with a malpractice claim for intraoperative awareness in the Closed Claim database include female gender, ASA physical class 1 and 2, less than 60 years of age, elective surgery, and obesity. (742)

23. The two main causes of intraoperative awareness in the Closed Claims database were light anesthesia and anesthetic delivery problems. (743, Table 46-3)

Chapter

43 QUALITY OF CARE AND PATIENT SAFETY

Anuj Malhotra, Vinod Malhotra

BASIC PRINCIPLES

1. What is the principle of nonmaleficence in regard to patient safety?
2. What elements constitute The Joint Commission National Patient Safety Goals and how often are these updated?
3. What is the triad of excellence in health care in the authors' opinion?
4. What is included in assessing quality of care?
5. What resources are available to measure quality and efficiency in the operating room (OR)?

ANESTHESIOLOGY AND PATIENT SAFETY

6. Why is anesthesiology often considered a leader in systematic improvement of patient safety in the OR?
7. What are examples of common safety features on anesthesia machines that promote the safe delivery of anesthesia?
8. What is the American Society of Anesthesiologists (ASA) Closed Claims Database?
9. What changes in practice have resulted, in part, from the findings of the ASA Closed Claims Database?
10. What are the goals of the Anesthesia Patient Safety Foundation and who does it include?
11. What are estimates of mortality from anesthesia in today's surgical population?

Patient Safety, Medical Error, Adverse and Sentinel Events

12. What broad types of medical or health care errors exist?
13. What is an adverse event?
14. What is a sentinel event?
15. What are the most commonly reported sentinel events?
16. What is a root cause analysis (RCA)?
17. How many patients die annually as the result of medical errors?
18. What is the National Surgical Quality Improvement Program (NSQIP)?
19. What are the primary tenets of the NSQIP?
20. What is the central venous catheter checklist advocated for use in intensive care units (ICUs)? What is the evidence for its efficacy?

The Joint Commission National Patient Safety Initiative

21. What is The Joint Commission?
22. How does The Joint Commission operate?

PREVENTING WRONG-SITE SURGERY

23. What is the definition of wrong-site surgery?
24. Is the incidence of wrong-site surgery increasing or decreasing?
25. What steps has The Joint Commission taken to prevent wrong-site surgery?
26. What are the essential elements of a preprocedural "time-out"?

Improved Patient Identification

27. How do the National Patient Safety Goals suggest that patient identification be confirmed?
28. When should patient identifiers be checked?

Improved Communication

29. What constitutes a "handoff" of patient care?
30. What is SBAR communication?

MEDICATION SAFETY

31. What is medication reconciliation in the context of anesthesia?
32. When should medication reconciliation be performed?
33. How should medication labeling be performed in the OR?
34. When should medication labeling be performed in the OR?
35. What elements of proper medication name and dose labeling help ensure patient safety?
36. How can look-alike and sound-alike drugs be differentiated?

FIRE SAFETY

37. What elements are requisite for a surgical fire and what are their sources in the OR?
38. What steps can be taken to prevent OR fires?

REDUCING HOSPITAL-ACQUIRED INFECTION

39. What practices can help limit hospital-acquired infections?

Surgical Care Improvement Project

40. What is the Surgical Care Improvement Project (SCIP)?
41. What are the current SCIP quality measures?

Never Events

42. What is a never event?
43. What are the current never events, per CMS?
44. What are the financial ramifications of a never event?

Culture of Safety

45. What are the components of a culture of safety?

High Reliability Organizations

46. What is a high reliability organization?
47. What are reporting guidelines for adverse events?

OPERATING ROOM EFFICIENCY

48. How can OR efficiency be improved by anesthesiologists?
49. What are the financial considerations of OR time?

PATIENT AND STAFF SATISFACTION

50. What is the link between staff satisfaction and patient satisfaction with health care?

ANSWERS*

BASIC PRINCIPLES

1. Nonmaleficence is a basic tenet of medical ethics based on the Latin *primum non nocere*, or "first, do no harm." (746)
2. The Joint Commission National Patient Safety Goals are updated yearly, and for 2010 include the following:
   a. Improve the accuracy of patient identification
   b. Improve the effectiveness of communication among caregivers
   c. Improve the safety of using medications
   d. Reduce the risk of health care–associated infections
   e. Accurately and completely reconcile medications across the continuum of care
   f. Reduce the risk of patient harm resulting from falls
   g. Reduce the risk of influenza and pneumococcal disease in older adults
   h. Reduce the risk of surgical fires
   i. Encourage patients' active involvement in their own care as a safety strategy
   j. Prevent health care–associated pressure ulcers
   k. Identify safety risks inherent in the organization's patient population
   l. Improve recognition and response in a patient's condition
   m. Universal Protocol: Prevent wrong person, wrong site, wrong procedure surgery (746-747, Table 47-1)
3. In the authors' opinion, (1) patient safety, (2) improved outcomes, and (3) improved patient satisfaction with their care constitutes the triad of excellence in clinical care. (747, Figure 41-1)
4. Quality of care includes not only the clinical care indicators, but also the measures of efficiency, such as timely starts, short turnaround times between cases, appropriate access for emergencies, and effective utilization of the ORs, equipment, and staff. (746-747)
5. The American Association of Clinical Directors has developed a Procedural Times Glossary to measure and compare OR efficiency benchmarks. The ASA also established the Anesthesia Quality Institute (AQI) in 2009 to establish standardized quality measures, promote research, and obtain useful data to improve the quality of patient care. (747)

ANESTHESIOLOGY AND PATIENT SAFETY

6. Anesthesiology has often been cited as an example of how a medical specialty has systematically improved patient safety. In 1954, Beecher and Todd's review of mortality during anesthesia found a mortality rate of 1 in every 1561 operations, and was one of the first studies to scientifically identify and quantify risks associated with anesthesia. Patient safety efforts have included features on the anesthesia delivery systems used in patient care (e.g., Pin Index Systems), founding of the ASA Closed Claims Database in 1985, and establishment of the Anesthesia Patient Safety Foundation (APSF) also in 1985. (747)
7. Many of the features of the anesthesia machine, such as Pin Index Safety Systems, oxygen fail-safe controls, prevention of hypoxic mixtures, and elimination of hanging bellows, were developed to enhance patient safety by avoiding critical technical failures. (747)
8. In 1985 the ASA established the Closed Claims Database with the goal of reviewing closed malpractice claims to identify sources of technical failure and human

*Numbers in parentheses: numbers refer to pages, figures, or tables in Miller RD, Pardo MC: *Basics of Anesthesia*, 6th ed. Philadelphia, Elsevier Saunders, 2011.

error that lead to patient injury, and to then share this information with the anesthesia community. (747)

9. Initial findings from the Closed Claims Database found that most claims were due to unrecognized esophageal intubation or other reasons for inadequate oxygenation. This finding accelerated the requirement for pulse oximetry and capnography as standard monitors for patients undergoing general anesthesia. Several additional ASA task forces, such as the Postoperative Visual Loss Registry, have been established to further address concerns identified by analysis of the Closed Claims Database. Further analysis of problems identified by the Closed Claims Database has led the ASA to publish clinical practice recommendations such as the ASA Difficult Airway Algorithm. The ASA currently has 23 practice advisories available. (747-748)
10. The Anesthesia Patients Safety Foundation is an independent, nonprofit corporation with the goal that "no patient shall be harmed by anesthesia." Board members include anesthesiologists, nurse anesthetists, equipment manufacturers, lawyers, and engineers. Its current mission statement identifies safety research and education, patient safety programs and campaigns, and national and international exchange of information and ideas as its continuing goals. Its quarterly newsletter is the most widely circulated anesthesia publication in the world, providing a forum to publicize advances in technology, as well as concerns regarding medications, patient issues, and common anesthesiology practices. (748)
11. Through the implementation of technical advances and practitioner education, mortality from anesthesia has improved to 1:250,000. However, as the population has aged and patients with more severe medical problems are undergoing surgery, mortality for the very ill is reported to be as frequent as 1:10,000 to 1:1500. (748)

Patient Safety, Medical Error, Adverse and Sentinel Events

12. Health care errors may be errors of *commission* (doing the wrong thing), *omission* (not doing the right thing), or *execution* (doing the right thing incorrectly). A defect in the delivery of care to a patient resulting in an unintended health care outcome is deemed a health care or medical error. (748)
13. An adverse event refers to any injury caused by medical care. Identifying something as an adverse event does not imply error, negligence, or poor quality of care. It simply indicates that an undesirable clinical outcome resulted from some aspect of diagnosis or therapy, not an underlying disease process. (748)
14. A sentinel event is an unexpected occurrence involving death or serious physical or psychological injury, or the risk thereof. Serious injury specifically includes loss of limb or function. The phrase "or the risk thereof" includes any process variation for which a recurrence would carry a significant chance of a serious adverse outcome. Such events are called "sentinel" because they signal the need for immediate investigation and response. (748)
15. From January 1995 through December 2009, The Joint Commission reviewed 6600 sentinel events; 68% of sentinel events included patient mortality. Among the 10 most frequently reported sentinel events were wrong site surgery (most common, 13.5%), operative/postoperative complication, medication error, and unintended retention of a foreign body. (748-749)
16. A Root Cause Analysis (RCA) is a structured process for identifying the causal or contributing factors underlying adverse events or critical incidents. (748-749)
17. The Institute of Medicine's reports "To Err Is Human: Building a Better Health System" (November 1, 1999) and "Crossing the Quality Chasm: A New Health System for the 21st Century" (March 1, 2001) indicated that 98,000 patients in the United States die annually as a result of medical errors. (748-749)

18. NSQIP began at the Veterans Administration hospitals and has expanded through the American College of Surgeons to many private institutions. The NSQIP initiative endeavors to improve the delivery of medical care at a systems level rather than at an individual level and is credited with improving postoperative surgical mortality by up to 31% and morbidity by 45%. NSQIP has demonstrated that while obvious errors can be detected on the local (hospital) level, subtle systems errors or deficiencies cannot be appreciated without comparison to data from peer institutions. (749)

19. NSQIP has identified three important patient safety observations:
    a. Safety is indistinguishable from overall quality of surgical care and should not be addressed independently of surgical quality.
    b. During an episode of surgical care, adverse outcomes, and hence patient safety, are primarily determined by the quality of systems of care.
    c. Reliable comparative outcome data are imperative for the identification of system problems and the assurance of patient safety from adverse outcomes. (749)

20. The checklist requires that practitioners should:
    a. Wash their hands with soap.
    b. Clean the patient's skin with chlorhexidine antiseptic.
    c. Put sterile drapes over the entire patient.
    d. Wear a sterile mask, hat, gown, and gloves.
    e. Put a sterile dressing over the catheter site.
    f. In a 2003 Michigan study, the median rate of ICU catheter-related bloodstream infections decreased by 68%. In the first 18 months, the authors estimated that 1500 lives and $100 million were saved. These results were sustained for almost 4 years. (749)

The Joint Commission National Patient Safety Initiative

21. The Joint Commission is an independent, not-for-profit organization, which accredits and certifies health care organizations and programs in the United States. The organization's mission statement is "to continuously improve health care for the public, in collaboration with other stakeholders, by evaluating health care organizations and inspiring them to excel in providing safe and effective care of the highest quality and value." (749)

22. The Joint Commission conducts unannounced surveys of hospitals on a regular basis with the goal of assessing structural attributes, policies, and staff to ensure patient safety and quality of care. The Department of Health and Human Services and the Center for Medicare and Medicaid Services recognizes The Joint Commission's accreditation as deeming hospitals, laboratories, and other medical care providers able to participate in Medicare and Medicaid programs. (749)

PREVENTING WRONG-SITE SURGERY

23. By definition, wrong-site surgery involves all surgical procedures performed on the wrong patient, wrong body part, wrong side of the body, or the wrong level of a correctly identified anatomic site. This includes anesthesia procedures such as regional or neuraxial blocks. (749)

24. According to The Joint Commission, the reports of wrong-site surgery or procedures are steadily increasing. The actual incidence of wrong-site surgery is unknown but is estimated to be 1:15,000 to 1:112,000. (749)

25. To prevent the occurrence of wrong-site surgery, The Joint Commission has issued a universal protocol which requires:
    a. Preoperative verification that uses two patient identifiers as well as the procedure, the site/side or vertebral level, and involves at least two health care providers (one of whom is the surgeon)

b. Site marking of the operative site by the surgeon using his or her initials or "yes" with patient involvement
c. "Time-out" right before starting the procedure (749)

26. The process of "time-out" is when all the services involved in caring for the patient (surgery, anesthesiology, and nursing) pause before beginning a procedure to ensure that the correct patient is undergoing the correct procedure on the correct location and all the necessary imaging studies and equipment necessary to safely complete the procedure are available. The essential elements for a preprocedural "time-out" are:
a. Identification of the patient using two identifiers
b. Correct side/site
c. Correct procedure
d. Correct position
e. Verification that implants, devices, and special equipment are available
f. Relevant images are properly labeled and displayed
g. Allergies
h. Antibiotics administered
i. Safety precautions based on fire, hazards, patient history, or medication use
j. Verbal agreement that all time-out elements have been met (749-750, Table 47-3)

Improved Patient Identification

27. National Patient Safety Goals have focused on improving patient identification by checking two independent identifiers, such as name and date of birth or name and medical record number. (750)

28. These patient identifiers must be checked every time a patient is to undergo a diagnostic test or procedure, or is to receive medication or blood products. (750)

Improved Communication

29. When a patient is transferred from the care of one practitioner to another, whether it is from floor nurse to the anesthesiologist in the operating room, anesthesiologist to postanesthesia care unit nurse, or within services from daytime team to an on-call team, structured systems to facilitate the transfer of vital patient information are essential to avoid errors. The Joint Commission has termed these transfers of patient care as "handoffs." (750)

30. Originally developed for U.S. Navy communications, situation-background-assessment-recommendation (SBAR) has been adapted by many health care organizations and is internationally accepted as an effective communication regarding a change in a patient's condition either from nurse to physician or among physicians. The elements of SBAR communication are:

Situation: The notifying health care practitioner identifies the patient and the problem or the change in the patient's condition.

Background: Relevant background information specific to the situation. For example, this could include the patient's diagnosis, his mental status, current vital signs, complaints, pain level, and physical assessment findings.

Assessment: This step of the communication provides the practitioner with the opportunity to offer an analysis of the problem or to convey more extensive data about the patient, such as changes from prior assessments.

Recommendation: What the practitioner believes would help resolve the situation or what is the desired response. (750)

MEDICATION SAFETY

31. Medication reconciliation refers to the process by which the medications the patient is on preoperatively are reviewed for any possible adverse reactions with any medications he or she might receive intraoperatively or postoperatively. (750)

32. Medication reconciliation should occur whenever the patient is admitted, transferred to another unit or service, or is discharged home. (750)

33. Medications should not be drawn into syringes until immediately prior to patient use and the syringes must be labeled with the drug name, drug concentration, and time medication is drawn up. Anesthesiologists have long adopted the use of color-coded labels to distinguish among different classes of medications in an effort to avoid medication administration errors. (750)

34. The Joint Commission recommends against the labeling of empty syringes in anticipation of future medication preparation since this does not obviate drawing the incorrect medication into a differently labeled syringe. A clarification on this recommendation was sought by the ASA, in response to which The Joint Commission will remove it from the FAQ section of their website. However, they have stopped short of a clear statement of reversing it. (750)

35. Additional requirements in ensuring medication safety are avoiding the use of abbreviations with regard to drug name and unit of dose. The use of decimal points followed by a trailing zero is also to be avoided while a zero must be placed in front of a decimal point to avoid dosing errors. Finally, the Do Not Use List prohibits the use of "u" for units, "iu" for international units, and Q.D. or Q.O.D. for daily or every other day dosing. (751)

36. Care must be taken to avoid using vials of drugs from manufacturers that look alike. If look-alike drugs cannot be avoided, such vials should not be placed near one another in any pharmacy drawer. In addition, TALLman lettering, such as EPInephrine may be used to distinguish it from EPHedrine. (751)

FIRE SAFETY

37. For a fire to start, each element of the fire triangle—heat, fuel, and oxygen—must be present. Heat is the by-product of electrocautery units, lasers, and endoscopes. Paper drapes, fabric towels, and gauze sponges provide ample fuel. Oxygen is often present at high concentrations in localized areas such as during facial plastic surgery or tracheostomy. Also, the newer, more effective skin preparation solutions often contain alcohol that is highly flammable and must be allowed to dry completely prior to placement of surgical drapes. (751)

38. Effective communication between all perioperative team members is essential in preventing OR fires. Skin preparation solutions must be completely dried prior to surgical draping, and lasers and endoscopes should be turned off or to standby when not in use. When there is a possibility that oxygen may come into direct contact with electrocautery, as in airway surgery or when administering oxygen in a non-closed circuit, oxygen should be administered at the lowest possible concentrations necessary for the patient to maintain oxygenation. Use of special endotracheal tubes may also be warranted in some cases. (751)

REDUCING HOSPITAL-ACQUIRED INFECTION

39. Prevention of hospital-acquired infections requires strict adherence to hand hygiene protocols, prevention of central line, and surgical site infections, and prevention against the spread of multidrug resistant organisms. Interventions by anesthesia providers may include appropriate selection of antibiotics, timely administration and dosing of antibiotics, proper hygiene and sterile technique where indicated, appropriate contact and respiratory precautions, and maintenance of normothermia. (751)

Surgical Care Improvement Project

40. The Surgical Care Improvement Project (SCIP) is a national partnership of organizations interested in improving surgical care by significantly reducing

surgical complications. The steering committee is comprised of 10 national organizations who have pledged their commitment and full support for SCIP:
- **a.** Agency for Healthcare Research and Quality
- **b.** American College of Surgeons
- **c.** American Hospital Association
- **d.** American Society of Anesthesiologists
- **e.** Association of Perioperative Registered Nurses
- **f.** Centers for Disease Control and Prevention
- **g.** Centers for Medicare & Medicaid Services
- **h.** Institute for Healthcare Improvement
- **i.** The Joint Commission
- **j.** Veterans Health Administration (751)

41. Current SCIP quality measures include the following evidence-based outcome improvement interventions:
- **a.** Prophylactic antibiotic received within one hour prior to surgical incision (quinolones or vancomycin may be administered within 2 hours)
- **b.** Prophylactic antibiotic selection for surgical patients
- **c.** Prophylactic antibiotic discontinued 24 hours after surgery end time (48 hours for cardiac surgery)
- **d.** Cardiac surgery patients with controlled 6 AM postoperative serum glucose (<200 g/dL)
- **e.** Surgery patients with appropriate hair removal (depilatory creams or clippers only, no razor)
- **f.** Urinary catheter removed on postoperative day 1 or postoperative day 2
- **g.** Surgery patients with perioperative temperature management (goal 36.0° C/ normothermia)
- **h.** Surgery patients on a β-blocker prior to admission received β-blockers during the perioperative period
- **i.** Surgery patients with recommended venous thromboembolism (VTE) prophylaxis ordered
- **j.** Surgery patients received appropriate VTE prophylaxis within 24 hours before and after surgery (747, 752, Table 47-2)

Never Events

42. Never events are 28 occurrences on a list of inexcusable outcomes in a health care setting compiled by the National Quality Forum (NQF). They are defined as adverse events that are "serious, largely preventable, and of concern to both the public and health care providers for the purpose of public accountability." The Centers for Medicare & Medicaid Services (CMS) also provides a list of never events, some of which coincide with the NQF. (752)

43. Per CMS, the list of never events includes:
- **a.** Foreign object left in patient after surgery
- **b.** Surgery on wrong patient
- **c.** Surgery on wrong body part
- **d.** Wrong surgery on a patient
- **e.** Death/disability associated with intravascular air embolism
- **f.** Death/disability associated with incompatible blood
- **g.** Death/disability associated with hypoglycemia
- **h.** Death/disability associated with a fall within facility
- **i.** Death/disability associated with electric shock
- **j.** Death/disability associated with a burn incurred within facility (752, Table 47-4)

44. If a never event occurs, CMS will not pay the hospital for the added cost of the extra care incurred as a result. (752)

Culture of Safety

45. A culture of safety enables any member of the health care team to contribute to patient safety. It is a key component of many high reliability organizations. Components of a culture of safety include:
    a. A blame-free environment where individuals are able to report errors or close calls without fear of reprimand or punishment
    b. An expectation of collaboration across ranks to seek solutions to vulnerabilities
    c. A willingness on the part of the organization to direct resources for addressing safety concerns (752-753)

High Reliability Organizations

46. High reliability organizations refers to organizations or systems that operate in hazardous conditions and have done so with nearly failure-free performance records, not simply better than average. Commonly discussed examples include air traffic control systems, nuclear power plants, and naval aircraft carriers. (753)

47. Compliance with patient safety initiatives involves either voluntary or mandatory reporting of adverse events. Reporting requirements are different in each state and for federal government programs as well. In 2002 Pennsylvania became the first state to establish a mandatory reporting system for not only serious adverse events, but "incidents" (near misses) as well. (753)

OPERATING ROOM EFFICIENCY

48. Anesthesiologists can be leaders in facilitating punctuality, on time starts, keeping turnaround times between cases to a minimum, and promoting expeditious surgery to improve the utilization of resources in the operating room. A systems approach and standardization of equipment and processes will not only streamline operations and improve efficiency but also improve patient safety, staff satisfaction, and patient satisfaction. (753)

49. The operating rooms are the most expensive units to run in a hospital and, if run inefficiently, can become a major financial drain. However, when run appropriately, ORs are also the best source of revenue for most hospitals. (753)

PATIENT AND STAFF SATISFACTION

50. Surveys have tracked a close link between staff satisfaction and patient satisfaction at health care facilities. For example, according to the National Surveys (Press Ganey), about one third of patients surveyed would not recommend the facility where they received care. Interestingly, about one third of health care employees at the hospitals surveyed were dissatisfied with their job. It should therefore be a goal for every facility to promote staff satisfaction and be intolerant of disruptive behavior so that the safest and best care is rendered to its patients. (753)

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